

Use of behavioral performance tests in the assessment of solvent toxicity

by Francesco Gamberale, PhD¹

GAMBERALE F. Use of behavioral performance tests in the assessment of solvent toxicity. *Scand J Work Environ Health* 11 (1985): suppl 1, 65–74. Common to all applications of psychometric techniques in toxicologic research is the assessment of behavioral performance changes which can be regarded as manifestations of the neurotoxic effect of the compound under study. Ever since the use of psychometric techniques made it possible to link together deterioration of behavioral performance in humans and the inhalation of solvent vapor, psychometric tests or batteries of tests have been widely and successfully used in the study of solvent toxicity. In fact, most of the evidence showing that low-dose exposure to industrial solvents can exert a depressant action on the nervous system has been obtained with psychometric tests. The present paper provides a short review of the main results obtained by the application of behavioral performance tests in the study of solvent toxicity. The studies reviewed are divided among (i) experimental laboratory investigations, (ii) quasi-experimental field studies, (iii) epidemiologic studies, and (iv) studies using data from clinical investigations. The paper also provides a discussion of the applicability of psychometric techniques to the different questions at issue in the study of the effects of solvent exposure on the nervous system. Special attention is focused upon the interpretation of behavioral performance changes with regard to factors associated with the type of test used, the condition under which the tests are performed, the subjects' characteristics, and the study design.

Key terms: behavioral performance, experimental studies, field studies, psychometric tests.

In the late 1960s Stewart and his co-workers adopted behavioral performance tests to assess possible effects on the nervous system of human subjects experimentally exposed to styrene (51) and 1,1,1-trichloroethane (52). A few years later, Hänninen used a comprehensive battery of behavioral tests to study the effects of long-term occupational exposure to carbon disulfide (26). After these seminal efforts, in which the use of psychometric techniques made it possible to relate behavioral performance decrements to the inhalation of solvent vapor, behavioral performance tests have been used with increasing frequency in the assessment of solvent toxicity. At present batteries of psychometric tests are used almost routinely during investigations of possible short- or long-term effects of occupational solvent exposure on the nervous system.

Another application of psychometric tests is also rapidly increasing, at least in the Scandinavian countries. It consists of the use of the tests as an important tool in the medical examinations performed to diagnose solvent-induced disorders in individuals.

Many hypotheses have been formulated and tested in empirical investigations concerning the nature of the effects to be expected from solvent exposure. These hypotheses cover a wide spectrum of impairments of the functional capacity of the nervous system. They range from a transitory depressant action on arousal to serious irreversible organic brain dysfunctions.

The choice of behavioral performance tests should depend on the hypothesis to be tested. A slight transient effect on arousal during short-term exposure to a low concentration of a solvent could probably only be detected by means of a very sensitive and reliable vigilance task. In the case of serious organic brain damage, on the other hand, almost any behavioral performance test would probably reveal a deficit. In the latter case, the sensitivity of the tests to detect solvent-induced performance changes would be of secondary importance. More important would be to evaluate the extent and nature of the damage, which would require the use of a comprehensive and differentiated battery of behavioral tests.

Although the preceding statements concerning the choice of performance tests should be obvious, a review of the literature shows very clearly that this has not always been the case. Thus too many investigations have been performed in which the researchers had no manifest hypotheses concerning the type of behavioral performance impairment to be expected as a result of the condition under study. Researchers in this field have frequently shown a profound lack of knowledge of the fundamentals of performance measurement and of the interpretation of psychometric results. There is also a tendency among researchers in behavioral toxicology to refer to the behavioral tasks they use in their investigations by the mental functions these tests are supposed to assess. More serious, however, is the fact that this confusion can very easily be transferred to nonspecialist readers. Thus it cannot be justified to call behavioral tasks by terms such as, eg "visual intelligence" or "logical memory" since these

¹ Research Department, National Board of Occupational Safety and Health, Solna, Sweden.

Reprint requests to: Dr F Gamberale, National Board of Occupational Safety and Health, S-171 84 Solna, Sweden.

Table 1. Types of investigations concerning solvent-induced effects on behavioral performance.

Type of study	Conditions	Subjects	Type of effect
Experimental study	Manipulation and control of exposure	One group, repeated measurements	Short-term effect on the central nervous system
Quasi-experimental field study	Control of exposure	Two groups, repeated measurements	Short-term effect on the central nervous system
Retrospective study	No control of exposure	Two or more groups	Long-term effect on the central nervous system
Clinical study	No control of exposure	N = 1	Long-term effect on the central nervous system

terms suggest the measurement of specific mental functions, while there is a total lack of empirical evidence for their existence. On the other hand, it seems reasonable to use terms such as, eg, "simple reaction time," "short-term memory," or "finger dexterity" to indicate specific performance tasks, as well as mental functions defined on the basis of empirical observations.

The present paper reviews the main results obtained from the application of behavioral performance tests in the study of solvent toxicity. The studies reviewed have been divided into four categories depending on whether they were (i) experimental laboratory investigations, (ii) quasi-experimental field studies, (iii) retrospective or epidemiologic studies, and (iv) clinical studies or studies using data from clinical investigations.

Some of the methodological characteristics of the aforementioned types of investigations are indicated in table 1. They are briefly discussed in this paper in connection with the presentation of the results from each of the four categories of investigations.

Experimental laboratory studies

A general feature of all human experimental studies in behavioral toxicology is examination, by means of behavioral performance tests, of the acute effects of a neurotoxic substance on the nervous system under conditions which are manipulated and controlled by the researcher. With an adequate experimental design and procedure it is possible to eliminate or control the potential effect of confounding factors, ie, factors which, although extraneous to the experiment, may affect performance. If properly performed, the experiment may provide results which can be directly interpreted in terms of a cause-effect relationship between exposure and performance.

Due to the fact that human experimental studies are both very expensive and difficult to conduct, they are few in number. It is therefore possible to produce a fairly representative summary of the results obtained even in a short review such as the present one. Table 2 illustrates some of the features and results of 35 hu-

man inhalation experiments² in which behavioral performance tests constituted the main criteria in the assessment of solvent toxicity. Experiments in which the evaluation of toxicity was primarily based on neurophysiological variables are not included.

As can be seen in table 2, the duration of exposure in the different experiments ranged between 1 and 8 h. This variation is considerable and should be taken into account when the results of the various studies are compared. From an analysis of table 2 some facts emerge. Behavioral performance was affected by exposure to relatively low concentrations of most of the solvents investigated, ie, methylene chloride, styrene, toluene, 1,1,1-trichloroethane, trichloroethylene, white spirit, and xylene.

Although the concentrations leading to manifest performance decrements are sometimes encountered in the work environment, they do appear to be above the present hygienic standards for the different solvents. As yet, no interactional effects of the nonadditive type on behavioral performance have been found for combined exposure to two solvents or for the combination of exposure to one solvent and the intake of alcohol or pharmaceuticals.

Many questions have been raised concerning the representativity and validity of the effects on behavioral performance observed in experimental laboratory investigations. Most of the criticism is directed toward aspects of experimental procedure and experimental control in general, and this criticism has not been discussed in this review. Two issues do, however, seem to be more specifically relevant to the type of experimental inhalation studies already referred to. The first issue concerns the number and choice of subjects participating in the experiments. For natural reasons only a very limited number of subjects can be studied in each experiment. Moreover, the subjects in most experiments have been chosen from young, healthy persons with a high educational background rather than from solvent-exposed workers. It is argued that this circumstance may have contributed to an increase in the number of experiments with negative results and

² The author would be grateful if any reader can provide further references to experiments of the type included in table 2.

Table 2. Experimental laboratory investigations of solvent-induced effects on behavioral performance.

Author	Solvent	Number of subjects	Duration of exposure	Lowest concentration with manifest performance decrement	Highest concentration with no manifest performance decrement
Putz-Anderson et al 1981 (41)	Methyl chloride	56	3 h	..	200 ppm
Di Vincenzo et al 1972 (12)	Methylene chloride	11	2 h	..	200 ppm
Winneke 1974 (57)	Methylene chloride	12 and 18	3 and 4 h	300 ppm	..
Gamberale et al 1975 (19)	Methylene chloride	14	4 × 30 min	..	800 ppm
Putz et al 1979 (39)	Methylene chloride	12	4 h	200 ppm	..
Stewart et al 1968 (51)	Styrene	5	60 min	375 ppm	200 ppm
Gamberale et al 1974 (23)	Styrene	12	4 × 30 min	350 ppm	250 ppm
Stewart et al 1970 (50)	Tetrachloroethylene	17	7 h	..	100 ppm
Stewart et al 1977 (53)	Tetrachloroethylene	12	5.5 h	..	100 ppm
Gamberale et al 1972 (21)	Alcohol	12	..	0.6 ml/kg	..
	Diazepam	12	..	10 mg	..
	Combinations	12	..	No interactions	..
	Toluene	12	4 × 20 min	300 ppm	100 ppm
Stewart et al 1975 (49)	Toluene	8	7.5 h	..	100 ppm
Winneke 1982 (58)	Toluene	18	3.5 h	..	100 ppm
Andersen et al 1983 (1)	Toluene	16	6 h	..	100 ppm
Cherry et al 1983 (6)	Toluene	8	4 h	..	80 ppm
	Alcohol	8	4 h	0.4 ml/kg	..
	Combination	8	4 h	0.4 ml alcohol and 80 ppm toluene (no interaction)	..
Iregren et al ^a	Toluene	12	4.5 h	..	80 ppm
	Alcohol	12	4.5 h	0.6 ml/kg	..
	Combination	12	4.5 h	0.6 ml alcohol and 80 ppm toluene (no interaction)	..
Dick et al 1984 (11)	Toluene	30	4 h	..	100 ppm
	Methyl ethyl ketone	20	4 h	..	200 ppm
	Combination	20	4 h	..	100 ppm toluene and 50 ppm methyl ethyl ketone
Anshelm Olson et al 1984 (4)	Toluene	16	4 h	..	80 ppm
	Xylene	16	4 h	..	80 ppm
	Combination	16	4 h	..	50 ppm toluene and 30 ppm xylene
Stewart et al 1969 (52)	Trichloroethane	5	7 h	500 ppm	..
Salvini et al 1971 (42)	Trichloroethane	6	2 × 4 h	..	450 ppm
Gamberale et al 1973 (22)	Trichloroethane	12	4 × 30 min	350 ppm	250 ppm
Vernon & Fergusson 1969 (55)	Trichloroethylene	8	2 h	1 000 ppm	300 ppm
Salvini et al 1971 (43)	Trichloroethylene	6	8 h	110 ppm	..
Nakaaki et al 1973 (38)	Trichloroethylene	4	6 h	..	100 ppm
Stewart et al 1974 (55)	Trichloroethylene	9	8 h	..	110 ppm

(continued on page 68)

Table 2. Continued from page 67.

Author	Solvent	Number of subjects	Duration of exposure	Lowest concentration with manifest performance decrement	Highest concentration with no manifest performance decrement
Konietzako et al 1975 (35)	Trichloroethylene	20	4 h	..	95 ppm
Eittema et al 1975 (15)	Trichloroethylene	15	2.5 h	..	300 ppm
Gamberale et al 1976 (17)	Trichloroethylene	15	70 min	..	200 ppm
Fergusson & Vernon 1970 (16)	Trichloroethylene and depressant drugs (alcohol)	8	2 h	300 ppm trichloroethylene and 0.5 ml/kg alcohol	..
Windemüller & Ettema 1978 (56)	Trichloroethylene and alcohol	15	2.5 h	..	200 ppm trichloroethylene and 0.4 ml/kg alcohol
Gamberale et al 1975 (18)	White spirit	14	4 x 30 min and 1 x 60 min	4 000 mg/m ³	2 000 mg/m ³
Gamberale et al 1978 (20)	Xylene	23	70 min	300 ppm xylene and work on a bicycle ergometer (100 W)	300 ppm
Savolainen et al 1979 (46)	Xylene	6	6 h/d 2 weeks	100 ppm first day	200 ppm fifth day
Savolainen et al 1980 (47)	Xylene	8	6 h	90 ppm	..
Savolainen 1980 (44)	Xylene	10	4 h	..	280 ppm
	Alcohol	10	..	1 ml/kg	0.5 ml/kg
	Combination	10	4 h	1 ml/kg alcohol and 280 ppm xylene	..
Savolainen et al 1981 (45)	Xylene	9	4 h	..	200 ppm
	Trichloroethane	9	4 h	..	400 ppm
	Combination	9	4 h	..	200 ppm xylene and 400 ppm trichloroethane (no interaction)

^a Iregren A, Åkerstedt T, Anshelm Olson B, Gamberale F, Wallén M. Experimental exposure to toluene in combination with ethanol intake: Psychophysiological and behavioral effects (to be published).

thus can lead to an overall underestimation of the potential capacity of solvent exposure to affect performance. The other issue concerns the ecological relevance of the experimental situation in general. Thus it is a basic limitation of the experimental approach that the exposure conditions which can be simulated in an exposure chamber are rarely if ever very representative of the conditions existing in the real work environment.

One way of studying the acute effects of solvent exposure and overcoming most of the shortcomings of the experimental approach is to conduct quasi-experimental studies directly in the field.

Quasi-experimental field studies

Only a few attempts have been made to evaluate the acute effects of solvents with psychometric tests directly at the worksite (2, 3, 5, 7, 10, 24, 25, 33). However the results obtained in these investigations clearly demonstrate the narcotic effects of exposure to a number of organic solvents. Furthermore, these investigations give an interesting illustration of how the assessment of performance changes during the workshift

may be of practical importance with regard to the monitoring and prevention of hazards to health.

A common characteristic of the designs adopted in the field investigations reviewed in the following discussion is that performance measures were collected both at the beginning and at the end of a workday. The rationale of this design is based on the underlying assumption that the effect of exposure during the day may manifest itself in an impairment of performance at the end of a workday, with a return to normal levels of performance by the beginning of the following day, after approximately 16 h free from exposure. If the action of exposure lasts long enough to bridge the exposure-free period between two consecutive workdays, performance should also be negatively affected at the start of a workday.

Some features of these field studies are presented in table 3.

In the study by Göttel and his co-workers (25) the performance on a reaction-time test of a group of workers exposed to an average of 150 ppm of styrene was compared to that of a reference group of unexposed workers of the same age. The mean reaction time of the exposed workers appeared to be affected both before and after a workday.

In another study (24), workers exposed to styrene in concentrations varying between 20 and 120 ppm in four factories building fiber-glass boats, were compared in regard to reaction time with age-matched workers from two mechanical industries. The workers exposed to styrene had a longer reaction time, a greater deterioration of reaction time over time, and a greater irregularity of performance on the test than the unexposed workers both before and after a workday. However these differences between the groups were more pronounced at the end of the workday.

The performance of a group of workers exposed to solvent mixtures at concentrations clearly exceeding the hygienic standards was studied by Binaschi and his co-workers (5). No reference group was studied in this investigation. However the effect of the exposure manifested itself in a pronounced deterioration of performance after a workday. This deterioration was observed in spite of the use of tests which, under control conditions, would have revealed a learning effect.

Kjellberg and his co-workers (33) were able to follow a group of styrene-exposed workers after the closing down of a fiber-glass boat factory. They found that the reaction time of the exposed workers was prolonged compared with that of a reference group of unexposed workers. This effect could still be observed 4 d after the cessation of exposure. No effect was noticeable 35 d after the cessation of exposure.

In the investigations by Cherry and her co-workers (7, 10) reaction time was found to be prolonged among styrene-exposed workers before the beginning of a workday. They also found that, after 2 d without exposure, the mandelic acid concentration in early morning urine correlated with the reaction time measured on arrival at work.

In a longitudinal investigation by Anshelm Olson and her co-workers (3) the reaction time of workers handling organic solvents and solvent-based paints in

the production of plastic-coated sheets was measured several times during a period of more than two years. The performance of the workers was found to improve over time as a result of changes in the ventilation system and work process; the changes had brought about a considerable reduction in the solvent vapor concentration at the workplace.

The effects of exposure to a mixture of organic solvents was also studied by Anshelm Olson (2) among workers in the paint industry. In this study the exposed group performed less well than the reference group on most of the behavioral tests used. The differences were evident for both morning and afternoon measurements. Particularly noticeable was a marked decrease in performance on a reaction-time test over the course of the day for the workers exposed to the highest solvent levels.

Consideration of the results obtained in the investigations reviewed makes it seem reasonable to regard the assessment of behavioral performance as constituting a potential means for monitoring and controlling exposure to neurotoxic substances in a specific work environment. The detection of work conditions leading to depression of the central nervous system would clearly indicate the need for improvements in the hygienic quality of the environment under investigation and would, therefore, be a valuable complement to traditional environmental monitoring. The use of performance tests for this purpose does, however, make special demands on the procedure.

Since measurements of performance have to be carried out at different times during the day, circadian rhythms may constitute a confounding factor that is as important or even more important than learning or motivation. However it does seem possible to minimize or control the effects of these confounding factors with operations of experimental control such as the use of an age-matched reference group and a balanced design. Such control was accomplished in some of the afore-

Table 3. Quasi-experimental field studies on solvent-induced behavioral performance changes.

Author	Exposure	Subjects	Performance tests
Götell et al 1972 (25)	Styrene, 150 ppm	17 exposed, 17 referents Mean age 28 years	Simple reaction time
Gamberale et al 1976 (24)	Styrene, 20–120 mm	106 exposed, 36 referents Mean age 33 years	Simple reaction time
Binaschi et al 1976 (5)	Solvent mixtures, 1.72 of hygienic standard	8 exposed	Battery of 10 tests
Kjellberg et al 1979 (33)	Styrene, 40–50 ppm	7 exposed, 7 referents Mean age 49 years	Simple reaction time, mental arithmetic, Bourdon
Cherry et al 1980 (10) & 1981 (7)	Styrene, 52–227 ppm	27 exposed, 27 referents Mean age 23–26 years	Simple reaction time, vigilance task, digit symbol, digit span, tapping
Anshelm Olson et al 1981 (3)	Solvent mixtures, 1.0–1.5 of hygienic standard	42 exposed Mean age 31 years	Simple reaction time
Anshelm Olson 1982 (2)	Solvent mixtures, 0.35–2.94 of hygienic standard	47 exposed, 47 referents Mean age 51 years	Simple reaction time, Bourdon, Benton, critical flicker fusion

mentioned investigations using a quasi-experimental study design, as presented in table 4.

As shown in table 4, half of the workers in the exposed and reference groups performed the tests before work the first time and after work the second time, whereas the other half performed the tests after work the first time and before work the second time. With the study balanced in this way, a single analysis of variance for each performance variable is sufficient to test the effects of (i) exposure, (ii) learning, and (iii) the circadian rhythm independently of each other and the possible effect of the interactions between them.

Epidemiologic studies

The evidence for the toxic effects of long-term occupational exposure to low concentrations of solvent

Table 4. Experimental design of field studies on acute effects of occupational exposure to neurotoxic substances. (Reference groups 1 and 2 = age-matched workers)

Measurement occasions		
Before work	After work	Before work
Exposed group 1	Exposed group 1	Exposed group 2
Reference group 1	Exposed group 2	Reference group 1
	Reference group 2	Reference group 2

vapor is based largely on the results from epidemiologic studies in which the behavioral performance of groups of exposed workers has been compared to that of reference groups. In order for such comparisons to be meaningful, the assumption of the comparability of the exposed groups to the reference groups as regards performance capacity prior to exposure must be valid. Unfortunately, in retrospective studies of this type, there is no means of validating this assumption. Therefore, no matter how rigorously the researchers perform the selection or matching of the groups, the comparability of the exposed to the reference group with regard to behavioral performance capacity will always be uncertain. A further contribution to this uncertainty is the fact that performance variables are usually highly correlated to background factors such as age, education, intelligence, etc. These factors are known to have a selective impact on an individual's choice of job. Further difficulties in the interpretation of the outcome of this type of retrospective study are related to the nature of the independent variable. Thus in most cases there is no true knowledge of what the exposure has been; instead it is estimated from uncertain historical information.

Due to the aforementioned methodological limitations, the results of each specific study should be interpreted with caution. Possibly a better understanding of the state of affairs can be achieved through an

Table 5. Epidemiologic studies of solvent-induced effects on behavioral performance.

Author	Exposure	Number of subjects		Measured functions ^a	
		Exposed	Referents	Affected	Nonaffected
Hänninen 1971 (26)	Carbon disulfide	(50) + 50	50	I, PM	M, P
Hänninen et al 1976 (27)	Solvent mixtures	100	101	M, I, P, PM	RT
Lindström et al 1976 (36)	Styrene	98	43	PM	M, I, P, RT
Hane et al 1977 (28)	Solvent mixtures	52	52	I, PM	M, P, RT
Knave et al 1978 (34)	Jet fuel	30	30	P, RT	M, PM
Elofsson et al 1980 (14)	Solvent mixtures	80	80	M, P, PM, RT	I
Cherry et al 1981 (9)	Methylene chloride	29	29	..	M, I, P
Anshelm Olson 1982 (2)	Solvent mixtures	47	47	M, P, RT	Critical flicker fusion
Iregren 1982 (31)	Toluene	34	34	RT	M, I, P, PM
Lindström & Wickström 1983 (37)	Solvent mixtures	219	229	M, RT	I, PM
Putz-Anderson et al 1983 (40)	Carbon disulfide	131	167	..	M, I, RT, PM
Cherry et al 1984 (18)	Toluene	59	59	I (reading test)	M, P, RT, PM
	Solvent mixtures	42	42	RT	M, P, PM

^a M = memory functions, I = other intellectual functions, P = perceptual functions, RT = reaction time, PM = other psychomotor functions.

analysis and comparison of the results of the different investigations.

Table 5 presents some features of a number of epidemiologic studies conducted to assess the long-term effects of solvent exposure. To facilitate the comparison between the studies, an attempt has been made to classify the performance effects observed in each investigation on the basis of whether the tests used were supposed to assess primarily (i) memory functions, (ii) other intellectual functions, (iii) perceptual functions, (iv) reaction time, or (v) other psychomotor functions.

Two of the studies listed in table 5 were conducted with groups of textile workers exposed to carbon disulfide (26, 40). The results of these two studies do not agree with regard to the effects on performance. In the study by Hänninen (26) the intellectual and psychomotor functions of the exposed workers appeared to be affected, while no such effect was observed in the investigation by Putz-Anderson and his co-workers (40). One explanation for this difference in results may be that the exposure conditions seem to have been more severe in the study by Hänninen.

Groups of painters were investigated with extensive batteries of behavioral tests in two Finnish and two Swedish studies (14, 27, 29, 37). Statistically significant differences in the performance of various tests were obtained between exposed and unexposed workers in all these studies. However some differences between studies should be especially noted. In the study by Hänninen et al (27) the performance of the exposed group was clearly poorer than that of the reference group in all but one of the tests used. On the whole, the higher intellectual functions seemed to be more affected by exposure than the psychomotor functions. In the study by Hane et al (28) the differences in performance between the painters and the referents were not so distinct. Only one test of intellectual ability and one of psychomotor functions revealed differences in performance. Moreover, on 5 out of 12 tests, the painters actually did a little better than the referents. In the two more recent studies, the one by Elofsson et al (14) and the one by Lindström & Wickström (37), there was no manifest decrements in intellectual functions among the exposed workers. The differences observed concerned perceptual and psychomotor functions, particularly reaction time.

Recently, exposure to paint solvents was also investigated by Anshelm Olson (2) among workers in the paint industry and by Cherry and her co-workers (8) among painters in a naval dockyard. Some features of the former study, which was designed for repeated measurements of performance, have already been presented. The only clearly consistent result of these two studies was that the exposed workers had longer reaction times than the unexposed workers in the reference groups. These results cannot definitely be interpreted as due to long-term exposure. Similar results were obtained by Iregren (31), who examined a group

of printers with a battery of tests, of which only a reaction-time task showed a decrement in performance.

In the remaining studies listed in table 5, either no effects of exposure were found, or the effects were restricted to perceptual and psychomotor functions.

A few conclusions can be drawn from a comparative analysis of the results of the epidemiologic investigations included in this review. It is evident that at least some aspect of performance was found to be impaired in the great majority of the studies. This fact can hardly be attributed to chance. The argument that systematic errors in the choice of reference groups can have created spurious differences in performance in so many independently conducted investigations is not very convincing. It should be noted, however, as has been shown by Lindström & Wickström (37) and by Cherry et al (8), that differences in performance between exposed and unexposed groups of workers do sometimes tend to disappear when the groups are matched with regard to the intellectual level of the workers before exposure. It is also interesting to observe that in both these studies the matching procedures did not affect the results of a test of simple reaction time showing a performance decrement among the exposed workers.

Clear evidence for the effects of long-term exposure to solvents is also found in the results of two studies of styrene-exposed workers (24, 36). In these studies the duration of exposure was found to be negatively correlated to performance on certain tasks independent of the age of the exposed workers.

There seems to be no real evidence that the effects on behavioral performance due to long-term solvent exposure are distinguishable from the effects which have been observed in laboratory experiments or in quasi-experimental field studies. In order to describe the existing differences between the acute and the long-term manifestation of solvent exposure, a more complex model is needed which integrates the assessment of behavioral performance with that of other behavioral variables, ie, neurobehavioral reactions, subjective symptoms, psychiatric observations, etc.

Clinical studies

Substantial evidence that long-term exposure to organic solvents may produce neuropsychological impairments derives not only from the investigation of behavioral performance changes in exposed workers, but also from case reports, clinical studies, and epidemiologic studies of workers on disability pensions. (For a review see reference 29.) The solvent-induced clinical conditions have been given different names. In Finland and Sweden, for example, the condition is called "psycho-organic syndrome," while in Denmark and Norway the diagnosis is labeled "presenile dementia." The nonspecific manifestation of the toxicity of solvents makes the individual clinical diagnosis very difficult however.

In Sweden the diagnostic recognition of solvent-induced disorders is mainly based on information concerning the exposure history of the worker/patient and on observations of his behavioral performance capacity. The observations are made systematically with the use of a battery of psychometric tests (30).

Essentially, the work in this case is very similar to that performed with psychometric methods in the assessment of the cerebral functional status of a patient with suspected minor brain damage.

The psychometric methods used in clinical investigations in the different Scandinavian countries are very similar. They have been designed on the basis of the results obtained in the epidemiologic investigations reviewed in the previous section. Further information useful in the development of the psychometric methods used in clinical investigations derives from the analysis of results of groups of patients referred to occupational health clinics for suspected solvent-induced functional impairments (13).

Concluding remarks

One of the conclusions which can be drawn from the present review is that many researchers have relied successfully on psychometric techniques to detect early signs of the toxicity of industrial solvents. Of course, other methods, such as neurophysiological measurements and systematic observations of subjective symptoms, have also been suitable for this purpose and have often been used together with the psychometric methods. However, it seems clear that the measurement of behavioral performance has produced consistent results and that it has been demonstrated to possess more general applicability in human studies than other methods have. Thus the demonstration in experimental laboratory studies that behavioral performance changes do or do not occur at certain solvent concentrations is very important information for the establishment and evaluation of occupational exposure standards.

The results of the application of psychometric techniques in quasi-experimental field studies have also been very promising. Probably the potentialities of these methods in the monitoring of hazards in the work environment have not yet been fully exploited. The use of the study design outlined in this paper, or the application of a similar strategy to collect measurements of performance directly at the worksite, appears to be practicable. Some behavioral tests suitable for this purpose are already available and others can be developed (48). To be suitable for use in the field, a performance test must satisfy a number of requirements. The test must be sensitive, short, reliable, simple to administer, and resistant to learning or training effects, and, most important, the performance measures obtained must be related to early signs of functional disorders.

The evaluation of the psychometric methods in assessing the long-term effects of solvents on the cen-

tral nervous system is more difficult. The difficulties, however, are not strictly related to specific characteristics of the psychometric methods. Instead, as discussed previously, they are mostly due to the limitations inherent in the epidemiologic method as such. With all likelihood a longitudinal approach with repeated measurements of performance over time would result in substantially more distinct results.

An important question, although difficult to answer, concerns the type of behavioral performance tests to be used in the study of the toxicity of solvents. Because of the complexity of the question no attempt has been made here to review this argument in detail. Only a few comments on this topic follow in these final remarks.

To begin with, it is not possible to give this question a fully valid answer because such an answer would have to be based on an understanding of the neurophysiological and neuropsychological mechanisms (affected by the solvents) — knowledge which we do not yet possess. Moreover it is important to keep in mind that, independent of their use, performance tests are supposed to provide measurements of the activity of underlying functional processes, of which in fact very little is known. For this reason it is often very difficult to define what is actually measured by different performance tests. Even the relatively simple classification of performance tests carried out in this paper (table 5) must be considered arbitrary. In fact, although a distinction is commonly drawn between different types of mental functions which can be measured by behavioral performance tests, the distinction is very difficult to maintain completely. Thus perception, decision, knowledge, judgment, and coordinated overt activity by the hands, organs of speech, or other effectors are involved in all performance tests. Usually the tests are defined and classified according to which mental function is supposed to play the most essential part in the performance. However, it should be observed that an impairment of performance need not necessarily be related to the mental function the test is supposed to assess.

Until the mechanisms of solvent toxicity are better understood, it is advisable to base the choice of behavioral tests on strictly empirical considerations. There is no doubt that the likelihood of detecting the adverse effects of solvent exposure will be enhanced if the performance tests used involve sensorimotor, vigilance, and perceptual functions rather than functions related to intelligence. Performance tests of intellectual functions could possibly be used for matching procedures. There is no doubt that psychometric methods can and need to be improved. A promising development consists in the computerization of test procedures. Computerized batteries of performance tests have already been used in experimental laboratory studies (4, 33) and have been found to have considerable advantages as compared to paper and pencil tests. In Sweden a collaboration is in progress

between the Research Department of the National Board of Occupational Safety and Health and some of the occupational health clinics with the task of evaluating the application of a computerized battery of psychometric tests for use in clinical examinations (32).

References

- Andersen I, Lundqvist GR, Mölhave L, Find Pedersen O, Proctor DF, Vaeth M, Wyon DP. Human response to controlled levels of toluene in six-hour exposures. *Scand J Work Environ Health* 9 (1983) 404—418.
- Anshelm Olson B. Effects of organic solvents on behavioral performance of workers in the paint industry. *Neurobehav Toxicol Teratology* 4 (1982) 703—708.
- Anshelm Olson B, Gamberale F, Grönqvist B. Reaction time changes among steel workers: A longitudinal study. *Int Arch Occup Environ Health* 48 (1981) 211—218.
- Anshelm Olson B, Gamberale F, Iregren A. Coexposure to toluene and p-xylene in man: Central nervous functions. *Br J Ind Med* 42 (1985) 117—122.
- Binaschi S, Gazzaniga G, Crovato E. Behavioural toxicology in the evaluation of the effects of solvent mixtures. In: M Horvath ed. *Adverse effects of environmental chemicals and psychotropic drugs*. Volume 2. Elsevier Scientific Publishing Co, Amsterdam 1976, pp 91—98.
- Cherry N, Johnston JD, Venables H, Waldron HA. The effects of toluene and alcohol on psychomotor performance. *Ergonomics* 26 (1983) 1081—1087.
- Cherry N, Rodgers B, Venables H, Waldron HA, Wells GG. Acute behaviour effects of styrene exposure: A further analysis. *Br J Ind Med* 38 (1981) 346—350.
- Cherry N, Venables H, Waldron H. British studies on the neuropsychological effects of solvent exposure. *Scand J Work Environ Health* 10 (1984): suppl 1, 10—12.
- Cherry N, Venables H, Waldron HA, Wells GG. Some observation on workers exposed to methylene chloride. *Br J Ind Med* 38 (1981) 351—355.
- Cherry N, Waldron HA, Wells GG, Wilkinson RT, Wilson HK, Jones S. An investigation of acute behavioural effects of styrene on factory workers. *Br J Ind Med* 37 (1980) 234—240.
- Dick RB, Setzer JV, Wait R, Hayden MB, Taylor BJ, Tolos B, Putz-Andersen V. Effects of acute exposure of toluene and methyl ethyl ketone on psychomotor performance. *Int Arch Occup Environ Health* 54 (1984) 91—109.
- Di Vincenzo GD, Yanno FJ, Astill BD. Human and canine exposures to methylene chloride vapor. *Am Ind Hyg Assoc J* 33 (1972) 125—135.
- Ekberg K, Hane M. Test battery for investigating functional disorders — The TUFF battery. *Scand J Work Environ Health* 10 (1984): suppl 1, 14—17.
- Elofsson S-A, Gamberale F, Hindmarsh T, Iregren A, Isaksson A, Johnsson I, Knave B, Lydahl E, Mindus P, Persson HE, Philipson B, Steby M, Struwe G, Söderman E, Wennberg A, Widén L. Exposure to organic solvents: A cross-sectional epidemiologic investigation on occupationally exposed car and industrial spray painters with special reference to the nervous system. *Scand J Work Environ Health* 6 (1980) 239—273.
- Ettema JH, Kleerekoper L, Duba WC. Study of mental stress during short-term inhalation of trichloroethylene. *Staub Reinhalt Luft* 35 (1975) 409—410.
- Ferguson RK, Vernon RJ. Trichloroethylene in combination with CNS drugs (effects on visual motor tests). *Arch Environ Health* 20 (1970) 462—467.
- Gamberale F, Annwall G, Anshelm Olson B. Exposure to trichloroethylene: III Psychological functions. *Scand J Work Environ Health* 4 (1976) 220—224.
- Gamberale F, Annwall G, Hultengren M. Exposure to white spirit: II Psychological functions. *Scand J Work Environ Health* 1 (1975) 31—39.
- Gamberale F, Annwall G, Hultengren M. Exposure to methylene chloride: II Psychological functions. *Scand J Work Environ Health* 2 (1975) 95—103.
- Gamberale F, Annwall G, Hultengren M. Exposure to xylene and ethylbenzene: III Effects on central nervous functions. *Scand J Work Environ Health* 4 (1978) 204—211.
- Gamberale F, Hultengren M. Toluene exposure: II Psychophysiological functions. *Work Environ Health* 9 (1972) 131—139.
- Gamberale F, Hultengren M. Methylchloroform exposure: II Psychophysiological functions. *Work Environ Health* 10 (1973) 82—92.
- Gamberale F, Hultengren M. Exposure to styrene: II Psychological functions. *Work Environ Health* 11 (1974) 86—93.
- Gamberale F, Lisper HO, Anshelm Olson B. The effect of styrene vapour on the reaction time of workers in the plastic boat industry. In: M Horvath ed. *Adverse effects of environmental chemical and psychotropic drugs*. Volume 2. Elsevier Scientific Publishing Co, Amsterdam 1976, pp 135—148.
- Götell P, Axelsson O, Lindlöf B. Field studies on human styrene exposure. *Work Environ Health* 9 (1972) 76—83.
- Hänninen H. Psychological picture of manifest and latent carbon disulphide poisoning. *Br J Ind Med* 28 (1971) 374—381.
- Hänninen H, Eskelinen L, Husman K, Nurminen M. Behavioral effects of long-term exposure to a mixture of organic solvents. *Scand J Work Environ Health* 2 (1976) 240—255.
- Hane M, Axelsson O, Blume J, Hogstedt C, Sundell L, Ydreborg B. Psychological function changes among house painters. *Scand J Work Environ Health* 3 (1977) 91—99.
- Hernberg S. Neurotoxic effects of long-term exposure to organic hydrocarbon solvents: Epidemiologic aspects. In: Holmstedt B, Lauwerys R, Mercier M, Roberfroid M, ed. *Mechanisms of toxicity and hazard evaluation*. Elsevier, Amsterdam, 1980 pp 307—317.
- Hogstedt C, Hane M, Axelsson O. Diagnostic and health care aspects of workers exposed to solvents. In: Zenz C, ed. *Developments in occupational medicine*. Year book Medical Publishers Inc, Chicago, London 1980, pp 249—258.
- Iregren A. Effects on psychological test performance of workers exposed to a single solvent (toluene) — A comparison with effects of exposure to a mixture of organic solvents. *Neurobehav Toxicol Teratology* 4 (1982) 695—701.
- Iregren A, Gamberale F, Kjellberg A. A microcomputer-based behavioural testing system. In: World Health Organization, Regional Office for Europe. *Neurobehavioural methods in occupational and environmental health: Second international symposium, Copenhagen, 6—9 August 1985*. Copenhagen 1985, pp 75—80.
- Kjellberg A, Wigaeus E, Engström J, Åstrand I, Ljungquist E. Långtidseffekter av styreneexposition vid en plaståtsindustri [Long-term effects of styrene exposure in a polyester plant]. *Arbetsarkivstyrelsen, Stockholm 1979*. (Arbete och hälsa 1979:18).
- Knave B, Anshelm Olson B, Elofsson S, Gamberale F, Isaksson A, Mindus P, Persson HE, Struwe G, Wennberg A, Westerholm P. Long-term exposure to jet fuel: II A cross-sectional epidemiologic investigation on occupationally exposed industrial workers with special reference to the nervous system. *Scand J Work Environ Health* 4 (1978) 19—45.

35. Konietzko H, Elster I, Sayer M, Weichardt M. Zentralnervöse Störungen durch trichlorethylen. *Staub Reinhalt Luft* 35 (1975) 240—241.
36. Lindström K, Härkönen H, Hernberg S. Disturbances in psychological functions of workers occupationally exposed to styrene. *Scand J Work Environ Health* 2 (1976) 129—139.
37. Lindström K, Wickström G. Psychological function changes among maintenance house painters exposed to low levels of organic solvent mixtures. *Acta Psychiatr Scand* 67 (1983): suppl 303, 81—91.
38. Nakaaki K, Onishi N, Iida H, Kimotsuki K, Fikabori S, Morikiyo Y. An experimental study on the effect of exposure to trichloroethylene vapor in man. *Jpn Sci Labour* 44 (1973) 449—463.
39. Putz VR, Johnson B, Setzer J. A comparative study of the effects of carbon monoxide and methylene chloride on human performance. *J Environ Pathol Toxicol* 2 (1979) 97—112.
40. Putz-Anderson V, Albright B, Lee S, Johnson B, Chrislip D, Taylor B, Brightwell S, Dickerson N, Culver M, Zentmeyer D, Smith P. A behavioral examination of workers exposed to carbon disulphide. *Neuro Toxicol* 41 (1983) 67—78.
41. Putz-Anderson V, Setzer JV, Croxton JS, Phipps FC. Methyl chloride and diazepam effects on performance. *Scand J Work Environ Health* 7 (1981) 8—13.
42. Salvini M, Binaschi S, Riva M. Evaluation of the psychophysiological functions in human exposed to the 'threshold limit value' of 1,1,1-trichloroethane. *Br J Ind Med* 28 (1971) 286—292.
43. Salvini M, Binaschi S, Riva M. Evaluation of the psychophysiological functions in humans exposed to trichloroethylene. *Br J Ind Med* 28 (1971) 293—295.
44. Savolainen K. Combined effects of xylene and alcohol on the central nervous system. *Acta Pharmacol Toxicol* 46 (1980) 366—372.
45. Savolainen K, Riihimäki V, Laine A, Kekoni J. Short-term exposure of human subjects to m-xylene and 1,1,1-trichloroethane. *Int Arch Occup Environ Health* 49 (1981) 89—98.
46. Savolainen K, Riihimäki V, Linnoila M. Effects on short-term xylene exposure on psychophysiological functions in man. *Int Arch Occup Environ Health* 44 (1979) 201—211.
47. Savolainen K, Riihimäki V, Seppäläinen AM, Linnoila M. Effects of short-term m-xylene exposure and physical exercise on the central nervous system. *Int Arch Occup Environ Health* 45 (1980) 105—121.
48. Söderman E, Kjellberg A, Anshelm Olson B, Iregren A. Standardisation of a simple reaction time test for use in behavioral toxicology research [In Swedish with English summary]. National Board of Occupational Safety and Health, Solna 1982. (Undersökningsrapport no 27).
49. Stewart RD. Toluene: Development of a biological standard for the industrial worker by breath analysis. National Institute for Occupational Safety and Health, Cincinnati, OH 1975. (NIOSH contract report no 99-72-84).
50. Stewart RD, Baretta ED, Dodd HC, Torkelson TR. Experimental human exposure to tetrachloroethylene. *Arch Environ Health* 20 (1970) 225—229.
51. Stewart RD, Dodd HC, Baretta ED, Schaffer AW. Human exposure to styrene vapor. *Arch Environ Health* 16 (1968) 656—662.
52. Stewart RD, Gay HH, Schaffer AW, Early DS, Rowe VK. Experimental human exposure to methyl chloroform vapor. *Arch Environ Health* 19 (1969) 467—472.
53. Stewart RD, Hake CL, Le Brun AI, Kalbfleisch JH, Newton PE, Peterson JE, Cohen H, Strube R, Busch KA. Effects of trichloroethylene on behavioral performance capabilities. In: Xintaras C, Johnson BL, Groot I, ed. *Behavioral toxicology: Early detection of occupational hazards*. US Department of Health, Education and Welfare, Washington, DC 1974, pp 96—126. (DHEW publication no (NIOSH) 74—126).
54. Stewart RD, Hake CL, Wu A. Effects of perchloroethylene drug interaction on behavior and neurological function. US Department of Health Education and Welfare. Washington, DC 1977. (DHEW (NIOSH) publication no 77—191).
55. Vernon RJ, Ferguson RK. Effects of trichloroethylene on visual-motor performance. *Arch Environ Health* 18 (1969) 894.
56. Windemüller FBJ, Ettema JH. Effects of combined exposure to trichloroethylene and alcohol on mental capacity. *Int Arch Occup Environ Health* 41 (1978) 77—85.
57. Winneke G. Behavioral effects of methylene chloride and carbon monoxide as assessed by sensory and psychomotor performance. In: Xintaras C, Johnson BL, de Groot I, ed. *Behavioral toxicology*. US Government Printing Office, Washington, DC 1974, pp 130—144.
58. Winneke G. Acute behavioral effects of exposure to some organic solvents — Psychophysiological aspects. *Acta Neurol Scand* 66 (1982): suppl 92, 117—129.