Evaluation of the Q16 questionnaire on neurotoxic symptoms and a review of its use

Ingvar Lundberg, Margareta Högberg, Hans Michélsen, Gun Nise, Christer Hogstedt

Abstract

***Objectives*—The questionnaire 16 (Q16) is commonly used to study prevalences of neurotoxic symptoms among workers exposed to organic solvents. It has also been recommended that exposed workers reporting more than six symptoms should be referred for further examination of possible chronic toxic encephalopathy. It would be useful to know whether symptoms reported in the questionnaire also reflect impairment of similar functions measured with objective or semiobjective methods in a formerly highly exposed group.**

***Methods*—135 painters and 71 carpenters answered the Q16, were interviewed about symptoms compatible with an organic brain damage, and took a battery of psychometric tests. A subsample of 52 painters and 45 carpenters were interviewed for psychiatric diagnosis according to Diagnostic and Statistical Manual for Mental Disorders, 3rd version (DSM III) and their vibration thresholds in hands and feet were measured. The entire group was followed up in the register of diagnoses at early retirement 1971–93. The lifetime exposure to organic solvents was assessed. Current exposure to organic solvents was found to be low or none.**

***Results*—The prevalence of people with more than six symptoms in the Q16 rose with increasing cumulative exposure to solvents. The sensitivity of the questionnaire (more than six symptoms) to detect people who were assessed to exhibit symptoms compatible with an organic brain damage was only 38%. One of seven people who had retired early with a diagnosis compatible with a chronic toxic encephalopathy, and two of five people with a psychiatric diagnosis compatible with this condition, had more than six symptoms in the Q16. The agreement between Q16 replies and psychometric test results, as well as other examinations, was low.**

***Conclusions*—The notable exposure-response relation indicates that the questionnaire is useful for comparison of groups with different exposures to organic solvents. There was low agreement between the number of symptoms on the questionnaire and the assessment of symptoms compatible with organic brain damage, as well as psychiatric or early retirement diagnoses compatible with chronic toxic encephalopathy. The questionnaire does not seem useful for screening of patients with chronic toxic encephalopathy in groups without ongoing exposure to organic solvents.**

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Department of Occupational Health, Karolinska Hospital, S-171 76 Stockholm, Sweden
I Lundberg
H Michélsen
G Nise
C Hogstedt

Department of Occupational Health, National Institute for Working Life, S-171 84 Solna, Sweden
I Lundberg
M Högberg
C Hogstedt

Correspondence to:
Dr Ingvar Lundberg, Department of Occupational Health, Karolinska Hospital, S-171 76 Stockholm, Sweden.

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Lead, mercury, manganese, certain solvents, and other agents may be toxic to peripheral nerves or the central nervous system at high exposures. Long term low level exposure may elicit chronic effects as exposed workers complain of vague and unspecific symptoms like tiredness, forgetfulness, inability to concentrate, and anxiety more often than non-exposed workers. Behavioural effects are often found as group differences between exposed and non-exposed workers in sensitive psychometric tests.[1]

Questionnaires have been developed to monitor early effects of neurotoxic exposures in working populations.[1] However, a validation procedure has been described only for the questionnaire 16 (Q16).[2] This questionnaire was developed to monitor effects on the central nervous system among workers exposed to solvents but it has also been successfully used on workers exposed to other neurotoxic agents.[3–7] It contains 16 short questions with yes or no response alternatives on symptoms commonly described by workers exposed to solvents. The understanding of the questions was investigated by physicians, psychologists, and workers. The reliability was studied by test-retest procedures. The validity was evaluated by investigating the power of the questions to discriminate between exposed and non-exposed groups and by comparisons of groups with and without a "psycho-organic syndrome".[2]

It is common practice in Sweden to monitor groups exposed to solvents for possible overexposure by noting their symptom rate in the Q16 compared with reference groups—for example, the questionnaire has been used to evaluate preventive programmes.[8] The Q16 has also been used to screen exposed people for chronic toxic encephalopathy due to exposure to organic solvents, which is a recognised occupational disease in Sweden.[9] It has been recommended that people with more than six

symptoms in the Q16 should be referred for further medical and psychiatric examination.[2]

This questionnaire has become commonly used in research on neurotoxic effects of exposure to organic solvents but it is unknown how positive responses to Q16 questions relate to other outcomes intended to measure similar effects.

We have studied the relation between Q16 replies and a physician's assessments of similar symptoms, psychometric test results, and some other outcome measurements among house painters with previous heavy exposure to mixed solvents, and among house carpenters. We have also compiled all studies published before 1996 that used the Q16 on groups exposed to neurotoxic agents.

Material and methods

SUBJECTS

Cohorts were collected of all male house painters and house carpenters born in 1925 or later, who were members of the Stockholm chapters of their unions in 1965, and who had been members for at least 10 years before 1971. Information on these criteria was obtained from the membership rosters of the unions. The criteria were met by 767 painters and 1212 carpenters.

From this group, those painters and carpenters who lived in Stockholm County on 31 December 1986, and who took their military conscription tests in 1949, '51, '53, '57, or '61 were chosen for a clinical examination of neurotoxic effects.

Altogether 149 painters and 85 carpenters, were called to the examination. The selection procedure has been outlined in detail in a previous paper.[10]

EXAMINATIONS AND QUESTIONNAIRES

The study group was called in random order for a physical examination, and 135 painters and 71 carpenters attended their examinations, corresponding to 91% and 84%, respectively, of those invited during the examination period in 1988–9.

Solvent exposure

An occupational hygienist carried out extensive individual interviews with all subjects to survey their lifetime exposure to organic solvents. The construction of a cumulative exposure index has been described elsewhere.[10] The 25% of the painters who had the highest cumulative exposure were categorised as the heavy exposure group, the 25% with the lowest cumulative exposure as the low exposure group, and the remaining 50% as the intermediate exposure group. All the carpenters had no, or a very low, cumulative exposure to solvents.

The solvent exposure during the year before the investigation was also assessed and the men divided into those who had been exposed (69 painters), and not exposed (66 painters, all carpenters), during that period.

Questionnaire 16

The participants were sent a questionnaire and asked to leave it completed with the receiving nurse. The questionnaire contained questions on solvent exposure, previous illness or disease, alcohol consumption, etc. The questionnaire also contained the Q16 questionnaire reproduced in table 1.[2] Those who participated in the vibrometry examination (see later) also answered the Q16 on a second occasion, on the morning of the same day as the examination was performed.

It is recommended that people with more than six symptoms in the Q16 should be further examined to exclude organic brain damage due to exposure to organic solvents.[2] Apart from examining the relation between replies to individual questions and the different outcomes we also examined the relation between six or more symptoms and the outcomes.

Medical interview

All the subjects were interviewed by the same physician in a structured way. During the interview the subject was asked whether he had noticed changes in neuropsychiatric symptoms that were related to solvent exposure—that is, impaired memory, impaired concentration, impaired intellect, emotional lability, irritability, mood change, decreased speed, loss of initiative, increased fatigue, anxiety and nervousness, sleeping problems, vegetative symptoms, sexual problems, unsteadiness and vertigo, and frequent headache. All the subjects were asked questions about each symptom: the time it was first noticed, if it appeared gradually or suddenly, and if it appeared in connection with some specific event.

In a summary index the subjects were classified as lacking symptoms of organically based functional decline of the central nervous system or as having slight or obvious symptoms. For the statistical analysis the summary index was dichotomised: those who lacked symptoms of organically based central nervous system damage and those who had such symptoms. All symptoms apart from headache and unsteadiness were included in the summary index. Details on the evaluation of symptoms may be found in our previous paper.[10]

Psychometric tests

Table 2 shows the psychometric test battery used and indicates the functions that each test was intended to measure. Details on how the

Table 1 The Q16 (subsequent tables the questions are referred to by the italicised words)

Question	Yes	No
1 Are you abnormally *tired*?	☐	☐
2 Do you have *palpitations* even when you don't exert yourself?	☐	☐
3 Do you often have a painful *tingling* in some part of your body?	☐	☐
4 Do you often feel *irritated* without any particular reason?	☐	☐
5 Do you often feel *depressed* without any particular reason?	☐	☐
6 Do you have problems with *concentrating*?	☐	☐
7 Do you have a *short memory*?	☐	☐
8 Do you *perspire* without any particular reason?	☐	☐
9 Do you have any problems with *buttoning* and unbuttoning?	☐	☐
10 Do you generally find it hard to get the *meaning* from reading newspapers and books?	☐	☐
11 Have your *relatives* told you that you have a short memory?	☐	☐
12 Do you sometimes feel an *oppression* of your chest?	☐	☐
13 Do you often have to *make notes* about what you must remember?	☐	☐
14 Do you often have to *go back* and check things you have done such as turned off the stove, locked the door, etc.?	☐	☐
15 Do you have a *headache* at least once a week?	☐	☐
16 Are you less interested in *sex* than what you think is normal?	☐	☐

Table 2 Psychometric tests

Function	*Test*	*Outcome variables (abbreviation)*
Verbal ability	Synonyms	Number of correct answers (SRB1)
	Conscription test A	Number of correct answers (CON1)
	Conscription test C	Number of correct answers (CON2)
Visuospatial ability	Block design	Sum of tasks solved and time used (BD)
	Wisconsin card sorting test	Number of mismatches (CARD1)
		Number of perseverative errors (CARD2)
		Number of categories (CARD3)
Memory	Benton	Number of mistakes (B)
	Claeson-Dahl	Weighted score (CD1)
		Number of words recognised (CD2)
		Number of words memorised (CD3)
	Corsi block	Number of correctly repeated series (forward) (C1)
		Number of correctly repeated series (backward) (C2)
		Sum for repetition forward and backward (C3)
	Digit span	Number of correctly repeated series (forward) (DSP1)
		Number of correctly repeated series (backward) (DSP2)
		Sum for repetition forward and backward (DSP3)
	Complex figure	Ability to copy (CF1)
		Ability to reproduce from memory (CF2)
	Digit symbol, memory	Number of digit-symbol combinations correctly reproduced (DS2)
Perceptual ability	Digit symbol	Number of tasks completed in 90 seconds (DS1)
	Trail making A	Time for completion (T1)
	Trail making B	Time for completion (T2)
	Simple reaction time	Mean of reaction times (RT)
Psychomotor capacity	Purdue pegboard	Number of movements, dominant hand (P1)
		Number of movements non-dominant hand (P2)
		Number of movements, both hands (P3)
		Combination (P4)

tests in the battery were selected have been presented elsewhere.[10] During the examination the subject retook two of the psychometric tests he had taken at conscription into military service. Conscription test A measured ability to follow verbal instructions, conscription test C was a word comprehension test.

Before the data analysis a list was made of combinations of Q16 questions and psychometric tests in which associations were considered likely—for example, a feeling of impaired memory should affect psychometric tests intended to assess memory.

Indices of the psychometric test results were constructed, based on the number of psychometric test outcomes outside the 90th percentile among the carpenters.

Computerised coordination tests

The computerised coordination ability test system (CATSYS) was used.[11] The CATSYS consists of a touch sensitive screen and a broad response key attached to a personal computer. The system was set up on a table in front of the subject. All the tests were taken with the dominant hand. The following tests were given:

Screen-nose point test—In the middle of the display screen there was a black dot, where the subject, with his eyes open, placed his fingertip. He was then asked to close his eyes and move the fingertip to the end of his nose, and then back to the black dot on the screen, 10 times. The average value for the distance between the black dot and the fingertip contacts was registered.

Hand supination-pronation test—The subject was asked to follow a rhythmic sound from a loudspeaker by lightly beating time on the broad response key, rotating his forearm to use alternately the backs and fronts of the four fingers. For 10 seconds the subject was asked to follow a rhythm that started at 2 Hz and increased linearly to 7 Hz. The highest frequency the person could follow was registered.

Finger tapping—The subject held his index finger directly above the response key. The test followed the same procedure as the hand supination/pronation test, except that here the maximum stimulus frequency was 8 Hz.

Details on the equipment and the measurements may be found in our previous publication.[10]

SECOND EXAMINATION

About a year after the first examination, the painters with the highest cumulative exposure to solvents as judged by preliminary estimates, and a group of carpenters with the same age distribution, were called to a second examination. This included the Q16, neurophysiological examinations and interviews for psychiatric diagnosis. Of the 58 painters and 53 carpenters invited, 52 painters and 45 carpenters participated.

Vibrometry

Determination of vibration thresholds was performed at three points bilaterally: the back of the hand (os metacarpale II), the upper part of the lower leg (ventromedial surface of the tibia) and the top of the foot (os metatarsale I). We have published details of the equipment and the measurements previously.[10]

Psychiatric diagnosis

All the subjects who participated in the vibrometry examinations were also interviewed for about two hours by a trained psychologist to test the criteria for psychiatric diagnoses given in the Swedish translation of Diagnostic and Statistical Manual for Mental Disorders, 3rd version (DSM III).[12,13] Before the examinations the interviewer was given training in DSM III diagnosis by an experienced psychiatrist. The examination procedure was described elsewhere.[10]

POTENTIAL CONFOUNDING FACTORS

Information was obtained on many potential confounding factors. Here we only give information, however, on those potential confounders that were included in the analyses presented. Details on the confounder information obtained may be found elsewhere.[10]

Age was dichotomised at 50 years, the median for the entire group. A measure of long term alcohol consumption was established, as described elsewhere, based on register information on alcohol misuse, serum γ-glutamyltranspeptidase activities, stated alcohol consumption, and questionnaire indications on possible alcohol misuse. The results of the conscription test C, at conscription, was used to take primary intellectual capacity into account. This test consists of 40 items in which each item contains five words. Four words are features of one common category, whereas the fifth word deviates. The fifth word is to be identified. The subjects were divided into those who reported that they had, or had not had concussion, regardless of how long they were unconscious.

The subjects were also divided into those who reported that they had, or had not consumed neuroleptics, antidepressants, tranquillisers, or sleeping pills, for a prolonged period.

STATISTICAL METHODS

Exposure-response relation

The relation between cumulative exposure to organic solvents and the replies to the Q16 questions was studied with logistic regression analysis in the EGRET computer package.[14] Age and alcohol consumption were included as potential confounding factors in all analyses and other potential confounding factors were added if they were associated with the outcome ($P < 0.10$) in univariate analyses.

Agreement between Q16 replies and other examinations

The agreement between symptoms stated in the Q16 and symptoms noted by the physician was studied by means of the odds ratio (OR—that is, ad/bc where a = number of people with a symptom according to both sources, b = number of people with a symptom according to Q16 but not the physician, c = number of people with a symptom according to the physician but not the Q16, and d = number of people without the symptom according to both sources. The OR provides an estimate of correlation independent of how skewed the 2 × 2 table marginals are.

The P values for departure of the OR from unity were calculated from the 2 × 2 tables with the Cochran-Mantel-Haentzsel statistics in the SAS computer program. None of the potential confounding variables were taken into account in these analyses.

Comparison of psychometric test results, computerised coordination tests, and vibration thresholds between those giving yes and no replies to the Q16 questions were compared in three ways.

(1) The mean test results in both groups were compared by *t* tests.

(2) The OR, with a P value, of obtaining a test result above the median result among the carpenters was calculated in the same way as for symptoms.

(3) The OR, with a P value, of obtaining a test result worse than the 10th percentile among the carpenters was calculated.

Unless otherwise stated a worse result among those responding yes or no to a Q16 question was considered to be present if a significantly ($P < 0.05$) worse result was obtained in at least one of the comparisons already described.

Analyses were made separately for the entire study group, for painters, carpenters, for the three cumulative exposure groups among painters and for painters exposed and unexposed to solvents during the past year before the investigation. None of the potential confounding variables were taken into account in the analyses. As there were no consistent differences between the results in the subgroups and in the entire group results are shown only for the entire group.

INFORMATION ON DIAGNOSES IN THE REGISTER OF DIAGNOSES AT EARLY RETIREMENT

This register contains all people in Sweden that have received an early pension. The study participants were followed up from the beginning of 1971 until the end of 1993. Diagnoses likely to cover the neuropsychiatric effects caused by solvents, as defined by Axelson *et al*,[15] were specifically looked for regardless of whether they were primary or secondary diagnoses.

LITERATURE REVIEW

All papers known by the authors to have used the Q16 were included. It was not possible to make a conventional literature search as the name Q16 was never included among the key words of any paper.

Results

EXPOSURE AND Q16 SYMPTOMS

The prevalence of positive responses to all Q16 questions increased with increasing cumulative exposure to solvents (table 3). Thus there was also a pronounced exposure-

Table 3 Cumulative exposure to solvents and Q16 symptoms (adjustments for age and alcohol consumption were made in all analyses)

		Painters' exposure					
	Carpenters (n = 71)	*Low (n = 34)*		*Intermediate (n = 67)*		*Heavy (n = 34)*	
Question	n_i	n_i	*OR (95% CI)*	n_i	*OR (95% CI)*	n_i	*OR (95% CI)*
Tired*	9	4	0·9 (0·3–3·4)	16	2·1 (0·8–5·4)	14	4·4 (1·6–12)
Palpitations*	6	1	0·3 (0·0–2·5)	7	1·4 (0·4–4·6)	5	2·0 (0·5–7·7)
Tingling†	21	9	1·0 (0·4–2·5)	23	1·3 (0·6–2·7)	16	2·2 (0·9–5·3)
Irritated*	11	2	0·3 (0·1–1·7)	16	1·6 (0·7–4·0)	10	2·2 (0·8–6·0)
Depressed‡	6	2	0·8 (0·1–4·2)	9	1·9 (0·6–5·9)	5	2·6 (0·7–10)
Concentrating	5	5	2·2 (0·6–8·3)	20	5·7 (2·0–16)	10	6·3 (1·9–21)
Short memory	20	13	1·6 (0·7–3·9)	26	1·6 (0·8–3·4)	23	5·2 (2·1–13)
Perspire	8	2	0·5 (0·1–2·5)	14	2·0 (0·8–5·1)	8	2·4 (0·8–7·2)
Buttoning*	6	1	0·4 (0·0–4·1)	2	0·2 (0·0–4·1)	2	0·4 (0·1–2·5)
Meaning	7	4	1·2 (0·3–4·5)	12	2·0 (0·7–5·6)	6	2·0 (0·6–6·7)
Relatives	20	9	0·9 (0·4–2·4)	21	1·1 (0·5–2·3)	16	2·2 (0·9–5·4)
Oppression	16	13	2·0 (0·8–4·9)	23	1·9 (0·9–4·1)	15	3·1 (1·2–7·5)
Make notes	9	6	1·6 (0·5–5·0)	21	3·0 (1·2–7·2)	17	6·1 (2·3–16)
Go back	14	7	1·1 (0·4–3·1)	21	1·7 (0·8–3·8)	16	3·4 (1·4–8·5)
Headache	7	3	0·9 (0·2–3·8)	8	1·2 (0·4–3·6)	11	4·1 (1·4–12)
Sex§	2	1	1·4 (0·1–17)	5	2·3 (0·4–13)	7	8·3 (1·5–45)
> 6 Yes replies	6	3	1·2 (0·3–5·2)	12	2·2 (0·8–6·4)	11	4·6 (1·5–14)

*Adjusted for age, alcohol consumption, and medicines with effects on the central nervous system.
†Adjusted for age, alcohol consumption, medicines with effects on the central nervous system and concussion.
‡Adjusted for age, alcohol consumption, and concussion.
§Adjusted for age, alcohol consumption, and result on conscription test C.
n_i = Number with symptom.
For full question see table 1.

Table 4 Sensitivity and specificity of Q16 in identifying men with symptoms of organically based functional decline according to physician's assessment (PA)

	Q16 symptoms, cut off ⩾ 6 symptoms			*Q16 symptoms, cut off ⩾ 3 symptoms*		
	> 6	*⩽ 6*	*Total*	*> 3*	*⩽ 3*	*Total*
Symptoms according to PA						
Yes	14	23	37	27	10	37
No	18	151	169	52	117	169
Total	32	174	206	79	127	206
Sensitivity	14/37 (38%)			27/37 (73%)		
Specificity	151/169 (89%)			117/169 (69%)		

response relation for the combined Q16 measure of more than six symptoms. Exposure to solvents during the year before the examination, compared with no exposure during this period, did not increase the prevalence of any symptom.

RELATION BETWEEN SYMPTOMS STATED IN THE Q16 AND SYMPTOMS ACCORDING TO THE INTERVIEW WITH THE PHYSICIAN

It is recommended that men with more than six yes replies in the Q16 should be referred for further examination. When comparing these with the physician's assessment of whether symptoms compatible with a chronic toxic encephalopathy were present or not, the sensitivity of the questionnaire was found to be 38% and the specificity 89%. If the limit was changed to more than three symptoms in the Q16 the sensitivity increased to 73% and the specificity decreased to 69% (table 4).

Individual symptoms were also compared between the Q16 and the physician's assessment. High correlation was obtained where it was expected. The highest ORs obtained (> 10) were for: (*a*) headache at least once a week on the Q16 compared with frequent headaches in the physician's assessment; (*b*) easily becoming irritated according to both sources; (*c*) frequent palpitation according to the Q16 and vegetative symptoms according to the physician's assessment; (*d*) difficulties concentrating according to both sources; (*e*) difficulties buttoning and unbuttoning according to the Q16 and unsteadiness according to the physician's assessment; (*f*) "do you often need to go back and check things you have done such as turned off the stove, locked the door, etc" according to the Q16 and memory impairment according to the physician's assessment; and (*g*) "are you less interested in sex than what you think is normal?" according to the Q16 and sexual problems according to the physician's assessment.

Five men, who were considered by the physician to have clear symptoms compatible with a chronic toxic encephalopathy, had four, four, six, eight, and 13 symptoms on the Q16.

Table 5 Q16 replies and psychiatric diagnoses at early retirement

Year of birth	*Occupation*	*Q16 symptoms n*	*Physician's assessment n*	*Early retirement*	
				Year	*Diagnosis (ICD-9)*
1930	Painter	4	2	1993	Other organic psychoses (294)
1930	Painter	4	2	1987	Narcolepsy (347)
1932	Painter	2	0	1989	Alcoholism (303)
1939	Painter	6	2	1988	Alcoholism (303)
1932	Painter	15	1	1990	Specific non-psychotic mental disturbances due to organic brain damage (310)
1939	Carpenter	0	0	1993	Depression NOS (311)
1943	Carpenter	6	0	1993	Depression NOS (311)

Codes for the physician's assessment: 0 = no, 1 = slight, 2 = pronounced symptoms compatible with organic brain damage.
ICD-C = international classification of diseases, 9th revision.

COMPARISON OF Q16 REPLIES, PSYCHIATRIC DIAGNOSES, AND DIAGNOSES AT EARLY RETIREMENT

Five painters and two carpenters had retired early due to a diagnosis compatible with neuropsychiatric effects of organic solvents. All of these diagnoses were primary. Only one of the men, a painter, had more than six symptoms according to the Q16. The physician had found clear symptoms compatible with organic brain damage among three of the five painters and slight symptoms in the painter also identified by the Q16 (table 5).

The three painters who got a DSM III psychiatric diagnosis compatible with a chronic toxic encephalopathy had four, six, and eight symptoms each. The painter with four symptoms was evaluated by the physician as having noticeable symptoms compatible with this diagnosis, but no symptoms were noted for the remaining two. The two carpenters who had six and seven symptoms each did not have symptoms compatible with a chronic toxic encephalopathy according to the physician.

RELATION BETWEEN Q16 SYMPTOMS AND PSYCHOMETRIC TEST RESULTS

Comparisons were made for the 448 possible combinations of the 16 questions in the questionnaire and the 28 psychometric test variables. In 81 of these combinations a worse result was obtained among those responding yes to the Q16 question and in 15 combinations a worse result was obtained among those responding no (table 6). Accordingly, in 352 combinations there was no difference in test results between those responding yes or no. Those who often felt irritated had worse results than those who did not in 13 of the psychometric test variables, although those who stated a decreased sexual interest, and those who stated that they generally found it hard to get the meaning from reading newspapers and books, had worse results than those who did not in 12 of the psychometric test variables.

There were 90 combinations of positive replies to Q16 questions and psychometric test results in which an association had already been considered very likely. There were significant differences in the expected direction in 14 of these combinations and in the unexpected direction in one case.

Generally there was almost no agreement between stated memory problems and test

Table 6 Comparisons of psychometric test results among those responding yes and no to the different Q16 questions

Question	Psychometric tests in which those with the symptom had a worse result	Psychometric tests in which those without the symptom had a worse result
Tired	DS1, BD, CF2, RT, CD3, P1	CF1
Palpitations	CD1, CD2, P3	
Tingling	DS1, P2, C2	B
Irritated	DS1, DSP1, DSP2, DSP3, BD, T2 RT, CD1, CD3, P2, P3, P4, CON1	
Depressed	DS2, BD, RT, CD1, CD2, CD3, P1	
Concentrating	DS2, DSP3, CD1, CD3, CON1	
Short memory	P1	SRB, CARD1, CARD2
Perspire	CON1	
Buttoning	DS2, DSP1, DSP3, CD1, CD2	CF2
Meaning	SRB, DS2, DSP1, DSP2, DSP3, RT, CD1, CD2, P1, P2, CON1, CON2	
Relatives	P1	CARD1, CARD2
Oppression		T1, CF1
Make notes		SRB, CF1, CARD2, CON2
Go back	DS1, DSP1, CD1, CD2, P3	SRB
Headache	DS2, DSP1, DSP2, DSP3, BD, CD1, CD2, P3	
Sex	SRB, DSP1, DSP2, DSP3, BD, B, CF2, RT, CD1, CD3, CON1, CON2	
> 6 Symptoms	DSP1, DSP3, BD, CD1, CD3	

For full questions see table 1, and for abbreviations see table 2.

results. In the five questions on memory, associations were found only for question 10 with digit span (all outcomes) and Claeson-Dahl (all outcomes), but the associations were weak (all ORs were below 3).

For the most pronounced associations between a yes reply to a Q16 question and an inferior psychometric test result (OR > 5) no association had been anticipated. The most notable associations were between: (*a*) Q16 question 5 and reaction time; (*b*) Q16 question 9 and the result in the digit symbol used as a memory test; (*c*) Q16 question 10 and conscription test A; (*d*) Q16 question 16 and digit span (repetition forward and sum for repetition forward and backward), Benton, conscription test A, and conscription test C. In all these associations the specificity (number giving a no reply to the Q16 question and having a good test result/the total number having a good test result) was $\geqslant$ 90% but the sensitivity was $\leqslant$ 40% in all cases.

Stating more than six symptoms in the Q16 resulted in very weak relations with the psychometric test indices, based on the number of psychometric test outcomes among the carpenters outside the 90th percentile. In these comparisons the sensitivity of the Q16 did not exceed 30%.

RELATION BETWEEN Q16 SYMPTOMS AND NEUROLOGICAL TESTS

There were weak associations between Q16 replies and neurological tests. The Q16 questions 3 and 9 were intended to reflect neuropathy. There were weakly significant associations between a positive response to question 3 and higher than median vibration threshold in the left hand (OR 2·6) and a higher mean for the vibration threshold in the right lower leg. A positive response to question 9 was significantly related to a higher than median vibration threshold in the right hand (OR 4·9) and vibration threshold higher than the 90th percentile among the carpenters in the right lower leg (OR 4·8).

A positive response to Q16 question 16 showed the most consistent relations to the coordination and vibrometry tests. There were significant relations between a positive answer to this question and a worse outcome for the screen-nose point test and vibration thresholds in the right and left hand.

LITERATURE REVIEW

We have found 14 papers published in international scientific journals which have used the Q16 and reported prevalences of symptoms in defined groups.[3-7 16-25] Eleven papers were about workers exposed to organic solvents,[7 16 25] three papers about workers exposed to neurotoxic metals,[3 4 7] and one paper about workers exposed to organophosphate insecticides.[5] Most studies involved simple comparisons between exposure and non-exposure and found that some symptoms were more common, or the total number of symptoms was higher, in the exposed than the non-exposed group. In two studies on organic solvents exposure-response analyses were performed but relations were not found.[7 17] In one paper on exposure to neurotoxic metals exposure-response relations were found for stated numbers of years of exposure to aluminium and manganese from welding.[4]

Discussion

There was a strong exposure-response relation between cumulative exposure to solvents and the number of Q16 symptoms, including the prevalence of more than six symptoms. We have previously shown a similar exposure-response relation for the physician's assessment of whether symptoms compatible with a chronic toxic encephalopathy were present or not.[10] However, there was limited agreement from the two methods of assessment in identifying men with symptoms compatible with chronic toxic encephalopathy.

The sensitivity of the questionnaire was only 38%, with a cut off point of more than six symptoms, in identifying those that were considered to have, mostly slight, symptoms compatible with a chronic toxic encephalopathy according to the physician. A high sensitivity of the questionnaire would be crucial if it were to be used as a screening instrument for further medical exploration. It is possible that the sensitivity would have been higher if only more severe symptoms had been identified by the physician but among the five painters who were considered by the physician to have clear symptoms compatible with a chronic toxic encephalopathy only two had more than six symptoms. Only one of the three painters with a psychiatric diagnosis compatible with a chronic toxic encephalopathy had more than six symptoms, although four out of five painters and carpenters with a psychiatric diagnosis compatible with this condition had more than five symptoms. Of those seven men who had retired early up to and including 1993 due to a diagnosis compatible with a chronic toxic encephalopathy, only one had more than six symptoms on the Q16. This suggests that the sensitivity of the questionnaire in detecting cases of chronic toxic

encephalopathy is low among those without considerable recent exposure to solvents.

The exposure-response relation found in this investigation was more notable than in any other study that used the Q16 to evaluate effects from exposure to organic solvents. Quantitative assessment of the exposure has only been reported in one previously published study.[7 16] Cumulative exposures in that study were low and no exposure-response relations were found. Other studies were mostly based on comparisons between exposed and non-exposed workers and most studies found that exposed workers had a higher mean symptom score or an excess of one or a few symptoms. This suggests that the questionnaire is a sensitive instrument to detect groups with high exposure to organic solvents among currently, as well as previously, exposed workers.

In this study many statistical analyses were performed. Thus many significant associations would be expected to occur by chance alone. However, we found plausible associations between replies to questions given to the physician and to the questionnaire. The associations between questionnaire replies and psychometric test results and other outcomes were generally weak for a few of the combinations and non-existent for remaining combinations. Our interpretation of the results is based on this overall picture and not on associations between specific questions and specific outcome tests. Thus the use of many statistical tests does not seem to have biased our conclusions.

There were few strong associations between Q16 symptoms and psychometric test results. The associations between giving more than six yes replies to Q16 symptoms and test results were very weak whereas stronger associations were found particularly for question 16 on decreased sexual interest and many psychometric tests results covering different functions. There were comparatively few yes replies. This question may thus reflect a more serious condition than other questions, although there were less yes replies to it. A yes reply to this question was associated with a worse result in the three psychometric verbal hold tests examined (SRB1, conscription tests A, and C). This could indicate that the verbal hold tests may be partly influenced by conditions of life, including the working environment, as we have suggested before,[26] or that those responding yes to this question constitute a selected group of vulnerable men.

In particular, there was little agreement when agreement had been expected. There was almost no agreement at all between memory test results and replies to Q16 questions on memory. In fact, for three of the four questions on memory, those who complained of memory problems had significantly better results in the vocabulary test (SRB1) than those responding no. This indicates that the questions on memory to some extent may reflect personal demands on a good memory or the need for a good memory due to for example, work demands.

It seems reasonable to conclude that replies to many Q16 questions, from middle aged male workers with low or no ongoing exposure to solvents, indicate something different from the psychometric test results intended to evaluate the same function.

There was also low agreement between the questions on polyneuropathy and vibration thresholds in the arms and legs and coordination tests. Again the most obvious associations were for the question on decreased sexual interest, which confirms that a yes reply to this question may reflect a more serious condition than a yes reply to the other questions.

In conclusion there was little agreement between symptoms according to the questionnaire and effects measured with semiobjective methods which were intended to study the same function. This suggests that non-specific symptoms of the kind monitored by the Q16 may often be experienced without objective or semi-objective correlates. It follows that symptom questionnaires or other assessments of symptoms are necessary in the evaluation of incipient, less serious effects of agents toxic to the nervous system.

Our findings in the register of diagnoses at early retirement do not indicate that the Q16 is a sensitive instrument in detecting men with a diagnosis compatible with a chronic toxic encephalopathy but without ongoing exposure. The same was true for the comparison of Q16 findings and psychiatric diagnoses and the physician's assessment of whether symptoms compatible with organic brain damage were present or not. Hence the investigation does not support the use of the Q16 as a screening instrument for chronic toxic encephalopathy in men without ongoing exposure. The number of men with a diagnosis, or notable symptoms, compatible with an organic brain damage was low and further validation is warranted.

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