

Long-term exposure to jet fuel

II. A cross-sectional epidemiologic investigation on occupationally exposed industrial workers with special reference to the nervous system

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KNAVE, B., ANSHELM OLSON, B., ELOFSSON, S., GAMBERALE, F., ISAKSSON, A., MINDUS, P., PERSSON, H. E., STRUWE, G., WENNBERG, A. and 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. Thirty jet fuel exposed workers selected according to exposure criteria and thirty nonexposed controls from a jet motor factory were examined, with special reference to the nervous system, by occupational hygiene physicians, psychiatrists, psychologists, and neurophysiologists. The controls and the exposed subjects were matched with respect to age, employment duration, and education. Among the exposed subjects the mean exposure duration was 17 years, and 300 mg/m³ was calculated as a rough time-weighted average exposure level. The investigation revealed significant differences between the exposed and nonexposed groups for (a) incidence and prevalence of psychiatric symptoms, (b) psychological tests with the load on attention and sensorimotor speed and (c) electroencephalograms. When the control group was selected, it was ensured that the two groups were essentially equivalent except for exposure to jet fuel. It is concluded, therefore, that the differences found between the groups are probably related to exposure to jet fuel.

Key words: epidemiology, jet fuel, occupational medicine, occupational neurology, occupational neurophysiology, occupational psychiatry, occupational psychology, organic solvents.

It is well known that exposure to petroleum distilled fuels may have effects on the nervous system in man. Numerous reports have been published on acute and chronic occupational intoxication due to

such fuels. Acute intoxication is followed by dizziness, drowsiness, nausea, vomiting, etc., i.e., a narcotic effect (19, 28, 39, 41). As a matter of fact, gasoline was tried, although less successfully, for general anesthesia more than 100 years ago (16). Symptoms have also been described in a case of inflight intoxication due to jet fuel fumes (13). Neurasthenia (24, 38, 44, 45, 46, 47) and polyneuropathy (9, 12, 15, 34, 38, 46) have been described as early manifestations of disease following chronic intoxication.

Recently 29 Swedish aircraft factory workers occupationally exposed to jet fuel

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were examined (32, 33). More than two-thirds of them reported recurrent acute symptoms (dizziness, respiratory tract symptoms, heart palpitations, a feeling of thoracic oppression, nausea, headache) upon exposure at work to jet fuel vapors. Furthermore, symptoms of neurasthenia and symptoms and signs of polyneuropathy were more frequent in the exposed group than in the reference groups. These findings were interpreted by the authors as a possible effect of long-term exposure to jet fuel on the nervous system. The authors stated, however, that further studies on other groups of workers exposed to jet fuel vapors and on matched control groups of nonexposed workers were needed before the validity of this interpretation could be established. The aim of the present study was to provide additional information on such groups.

A jet motor factory was chosen for this purpose. In some areas of the factory parts of the engine are manufactured, and the workers concerned are not exposed to jet fuel. In another part of the plant motor parts are assembled, and the motor is run under simulated inflight conditions. Workers involved in these procedures are exposed to jet fuel. Thus, it was possible to compare exposed and nonexposed groups of subjects employed in the same factory.

THE WORKPLACE

Exposure to jet fuel vapors regularly occurs, particularly in the units or sites of the factory where the fuel systems of engines are produced. These fuel systems consist of a large number of single components. During the production process the components are gradually assembled to constitute the end product. During this process the various components and the fuel system as such undergo a variety of standardized testing procedures for the assessment of function, technical quality, and security. During the tests jet fuel flows through the test object in order to create a situation which can be regarded as equivalent to real flying conditions. In performing these tests, some categories of personnel are exposed to jet fuel vapors.

WORK CONDITIONS

Testing of fuel systems (component testing)

Fuel systems are tested on special premises (i.e., in test houses). The various components to be tested are attached to a testing device ("rig"). The actual test is performed and supervised by one man and consists of readings and manipulations and adjustments on the test object during the course of the test. There is a large variety of components, and the testing periods can vary from 10–15 min to a whole day, depending on the type of object and the length of the standardized testing protocol. Common test objects are: main fuel controls, after-burn pumps, exhaust nozzal controls, after-burn fuel controls, ignition valves, pressure radio bleed controls or valves, computers, etc.

Performing these tests and control procedures is manual work requiring high standards of precision; the work implies that the person performing it is positioned with his face 20–40 cm from the test object. The object is constantly perfused with jet fuel. For a tester roughly 50 % of the total work time is spent in this manual work with direct exposure to fuel vapors. The rest of the time is spent supervising the test at a distance (from behind a window), writing protocols, etc., with a minimum of exposure. The testing personnel consistently give the same description of their work situation and practices. They circulate freely from one part of the premises to another, and they do not specialize in any particular kind of test item.

Engine testing

The engines, when assembled, are also subject to testing and control procedures under conditions simulating real flying. The engines, with their installed fuel supply systems, are put up in a stabilizing frame and run through a standardized testing procedure. To a large extent the testing is maneuvered from a protected room with distant-control systems. During some moments (connection and disconnection of fuel supply, control and cleaning of fuel filters, adjustments, etc.), the testing

personnel handle the fuel system and are directly exposed to fuel vapors. The personnel consistently report that the exposure periods take roughly 35 % of their total work time. The engine tests can last from one or two to ten days. Usually they take three days.

Other kinds of work

After having undergone the testing procedure, which may be repeated after adjustments, the test object is passed on to special personnel (mechanics) for disassembling, cleaning and reassembling. These tasks require precision and are performed with the breathing zone of the worker in the immediate vicinity of the engine and component parts drenched with fuel. The personnel give the round figure of 35 % as the amount of work time spent at these tasks.

The testing of component parts, as already described, implies the use of instruments and devices for observing and registering the course of the testing procedure for evaluation purposes. The instruments need almost constant supervision and calibration for accuracy and reliability. Instrument checks are performed by special personnel who, from a practical point of view, work under similar conditions and routines as the component testers.

There is also a constant need of instrument and testing service repairs. This work is performed by one mechanic who works in the testing area. The nature of this work is very similar to that of the component testers with the difference that, when repairs are done in the testing area, the flow of fuel is regularly stopped.

EXPOSURE

Jet fuel is an aviation turbine fuel with the approximate distillation range of 50 to 250°C. Since 1972 fuel with the following composition has been used:

Aromatic hydrocarbons	12 vol. %
Olephin hydrocarbons	0.5 vol. %
Saturated hydrocarbons (paraffins, cycloparaffins, etc.)	87.5 vol. %

The aromatic hydrocarbons include benzene (0.3 vol. % of the total), toluene (1 %). The fuel contains no lead compounds.

In the present study the assessment of exposure to jet fuel vapors is based on (a) time of employment in work implying exposure, (b) analysis of work practices, and (c) measurements of fuel contents in the air of the worker's breathing zone during exposure. Time of employment in work implying exposure to fuel vapors was obtained from a personal interview and verified with the aid of the records of the company. At the interview a detailed account was obtained of the work habits and practices of the individual throughout the years during which exposure to fuel had occurred. Also, at this time, the moments of work when such exposure reasonably could occur were determined. On the basis of these interviews various moments of the work procedures were selected for quantitative measurement and analysis. The interview, moreover, constituted the basis for a gross overall approximation of the percentage of time occupied by work during which any considerable extent of exposure occurred to jet fuel vapors.

During 1975 a program of technical improvements was performed at the factory. The fuel vapor concentrations were thus decreased by improved ventilation and other protective arrangements, particularly in the areas of component testing. The results of these improvements are illustrated in fig. 1.

Quantitative measurements

In assessing exposure, we used measurements made of jet fuel concentrations in the air before the technical improvements were accomplished. Measurements were also performed during work procedures which had not undergone technical change.

Air concentrations of fuel vapors were measured with a flame ionization detector (Ratfish Instrument, Model RS 5). These measurements were performed to give a result relevant to exposure during work. The test person had an air sampler attached to him during work, and the sampling point was positioned immediately in front of his nose. The teflon sampling

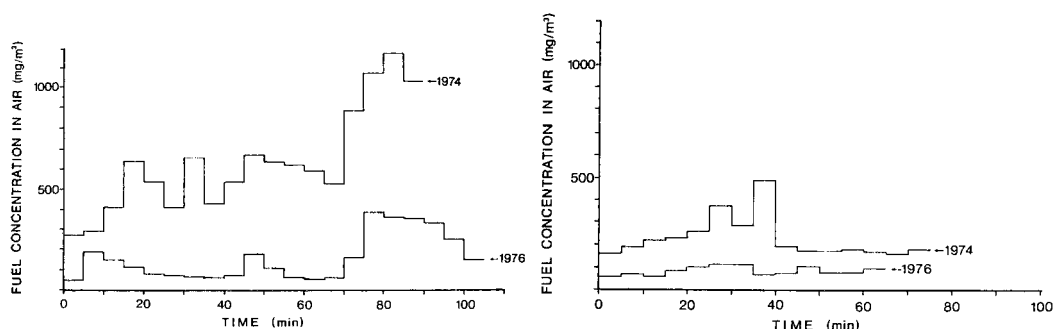


Fig. 1. Levels of fuel concentration in the worker's breathing zone during component testing with adjustment of a high pressure body (figure on the left) and a computer (figure on the right) as the test object in 1974 (upper lines) and 1976 (lower lines). The levels are given as the time-weighted average for each 5-min period.

tube measured 4 mm in internal diameter and 7 m in length. It was considered not to interfere with the routine course of the work procedure. The air flow in the tube during sampling was 2 l/min.

In November 1974 measurements of air concentrations of jet fuel were performed during some component-testing procedures. The test objects were selected to give a representative mixture of the work situation for exposed personnel. The

results as to component testing, engine testing, and relevant work procedures performed by mechanics are shown in table 1.

In the table the calculation of the average of the whole measurement is based on the time-integrated average concentration for each 5-min period of current measurement. For the registration of the time-integrated averages, an integrator device (Rikadenki Computer Recorder) was used.

Table 1. Jet fuel concentrations (mg/m³) in the breathing zones of personnel at work.

Test object	Time (t) (min)	Maximum	Minimum	Mean ($\bar{x}$)
<i>During component testing</i>				
Adjustment of flow control	40	343	157	209
Adjustment of computer	77	488	160	229
Adjustment of high pressure body	55	128	51	85
Adjustment of exhaust nozzle control	90	1,168	270	630
Adjustment of after-burn pump vent	20	594	422	510
Flow testing spread-ring	19	221	178	200
End control after-burn vent	19	824	284	580
Adjustment of main fuel control	97	3,214	111	925
Control of component in after-burn pump	87	413	41	125
<i>During engine testing</i>				
Final control of fuel filter	33	237	58	140
Regular control of fuel filter	54	272	29	110
Disconnecting fuel tubing, emptying of engine	30	240	41	147
<i>During routines implying exposure to fuel vapors</i>				
Collection of spill fuel	10	— ^a	— ^a	480
Repair of leaking fuel tube	10	— ^a	— ^a	149
Trimming of locking device	40	253	142	185
Change of filter	55	3,226	56	974

^a Not given.

Assessment of exposure

The exposure of different categories of personnel can be expressed as a time-weighted average air concentration in the breathing zone during the time periods when exposure occurs. This average value (C) was calculated to be as follows: 423 mg/m³ for the component testers, 128 mg/m³ for the engine testers, and 185–248 mg/m³ for the mechanics. The figures for the mechanics are given as the range due to the fact that the group was heterogeneous with respect to exposure conditions. C is calculated from the results of the performed measurements of air concentrations (table 1), and the registered time length of each test operation, with the following formula:

$$C = \frac{\sum (tx\bar{x}) n}{\sum t} \quad ^4$$

The entity (C) bears the character of a crude approximation and is demonstrated with the purpose of describing the levels of exposure in terms of magnitude.

EXAMINED GROUPS

Exposed workers

A committee was formed with representatives of the management, the trade unions, and the health department of the plant. The committee, acting on our instructions, selected 30 of the most heavily exposed workers from all the employees in regular or intermittent contact with jet fuels. The selection was based on accurate knowledge of the work conditions of all the jobs concerned. The exposure criteria were intensity and duration of exposure.

There was a consensus of opinion within the committee on the selection, and all

selected individuals agreed to participate in the study. In this group 15 were fuel system testers (5 foremen), 7 engine testers (2 foremen), and 8 mechanics (4 foremen). The fuel system testers were considered to be more exposed than the engine testers and mechanics. The duration of exposure varied between 2 and 32 years (mean = 17.1, median = 18.5).

Control groups

Originally, an age-matched control group of 30 subjects (age range 27–66 years, mean = 46.4, median = 44.0) was selected by the former plant physician. In this selection procedure "general state of health" was also used as a matching criterion. The level of education was disregarded. Since this procedure is open to objections, another control group had to be selected.

The final control group was chosen under the supervision of the Department of Statistics, the University of Stockholm. Subjects eligible for inclusion in the control group were drawn from the employment records according to the following criteria: (a) no exposure to jet fuel, (b) same age (± 1 year), and (c) similar duration of employment (± 1 year for short and ± 5 years for long durations) as each of the exposed subjects. From this pool of subjects ($n = 162$), one control candidate for each of the exposed foremen and three control candidates for each exposed worker were drawn by lots. The level of education and any trade union activity were established in this subgroup, since these factors were considered important to match. All 30 control subjects thus selected participated in the study.

The exposed group and the final control group, pairwise matched, were each composed of 19 workers and 11 foremen, all males, with an age range of 27–66 years. The mean age was 46.4 in the exposed group and 46.2 in the control group. The median age was 43.5 years in both groups. The exposed group had been employed 17.7 (mean) years and the control group 19.8 (mean) years. The corresponding median values were 19.0 and 21.0 years, respectively.

⁴ The formula is applied to the measurement results of component testing in table 1 as follows: $[(40 \times 209)/504] + [(77 \times 229)/504] + [(55 \times 85)/504] + [90 \times 630]/504 + [(20 \times 510)/504] + [(19 \times 200)/504] + [(19 \times 580)/504] + [(97 \times 925)/504] + [(87 \times 125)/504 = 422.6 \text{ mg/m}^3$.

METHODS

Medical history, standardized interview and neurological examination (investigator: B. K.)

Information was collected on heredity, previous and current health, occupational history, tobacco smoking, use of alcohol, etc., as well as on acute symptoms associated with exposure to jet fuel. Data on the incidence of symptoms such as neurasthenia, anxiety, and/or mental depression and on confounding and effect modifying factors were collected with a standardized interview, the contents of which were agreed upon in a Scandinavian meeting on health hazards in the use of solvents (3). Moreover, in the present investigation we were able to obtain further information from the medical records of the factory. Nearly all the subjects had been employed at the plant almost all their adult life (cf: mean age about 46 years and mean duration of employment about 19 years), and during this time they had been referred to the plant physician (who had been employed at the factory for 27 years) when ill. Therefore symptoms of neurasthenia, anxiety and/or mental depression were recorded and evaluated also from notations in the medical records of the factory health department.

When polyneuropathy was being studied, we used the standardized questionnaire applied in the first jet fuel investigation (32, 33) and supplemented the clinical neurological examination with an examination especially designed to detect early signs indicative of polyneuropathy. A basis for such an evaluation was developed by Lindblom in studies on uremic patients with subclinical and manifest polyneuropathy (7) and was later used in investigations on industrial workers (29, 30, 31, 32, 33, 40). Findings are scored between 0 = normal, 1 = mild changes, 2 and 3 = different severity of manifest disease. A score of 1 may be "normal," however, particularly for the elderly.

Psychiatric interviews and ratings (investigators: P.M. and G.S.)

The interview and first evaluation. All interviews were made during the summer 1976 by a psychiatrist who had no knowledge of the examined workers' previous diseases or symptoms. The workers were interviewed in random order. The interview lasted about 45 min. The medical history was first obtained; in it life events and illnesses promoting mental symptoms were emphasized. The contents (items) of the interview are shown in part A of the appendix. The second part of the interview concerned the prevalence of certain psychiatric symptoms. A record of 37 different symptoms (items) was obtained with a modified version of the Comprehensive Psychopathological Rating Scale (CPRS) (1). Each item was rated on a 7-grade scale of increasing severity; the rating depended on the intensity, frequency and duration of the symptoms in question. The items are shown in part B and the rating scale in part C of the appendix.

Taping procedures and second evaluation. The interviews were recorded on tape. The psychic symptoms were reevaluated by the interviewer on the basis of the tape recording, and then separately by another psychiatrist with no previous contact with the examined workers. The scores of each item (individual score) were added and the sum formed the measure of the prevalent symptoms in each subject. The mean of the two independent secondary evaluations was regarded as the measurement result.

Assessment of interrater reliability in the evaluation produced the following results: (a) The product-moment correlation between the scores of mental symptoms rated during the interview and those after evaluation of the tapes by the interviewer was $r = 0.79$. (b) The product-moment correlation between the interviewer's evaluation of the tapes and a similar rating by the other psychiatrist was $r = 0.87$ (assessed for 16 of the 60 tape recordings). (c) When observer bias was estimated, information on work conditions in the last 42 tapes was withheld from the second psychiatrist. In this situation

the correlation between the ratings made by the interviewer and the second psychiatrist was $r = 0.73$. The examinee's work conditions were misjudged by the second psychiatrist in half of the cases. After evaluation of the tapes the overall credibility of the reports given during the interview was found to be fairly good and not related to the individual's score.

The first part of the interview was summarized in a medical record, on the basis of which five items (part A of appendix) were rated (part C of appendix) independently by both psychiatrists. The resulting score was considered to be an index of the individual's liability for mental symptoms. For the comparison between the exposed and control groups, factors concerning previous mental health (item 3) were omitted. The differences in the index between matched pairs were calculated. In order to reduce random error, we considered only differences larger than one (2). With this evaluation procedure, the accordance between raters was good. (In 25 of 30 cases there were similar conclusions.)

Statistical procedure. The difference between the scores of the matched pairs was tested by the sign test. In addition, the difference in mental symptoms between the groups was tested by means of ranking the individuals (Mann—Whitney). The quantitative difference in psychic symptoms between matched individuals was tested by Student's *t*. Similar tests for the difference between the groups were also used for various categories of items.

Psychological tests (investigators: F. G. and B.A.O.)

Six performance tests were carried out individually by each subject within 1 h. The subjects were studied in such an order as to obtain comparability between the exposed and nonexposed groups with regard to time of day and day of week for the examination. The tests were performed by each subject in the order in which they are presented.

RT Addition (RT = reaction time). The RT Addition task was carried out with the aid of an electronic instrument and a

display-control panel. The test was conducted so that three single-digit numbers were presented simultaneously to the subject for 1 s. The subject was to add the three numbers and indicate the result on a keyboard. Forty-six trials were performed. The mean reaction time and standard deviation were calculated for each subject based on the last 40 trials.

Simple RT. The Simple RT task was performed with a stimulus/response panel placed horizontally to the subjects. The subjects were instructed to respond to a visual signal (stimulus) by pressing a switch with their fingertips as quickly as possible. The interval between stimuli averaged 3.75 s with a maximum variation of ± 1.25 s. Each session lasted about 10 min, during which a total of 160 stimuli were administered; thus there were 16 signals/min. The signals were administered electronically, and an electronic timer was used to record the reaction time. The mean reaction time and standard deviation were calculated for each subject based on the last 9 min of the task. Furthermore the mean reaction time was calculated for each time block (1-min period) to be used in an analysis of change in performance over time.

Memory test (recognition). For the testing of memory recognition, the same apparatus was used as for RT Addition. A series of 20 meaningless but pronounceable three-letter syllables, each lasting 2 s and at an interval of 1.5 s, was presented to the subject on the display panel twice. The same 20 syllables were thereafter presented to the subject once again randomly mixed with another 20 syllables which had not appeared before. The task of the subject consisted of indicating whether each of the 40 syllables had or had not been presented previously. The number of correct answers was recorded.

Manual dexterity (Santa Ana). The manual dexterity test consisted of a board (22×75 cm) with four rows, each row consisting of 12 square holes. Into each hole a knob could be fitted, the upper part of which was cylindrical. The task consisted of lifting the knobs one at a time from the hole, turning them 180° , and putting them

back in the hole. Five trials, each lasting 30 s, were carried out, two with each hand and one with both hands simultaneously. The number of knobs correctly replaced was recorded.

Perceptual speed (Bourdon—Wiersma). A modified version of the Bourdon—Wiersma Vigilance Test was used to test perceptual speed. The test material consisted of one full page with groups of 3, 4 or 5 dots arrayed in 30 lines, with 25 dot groups per line. The task of the subjects was to draw a line over each group of four dots, working from left to right, line by line. The subjects were instructed to work both rapidly and accurately. The task lasted 5 min. The mean time per line was calculated. Furthermore mean performance was calculated for each time block (1-min period) to be used in an analysis of change in performance over time.

Memory test (reproduction). When memory reproduction was tested, the same apparatus as for RT Addition and memory recognition was used. A series of letters and numbers was presented on the display panel during 4 s. The task of the subject was to reproduce the combination as accurately as possible. A total of 17 trials with combinations of increasing length were performed successively. The number of correctly reproduced combinations and the number of correctly reproduced elements were recorded.

The Simple RT, manual dexterity, and perceptual speed tests have all been used in previous studies (17, 18, 22, 36). The two memory tests and RT Addition were specially devised for the present study.

Neurophysiological examinations

(a) Electroencephalograms (investigators: A.W. and A.I.)

The electroencephalograms (EEGs) were recorded by means of an 8-channel Siemens—Elema EEG machine. The subjects were awake in a semireclined position with eyes closed during the recording. The electrodes were placed according to the 10/20 system. For computer analysis six derivations were stored on a 6-channel

analogue FM tape recorder (Precision Instrument): F7-T3, T3-C3, P3-O1 and F8-T4, T4-C4 and P4-O2.

The paper recordings were evaluated in the following way: (a) They were visually examined according to the clinical routine procedure. (b) From each EEG recording a typical 10-s section (8 channels) was selected. These sections were ranked without any knowledge of which subjects they belonged to. This ranking procedure was carried out so that the EEGs showing a distinct, stable alpha activity were given low ranks while higher ranks were

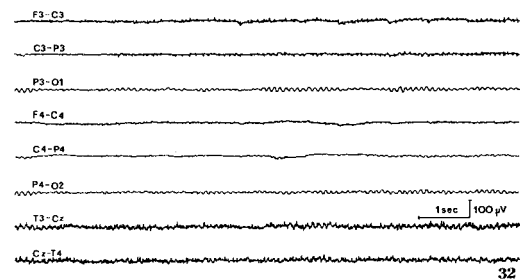
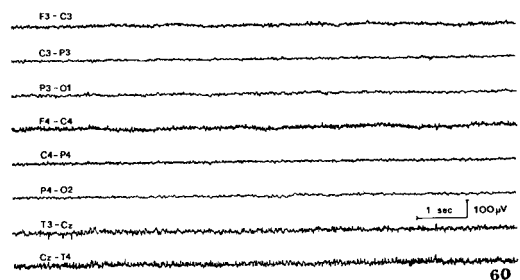
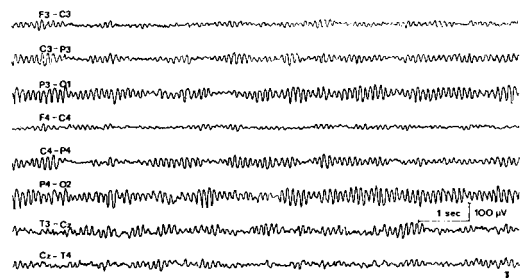


Fig. 2. EEG recordings from eight leads with ranks 1, 32, and 60 assigned after visual inspection.

assigned to EEGs with a decreasing amount of rhythmic activity. Fig. 2 shows three examples with different ranks (1, 32 and 60, respectively).

The recorded signals were computer processed by a method called Spectral Parameter Analysis (SPA) (48, 49). The SPA is a linear filter model adapted to the EEG signal, and it describes the spectral properties of the EEG by a limited number of components. As a rule, each component corresponds to a certain type of activity in the EEG. For this reason the components are labeled delta, alpha and beta, as in usual clinical EEG nomenclature. Each component is characterized by three parameters: (a) the peak frequency (f , Hz), (b) the bandwidth (σ , Hz), and (c) the power (G , percentage of total power). By definition the peak frequency of the delta component is zero; therefore this component is described by two parameters only. The total power spectrum of the EEG is thus characterized by eight parameters ($2 + 3 + 3$), as can be seen in fig 3. To these another parameter is added which expresses the ratio between the mean square deviation of the model to signal adaptation and the variability of the spectral properties of the signal (a model fit parameter). For good adaptation this parameter should be smaller than 1.00, and it decreases with increasing degree of adaptation. The main features of the SPA procedure have been described by Isaksson (26).

For the purpose of the present study, artifact-free EEG signals for computer analysis were provided by the visual selection of EEG sections of 10-s duration and free of artifacts such as muscle activity, arterial pulsations, eye and electrode movements. After the SPA analysis of these sections the parameters in question were inspected. Some of the results were finally canceled due to the following criteria: (a) poor model adaptation, i.e., a model-fit larger than 1.25, (b) strongly deviating parameters, i.e., negative power parameters, double peaks, etc.

After these selection procedures 8—14 sets of parameters remained for each subject from the leads P3-01 and P4-02 for 22 out of the 30 couples. This material was then subject to the following statistical procedures.

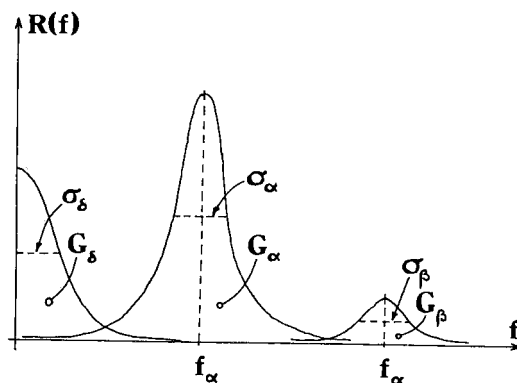


Fig. 3. Spectral power $R(f)$ as a function of frequency (f).

1. For each parameter the mean and standard deviation were calculated for each subject. Then the sets of parameter means were used to characterize the subjects. Based on each parameter separately, the hypothesis "equal means for exposed and control subjects" was tested with the analysis of variance, and the differences in standard deviations were tested with Fisher's F test.

2. The parameter means of all the subjects were ranked for each parameter separately. In addition a total ranking was performed in which each subject was ranked according to the sum of all his parameter ranks. The differences in rank between the exposed subjects and the controls were tested by means of the Mann—Whitney rank test.

3. The original sets of parameters were used to characterize the subjects. For each matched couple, it was determined whether the exposed subject was significantly different from the control. This procedure was carried out for each parameter separately by means of the analysis of variance. For statistical references the reader should consult Lindgren's *Statistical Theory* (35).

(b) *Peripheral nervous system examinations (investigator: H.E.P.)*

The functional state of peripheral nerves in the examined subjects was assessed by means of measuring conduction velocities and compound nerve action potential amplitudes in sensory nerves, conduction velocities in motor nerves, and sensation thresholds of vibration in the extremities.

Conduction velocities and nerve action potential amplitudes in peripheral nerves. Four peripheral nerves (n medianus, n ulnaris, n peroneus and n suralis) were investigated with electroneurographic (ENeG) methods (fig. 4) recommended in a Scandinavian meeting on health hazards in the use of solvents (3). The ENeG methods have earlier been used in studies on jet fuel exposed personnel (32, 33) and on other industrial workers (29, 30, 31, 40), but the present investigation was more extensive.

The sensory nerve conduction velocities (SCVs) and nerve action potential (NAP) amplitudes were measured in a distal (index finger-wrist; dse-S1 in fig. 4) and a proximal section (wrist-elbow; S1—S2 in fig. 4) of the left median nerve, and in a distal section of the left ulnar (dig V manus-wrist; dse-S1 in fig. 4) and sural nerves (mid lower leg — ankle region;

S2—S1 in fig. 4). Orthodromic measurements were made of all SVCs and NAPs with the exception of those of the sural nerve, in which antidromic methods were used. The measurements of the maximal conduction velocities (MCVs) in the motor nerves were made in the left median (elbow-wrist; S2—S1 in fig. 4), ulnar (elbow-wrist; S2—S1 in fig. 4) and peroneal nerves (knee-ankle; S2—S1 in fig. 4). The conduction velocity of the slow motor fibers (CVSF) was determined in the left ulnar nerve (elbow-wrist; S2—S1 in fig. 4). An anatomical illustration is presented in fig. 4.

The measurements of the MCV, SCV and NAP were made according to routine clinical methods (10, 20, 37, 42). The technique of measuring the CVSF in the ulnar nerve has previously been described by Seppäläinen and Hernberg (43). All the recordings were made with surface electrodes. Two MCV and CVSF values and four SCV and NAP values were recorded from each nerve segment of the examined persons.

Sensation thresholds of vibration in the extremities. The vibration thresholds were determined at three different locations of the extremities, i.e., the bony parts of the dorsum of the foot (represented in the tables by tarsal), lower leg (tibial) and wrist (carpal).

The measurement of vibration thresholds has earlier been used in investigations on industrial workers (29, 30, 31, 32, 33, 40). An electromagnetic biothesiometer with a plastic stimulator shaft, 6 mm in diameter, provided a 100-Hz sine wave stimulus with a variable amplitude (0—25 μ m). The stimulus amplitude was displayed digitally in micrometers peak to peak with the aid of an accelerometer mounted on the shaft of the stimulator. The stimulator was applied in a vertical position and perpendicular to the skin surface with the pressure of its own weight (440 g) on the skin surface over the underlying bone where the subcutaneous tissue was thinnest. This application minimized variation in repeated tests.

Differences in the parameters of ENeG and vibration thresholds between matched subjects were tested by parametric methods.

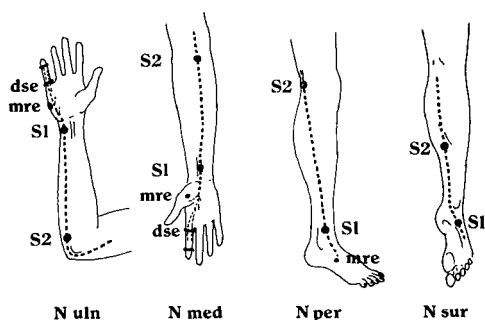


Fig. 4. Schematic illustration showing the positions of the stimulating and recording electrodes on the four investigated peripheral nerves. (N uln: nervus ulnaris; N med: nervus medianus; N. per: nervus peroneus; N sur: nervus suralis; S: position of stimulating and/or recording electrodes; dse: position of distal stimulating electrodes; mre: position of muscle response recording electrodes)

Table 2. Acute symptoms.

Symptom	Fuel system testers (n=15)	Motor engine testers and mechanics (n=15)	All subjects in the exposed group (n=30)
Dizziness	9	6	15
Fatigue	5	8	13
Headache	4	3	7
Nausea	1	3	4
Palpitations, thoracic oppression	3	1	4
Respiratory tract symptoms	2	1	3

General comment

In most of the investigations (i.e., when possible) the investigators did not know whether the person being examined belonged to the exposed or nonexposed group. The different investigations were performed and evaluated separately and independently of each other.

RESULTS

Medical history, standardized interview and neurological examination

(a) *Acute symptoms*

Twenty-one of the 30 exposed subjects stated that they had experienced recurrent acute symptoms upon exposure (table 2). The symptoms consisted of dizziness, headache, nausea, respiratory tract symptoms ("pain upon inhalation," "feeling of suffocation," "slight cough"), palpitations, and a feeling of thoracic oppression. Thirteen subjects also reported fatigue during work with jet fuel and afterwards, especially in the evenings. Altogether only four subjects in the exposed group did not report acute symptoms on exposure. As can be seen in table 2, no remarkable differences were found between the component testers on one hand and the motor engine testers and the mechanics on the other.

(b) *Nonacute symptoms*

Incidence of neuropsychiatric symptoms during employment at the factory. Nearly all of the examined subjects had been employed at the plant almost all their adult life. The incidence of neuropsychiatric ill health during this time was determined. The determination was based on the medical history and the standardized interview, but also on notes in the plant physician's medical records. Only events before September 1974 were considered in the incidence studies since at that time jet fuel was recognized as a potential health hazard in Sweden.

The results are shown in tables 3 and 4, in which comparisons are made between the exposed group and the control groups, and the differences are expressed as significance levels (p). Comparisons are made between the exposed group (n = 30) and the original control group, as well as with the final control group (n = 2 × 30). It appears from the tables that the two control groups are very similar in regard to incidence of symptoms. The incidence of symptoms in the exposed group differed significantly, however, from those of the control groups, as evaluated from the medical history and standardized interview, as well as from the plant physician's medical records.

Significant differences (based on group-wise as well as pairwise comparisons) were found when symptoms of neurasthenia, anxiety and/or mental depression were recorded whenever information was available on their existence and whenever

Table 3. Symptoms of neurasthenia, anxiety and/or mental depression in the exposed group and the control groups as recorded from medical history and standardized interview (upper row of figures) and medical records of factory health department (lower row).

Symptom	Exposed group (n=30)	Final control group (n=30)	Statistical difference (p)	Original control group (n=30)	Statistical difference (p)	Original and final control groups (n=60)	Statistical difference (p)
Neurasthenia, anxiety and/or mental depression	24 23	10 10	0.0008 0.0018	11 12	0.0017 0.0089	21 22	0.0001 0.0008
Diagnosed and treated by physician	19 23	7 10	0.004 0.0018	8 12	0.0095 0.0089	15 22	0.0009 0.0008
On several occasions	14 19	4 6	0.011 0.0017	4 4	0.011 0.0002	8 10	0.0014 0.0001
Anxiety and/or mental depression on one occasion	3 4	3 4		7 7			

Table 4. Symptoms of neurasthenia in the exposed and control groups as recorded in the standardized interview.

Symptom	Exposed group (n=30)	Final control group (n=30)	Statistical difference (p)	Original control group (n=30)	Statistical difference (p)	Original and final control groups (n=60)	Statistical difference (p)
Fatigue	13	1	0.0003	1	0.0006	2	< 0.0001
Depressed mood, lack of initiative, etc.	10	1	0.0076	1	0.0076	2	0.0003
Dizziness	10	2	0.024	1	0.0076	3	0.0010
Palpitations, thoracic oppression	9	1	0.015	2	0.046	3	0.0031
Sleep disturbances	9	2	0.046	1	0.015	3	0.0031
Headache	5	1	0.20	0	0.061	1	0.025
Memory impairment	5	0	0.061	3		3	0.15
Irritability	4	1	0.35	2		3	0.33
Respiratory tract symptoms (feelings of suffocation, etc.)	3	0	0.24	2		2	0.42
Sweating	3	2		0		2	0.42

Table 5. Symptoms of gastritis in the exposed and control groups as recorded in the standardized interview (upper row) and plant physician journals (lower row).

Exposed group (n=30)	Final control group (n=30)	Statistical difference (p)	Original control group (n=30)	Statistical difference (p)	Original and final control groups (n=60)	Statistical difference (p)
15	10		10		20	
22	15		16		31	0.08

Table 6. Eye irritation in the exposed and control groups as recorded in the standardized interview.

Exposed group	Final control group	Statistical difference	Original control group	Statistical difference	Original and final control groups	Statistical difference
(n=30)	(n=30)	(p)	(n=30)	(p)	(n=60)	(p)
9	1	0.015	3		4	0.0081

the subjects had consulted a physician and been treated for the symptoms. Significant differences were also found when the number of subjects who had experienced ill health on several occasions were compared. No difference was found for the incidence of one single attack of anxiety and/or mental depression.

Table 4 shows the incidence of symptoms in the exposed and control groups as recorded from the standardized interview. Among the neurasthenic symptoms (including the neurovegetative ones) the most obvious differences between the exposed and nonexposed groups were found for fatigue, depressed mood, lack of initiative, and dizziness. Other symptoms which differed markedly between the groups were palpitations, thoracic oppression, sleep disturbances, and headache.

Incidence of gastritis and eye irritation in the exposed and control groups during employment at the factory. In the standardized interview, questions were included on symptoms of gastritis and eye irritation since gastritis is a psychosomatic disease and eye irritation has been described as one of the first symptoms to appear on exposure to relatively low concentrations of gasoline in experimental studies (14). The results are shown in tables 5 and 6, respectively. Gastritis symptoms were more frequent in the exposed group than in the nonexposed groups, especially when the notations in the plant physician's journals were evaluated and the two control groups were combined to form the reference group ($p < 0.1$). As for eye irritation, significantly more subjects in the exposed group complained of symptoms when compared

with subjects of the genuine control group ($p < 0.05$) and the two control groups together ($p < 0.01$). The eye irritation, as described by the examined subjects, could be defined as symptoms of chronic conjunctivitis and, thus, were not necessarily associated only with exposure to jet fuel.

Occurrence of symptoms and signs possibly indicative of polyneuropathy. The occurrence of symptoms possibly indicating polyneuropathy ("restless legs," muscle cramps, diffuse pain in the extremities, distal paresthesia and numbness, and paresis), was determined from data collected with the polyneuropathy questionnaire described elsewhere (32). A symptom was scored as "positive" when the subject experienced it more often than once a month. It should be emphasized that "positive symptoms," according to these criteria, do not necessarily indicate manifest disease in terms of a clinical evaluation (32). Subjects who experienced at least one of the symptoms were classified as "positive." As shown in table 7, subjects with such symptoms were more frequent in the exposed group than in the control groups ($p < 0.1$).

In the standardized neurological examination signs scored 0 and 1 were found. As shown in table 7, no significant differences were found between the exposed and nonexposed groups.

(c) Possible confounding and effect modifying factors

As to possible confounding and effect modifying factors (use of tobacco and drugs, incidence of anesthesia in connec-

Table 7. Symptoms (upper row) and signs (lower row) possibly indicative of polyneuropathy in the exposed and control groups, as recorded in the standardized questionnaire and standardized neurological examination.

Exposed group	Final control group	Statistical difference	Original control group	Statistical difference	Original and final control groups	Statistical difference
(n=30)	(n=30)	(p)	(n=30)	(p)	(n=60)	(p)
12	5	0.086	7		12	0.077
18	15		12		27	

tion with surgery, meningo-encephalitis, concussion with or without unconsciousness, sciatica, anemia, hypertension, hyperlipemia and serious systemic diseases), the observed frequency was of the same order of magnitude in the exposed and non-exposed groups. For the use of alcohol, however, a quantitative estimation revealed a higher monthly average consumption in the nonexposed than in the exposed group: 188 and 120 gm, respectively ($p = 0.12$).

Psychiatric interviews and ratings

Prevalence of mental symptoms. The evaluation of the psychiatric interview yielded a score estimating the amount of symptoms in the individual. The individual scores and the difference in the scores of the matched subjects are given in table 8. The score for the exposed workers was larger than that of the controls in 20 of 30 pairs. In two pairs the scores were equal. In eight pairs the control's score was larger than that of the exposed worker. The average score of the exposed group ($\bar{S}_E = 8.6$) exceeded that of the control group ($S_C = 5.6$). The average difference was $d = 3.0$.

The results show that exposed individuals have more psychiatric symptoms than the controls (sign test, $p < 0.01$, Mann-Whitney $p < 0.01$, Student's t $p < 0.001$).

The presented scores show the sum of all rated items (1—37). The total score for each item in the exposed and control groups is illustrated in fig. 5. It can be seen that some of the items do not contribute to the difference mentioned. The relative importance of the rated items was tested after the items were grouped into

five categories (fig. 5). Neurasthenic symptoms (items 3—5, 13—16, 18, 19, 22 and 23) showed the largest differentiation between the groups, followed by neurotic disturbances (items 8, 10, 11 and 12). Dysmnnesia,

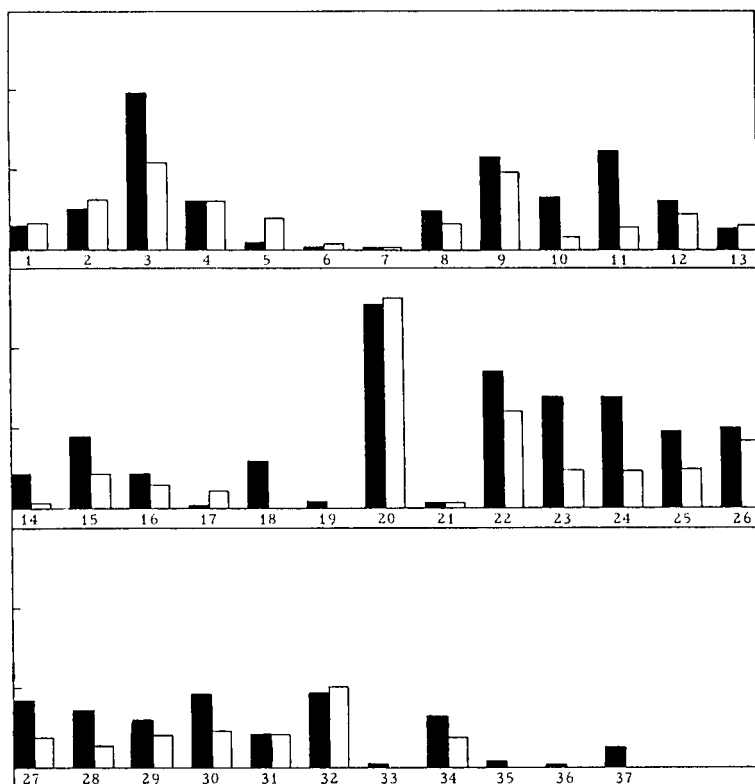
Table 8. Individual scores of mental symptoms for exposed workers (S_E) and controls (S_C). Difference in score indicated by d .

Pair no.	S_E	S_C	d
1	4.00	3.00	1.00
2	15.25	7.25	8.00
3	6.25	2.50	3.75
4	5.25	5.00	0.25
5	3.25	5.75	— 2.50
6	4.50	5.50	— 1.00
7	3.75	4.00	— 0.25
8	9.00	6.50	2.50
9	8.50	13.50	— 5.00
10	9.25	10.50	— 1.25
11	4.50	3.50	1.00
12	4.75	0	4.75
13	11.00	7.50	3.50
14	10.25	3.00	7.25
15	5.00	6.25	— 1.25
16	15.50	12.50	3.00
17	15.50	11.50	4.00
18	4.00	3.50	0.50
19	8.25	4.00	4.25
20	15.00	3.75	11.25
21	3.25	3.25	0
22	12.50	5.00	7.50
23	3.75	1.75	2.00
24	21.25	1.00	20.25
25	1.25	4.50	— 3.25
26	6.00	6.50	— 0.50
27	6.75	3.75	3.00
28	9.75	9.75	0
29	18.75	8.25	10.50
30	10.50	6.00	4.50
$\bar{S}_E = 8.6$	$\bar{S}_C = 5.6$	$d = 3.0$	

somatic symptoms, and items depending on personality traits, did not differentiate between the examined groups.

Medical history. The evaluation of the medical history yielded an index of liability for the psychiatric symptoms of each subject. No difference in the liability index of the examinees was found in 17

pairs. The exposed workers showed a lower index than the controls in nine pairs, whereas the reverse result was obtained for four pairs. Thus, no preponderance of individuals with a high liability for psychiatric symptoms (i.e., indices) was found in the exposed group. No relation between the individual's score and index was found.



Category no. and items	P	NP
1. Temperament, 1, 2, 6, 7, 35, 36	—	—
2. Somatic, 26, 28—34, 37, 17, 20, 21	—	—
3. Dysmnnesia, 24, 25, 27	—	*
4. Neurotic, 8, 10, 11, 12	*	—
5. Neurasthenic, 3—5, 13—16, 18, 19, 22, 23	*	*

* $p < 0.05$

Fig. 5. Histogram of relative prevalence of different mental symptoms in the exposed (dark) and control groups (white). The items are numbered according to the listing in the appendix. Below the histogram are the results of the test of difference between the examined groups after the items (1—37) were classified into five categories. Item numbers are listed for each category. Results of the nonparametric (NP) and parametric tests (P) are indicated.

Psychological tests

The statistical analysis of the results of the performance tests was carried out as follows.

The sampling distribution of each performance variable was inspected with regard to normality. The significance of the differences between the exposed and nonexposed groups was tested with regard to the homogeneity of variances and to the mean value of each performance variable. The statistical tests were performed

both under the assumption that the groups were independent samples and under the assumption that the groups were correlated samples (matched pair). Furthermore, a nonparametric test (Mann-Whitney *U* test) was applied to the data as a complement to the parametric tests. Two of the performance tests, Simple RT and Bourdon—Wiersma, could be analyzed for performance changes during the test period. For these two tests a two-way analysis of variance with repeated measurements was employed in which the

Table 9. Mean values (M) and standard deviations (SD) of the performance on different tests for the exposed and nonexposed groups.

Test	Exposed group		Nonexposed group	
	M	SD	M	SD
Simple RT (ms)				
Speed (M)	275	44	270	31
Regularity (SD)	19	9	19	13
RT Addition (s)				
Speed (M)	3.0	1.0	2.8	1.0
Regularity (SD)	1.2	0.4	1.0	0.4
Memory test: recognition				
Number correct	29.5	2.9	28.7	4.0
Memory test: reproduction				
Criterion 1 ^a	8.0	3.3	8.2	3.7
Criterion 2 ^b	53.8	10.2	54.6	10.3
Manual dexterity: Santa Ana				
Right	49.1	7.9	48.0	6.8
Left	47.0	7.4	45.2	6.1
Coordination	31.6	8.4	31.3	7.5
Perceptual speed: Bourdon-Wiersma (s)				
Mean time per line	14.0	2.5	12.8	2.1

^a Criterion 1: Number of correctly reproduced combinations.

^b Criterion 2: Number of correctly reproduced elements.

Table 10. Analysis of variance of mean reaction time in the Simple RT test and mean time per line in the Bourdon-Wiersma test.

Source	Simple RT			Bourdon-Wiersma		
	df	Mean square	F	df	Mean square	F
G (groups)	1	3,256.07	0.26	1	312.53	4.16*
I (individuals)	58	12,544.56		58	75.22	
T (1-min time blocks)	8	5,179.46	13.10***	4	70.18	22.21***
G x T	8	461.86	1.17	4	3.94	1.25
Residual I	464	395.48		232	3.16	
T linear trend	1	39,441.96	55.79***	1	200.91	33.57***
G x T linear trend	1	2,704.00	3.82	1	7.22	1.21
Residual II	58	707.02		58	5.98	

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

trend of the performance changes over time was introduced as a further source of variation.

Table 9 presents the mean values and standard deviations of the performance variables for the exposed and nonexposed groups. The analysis of variance for the two memory tests and for the manual dexterity test yielded F ratios that were very close to unity, and thus no differences in the performance of the groups were revealed on these tests. In the RT Addition test the exposed group had a longer reaction time and a greater intraindividual variation on the average than the nonexposed group. However, only the latter performance variable, i.e., the regularity of the individual performance on the test, resulted in a statistically significant difference in the analysis of variance [$F(1,59) = 4.12$; $p < 0.05$] and in the Mann-Whitney U test ($z = 2.22$; $p < 0.05$). The analysis of the results of the Simple RT test and the Bourdon-Wiersma test are given in table 10. There was no significant difference between the groups with regard to mean reaction time in the Simple RT test. As expected from the use of this test in previous research (17, 18), there was a significant linear trend over the time blocks [$F(1,58) = 55.79$; $p < 0.001$], i.e., the subjects' reaction time increased linearly during the test period. The analysis also showed that the linear change of the reaction time over the time blocks interacted with the groups [$F(1,58) = 3.82$; $0.05 < p < 0.10$]. In other words, time on task appears to affect the exposed subjects more than the nonexposed (see fig 6).

The Bourdon-Wiersma test also showed a performance decrement over time, but no differences in this respect were found between the groups. However, the analysis showed a significant difference in the mean performance between the groups [$F(1,58) = 4.16$; $p < 0.05$], the performance of the exposed subjects being poorer. The same result was also obtained with the Mann-Whitney U test ($z = 2.17$; $p < 0.05$).

To summarize, in the psychological investigation differences between the groups were found in three of the tests which made high demands on attention and sensorimotor speed. The investigation did

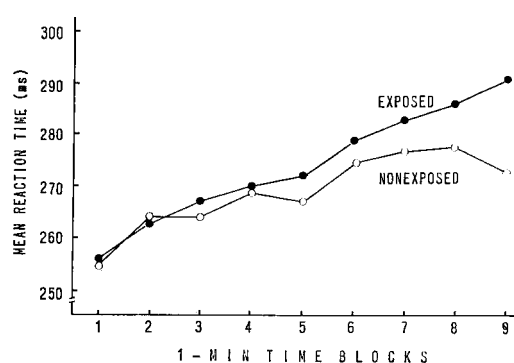


Fig. 6. Change in mean reaction time over time (1-min time blocks) for the exposed and nonexposed groups.

not reveal any difference between the groups in the tests concerning memory and manual dexterity function.

Neurophysiological examinations

(a) Electroencephalograms

The evaluation of the EEG recordings yielded the following results: At visual inspection all the EEGs were classified as normal except five in the exposed group and four in the control group. All abnormal findings in the exposed group were slight or moderate, episodic deviations within the frontotemporal areas with a left hemisphere dominance. The same type of abnormality was found also in the control group, except for one person who had a moderate abnormality within the right temporal region.

It is well-known, however, that the concept "normal EEG" of the clinical routine covers many types of EEG. It was the case also in this material. Despite the fact that the EEG recordings were judged as normal, sometimes their characters seemed to be widely different, as illustrated in fig. 2. Fig. 7 shows the visual ranking and the cumulative rank distribution. As can be seen, the control subjects tend to cluster to the left while the exposed ones gather at the right end. There is a significant difference between the two groups (Mann-Whitney, $z = 2.03$, $p < 0.05$).

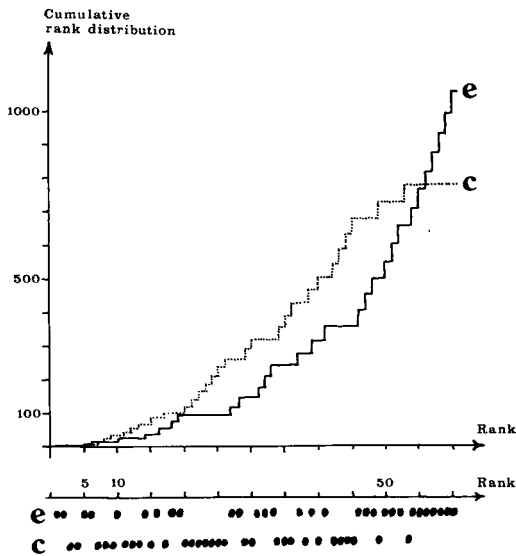


Fig. 7. Visual ranking and cumulative rank distribution of all EEGs. (e: exposed subjects; c: controls; N = 60 subjects)

Table 11 shows the means and standard deviations of the SPA parameters in the exposed and control groups for the leads P3—01 and P4—02. It can be seen that in comparison with the controls the exposed subjects showed a larger value for (a) the delta bandwidth (σ_δ) in P4—02, (b) the delta power (G_δ) bilaterally, (c) the alpha peak frequency (f_α) bilaterally, (d) the alpha bandwidth (σ_α) bilaterally, and (e)

the model-fit parameter in P4—02 and a smaller value of the alpha power (C_α) bilaterally. The differences were not significant. The exposed group, however, showed a larger interindividual variation (standard deviation) than the controls (F test, $p < 0.05$).

The ranking based on the different SPA parameters separately showed differences between the exposed and control subjects only for the alpha peak frequency (f_α), which was higher for the exposed subjects (Mann—Whitney, P3—01: $p < 0.05$ and P4—02: $p < 0.08$). The total ranking of all the subjects based on the sums of all parameter ranks of each subject showed no differences between the two groups. It is, however, interesting to note that out of the 16 subjects excluded from the SPA analysis, 10 were assigned visual ranks over 40 (maximum rank was 60). The result of the visual inspection was, however, not dependent on the 16 subjects excluded from the SPA processing. Both for 60 and 44 subjects differences were obtained between exposed and control subjects (Mann—Whitney, $p < 0.05$).

When the results of the SPA analysis were compared between the matched subjects and not between the examined groups as before, significant differences were obtained (analysis of variance, $p < 0.05$). Each parameter was tested within each matched couple. Fig. 8 shows the results of this study.

Table 11. Means and standard deviations of the SPA parameters of the exposed and control groups for the leads P3-01 and P4-02.

Lead	Subjects	Spectral parameters								Model fit
		σ_δ Hz	G_δ %	f_α Hz	σ_α Hz	G_α %	f_β Hz	σ_β Hz	G_β %	
P3-01	Controls									
	Mean	1.80	18	9.29	0.56	69	16.9	2.93	13	0.56
	SD	0.90	8	0.71	0.33	14	1.9	1.24	11	0.20
	Exposed									
P4-02	Mean	1.99	24	9.62	0.84	59	16.7	3.05	17	0.59
	SD	1.30	15	1.39	0.89	22	2.4	1.66	15	0.25
	Controls									
	Mean	1.74	21	9.39	0.55	65	16.3	3.54	14	0.51
	SD	1.33	11	0.73	0.29	15	2.3	1.66	10	0.20
	Exposed									
	Mean	2.05	28	9.72	0.88	56	16.3	3.84	16	0.61
	SD	1.40	18	1.40	0.91	22	2.5	1.98	15	0.22

(b) *Peripheral nervous system examinations*

Conduction velocities and compound nerve action potential amplitudes in peripheral nerves. Table 12 presents the ENeG findings for the exposed and nonexposed groups expressed as the mean differences between the matched subjects. The results showed that the NAP of the sural nerve was lower in the exposed than in the nonexposed group ($p < 0.03$). The SCV of the

distal part (dse—S1 in fig. 4) of the ulnar nerve was slower in the nonexposed group when compared with that of the exposed group ($p < 0.04$) and, in addition, the MCV of the median nerve was slower in the nonexposed group ($p < 0.06$). The other parameters did not differentiate between the examined groups. (Only p values ≤ 0.10 in the table).

Sensation thresholds of vibration in the extremities. Table 13 presents the sensation thresholds of vibration for the exposed and nonexposed groups expressed as the mean differences between the matched subjects. The vibration thresholds were, on the average, constantly lower in the nonexposed group, although not statistically significantly lower.

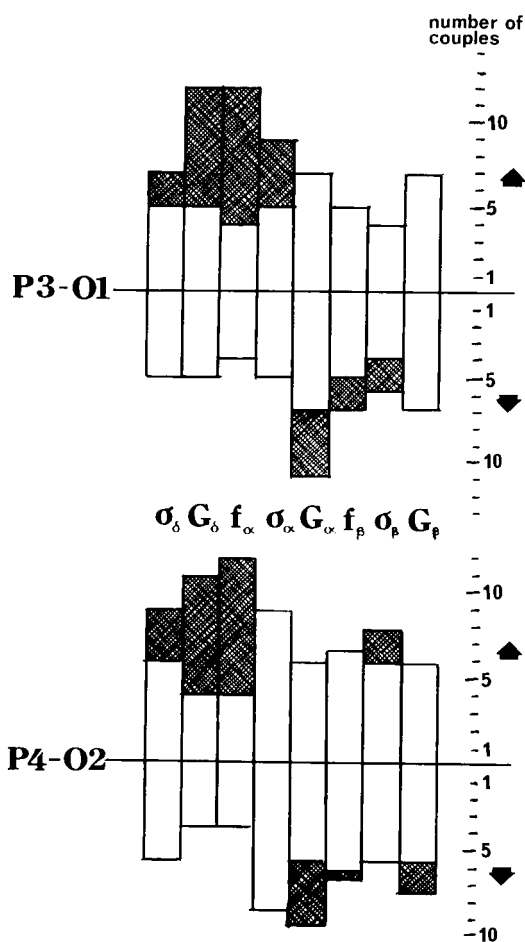


Fig. 8. Diagram showing the number of couples significantly differing in the SPA parameters. Upward column: Number of couples in which the exposed subject showed a significantly larger value than the control. Downward column: Number of couples in which the exposed subject showed a significantly smaller value than the control. For each parameter the difference in column sizes is indicated by a shadowed area.

DISCUSSION

Exposure

Exposure is a complex concept and includes parameters such as exposure intensity in terms of air concentrations of contaminant, duration of exposure, frequency of exposure at peak intensities, time lapse from first exposure to point of observation (latency period). Also, it may be subject to changes over long periods of time. Obviously, for an analysis of exposure in an epidemiologic context all such parameters would have to be considered. In view of the limited size of the studied groups, it has not been considered meaningful to divide the exposed group into subgroups according to these various parameters. The data at hand do not provide sufficient material for such an analysis.

It was, however, found that the exposure conditions in the work procedures studied were reasonably stable. It was observed that the variations of concentration around a mean value were not impressive and were slow and continuous. Therefore it was considered appropriate to describe the exposure to the factor under study as a calculated time-weighted average air concentration during work with relevant exposure. This entity is obviously an approximation. It is based on a limited number of measurements. The results are general-

Table 12. The ENeG findings for the exposed and nonexposed groups as expressed in the mean differences ($\bar{D}$) between the matched pairs. A positive mean difference indicates a smaller value for the exposed group.

ENeG parameters ^a	Number of matched pairs	D	SD	Statistical differences (p)	
<i>N suralis</i>					
NAP (S2—S1)	29	2.24	5.4	0.03	
SCV (S2—S1)	26	— 1.23	6.0		
<i>N peroneus</i>					
MCV (S2—S1)	30	1.07	6.7		
<i>N medianus</i>					
NAP (dse—S1)	29	0.48	5.5	0.06	
SCV (dse—S1)	27	— 2.19	7.0		
NAP (S1—S2)	29	4.28	18.9		
SCV (S1—S2)	29	— 0.83	4.8		
MCV (S2—S1)	30	— 2.07	5.8		
<i>N ulnaris</i>					
NAP (dse—S1)	30	0.50	5.1		0.04
SCV (dse—S1)	29	— 3.45	8.5		
CVSF (S2—S1)	30	1.40	5.9		
MCV (S2—S1)	30	— 0.43	6.3		

^a See fig. 4 for an explanation of the points in parentheses.

Table 13. The sensation thresholds of vibration for the exposed and non-exposed groups expressed as the mean differences ($\bar{D}$) between the matched subjects. A positive mean difference indicates a higher vibration threshold value for the exposed group.

Vibration thresholds	Number of matched subjects	$\bar{D}$	SD	Statistical differences (p)
Carpal	30	0.19	0.74	
Tibial	30	0.22	4.91	
Tarsal	30	0.51	8.22	

ized to describe a typical exposure for categories of personnel. Thus, the results are not truly individually based in the sense that every member of the exposed group has not had his personal work situation subjected to measurements.

Medical history, standardized interviews and neurological examination

All but four subjects in the exposed group reported recurrent acute symptoms upon exposure to jet fuel vapors during work (dizziness, fatigue, headache, nausea, respiratory tract symptoms, palpitations and

thoracic oppression). The incidence of neurasthenia, anxiety and/or mental depression during employment at the factory was significantly higher in the exposed than in the nonexposed groups as recorded in (a) the medical history and a standardized interview and (b) notations in the medical records of the factory health department when the employees had consulted, and been treated by, the plant physician for such symptoms. Among the neurasthenic symptoms fatigue, depressed mood, lack of initiative, and dizziness dominated, but significant differences were also found for palpitations and thoracic oppression, sleep disturbances,

and headache. Also symptoms of gastritis and eye irritation were more frequent in the exposed than in the nonexposed groups ($p < 0.1$ and $p < 0.01$, respectively). As to the occurrence of symptoms and signs possibly indicative of polyneuropathy, trends towards higher prevalences were found in the exposed group.

In this part of the investigation it is worth emphasizing that the standardized interview and the information collected from the medical records of the factory health department yielded more or less identical results as to incidence of neuropsychiatric ill health among the examined. The fact that differences existed also when the medical records were scrutinized seems to rule out any bias of the observer as well as of the examined subjects. The increased incidence of symptoms in the exposed group is furthermore strengthened by comparisons with the original control group. It appears from the results that the original and final control group are very similar as regards incidence of symptoms.

Psychiatric interviews and ratings

After evaluation of the tapes all interviews were considered to be adequate for further analysis. No relation between reliability and amount of mental symptoms was noted. This finding suggests that overstatements by the interviewer or examinee did not significantly contribute to the results. In addition, there was good agreement between the first and second evaluation of the psychic symptoms by the interviewer, and also between independent raters with and without knowledge of the occupation of the examinee. Thus the evaluation does not seem to have been influenced by observer bias. No general inclination for complaining was found for the exposed group, since the difference between the examined groups was mainly due to neurasthenic symptoms.

The rating scale used to estimate the degree of the psychic symptoms was similar to that of another scale [CPRS (1)]. The CPRS was constructed to measure symptoms before and after pharmacological treatment of depressed and schizophrenic patients, and its reliability for this purpose was found to be high. In

the present study, items of the CPRS concerning psychotic symptoms were replaced by other items concerning neurasthenia. The previously mentioned assessment is probably valid for the modification used since its structure was similar to that of the CPRS, which has also been used for volunteers without psychiatric disease (1).

It may be argued that the difference in psychic symptoms between the exposed and control groups is due to social or mental factors. However, no preponderance of large indices was found for the exposed group. Good agreement between independent index raters was observed. The validity of the index as a measure of probability for mental ill health has not been assessed. However, patients with a large amount of some previous somatic diseases and other items used are known to run a higher risk for the development of psychiatric symptoms. The result indicates that previous illness or constitutional factors did not contribute to the difference in amount of mental symptoms found between the groups.

The results thus show a higher prevalence of neurasthenic symptoms in workers exposed to jet fuel.

Psychological tests

The results of the examination using behavioral performance tests indicated a difference in performance capability between the groups. The exposed subjects had a greater irregularity of performance on a test of complex reaction time, a greater performance decrement over time in a simple reaction time task and poorer performance in a task of perceptual speed than the nonexposed subjects. No differences between the groups were found in two tests of memory functions and in a manual dexterity test.

When the psychological test results are interpreted, two circumstances should be noted which reduced the power of the statistical analysis of the results, i.e., the theoretical probability of finding statistically significant differences between the exposed and nonexposed groups of subjects. The first is that the analyses were based on relatively small samples. The second is that the examined groups were somewhat more heterogeneous with re-

spect to education and, consequently, even with respect to mental performance capability than most of the groups examined in previous studies on the effects of long-term exposure to industrial solvents (17, 18, 22, 23, 36). This fact was confirmed by the comparison which could be made for two of the tests with the results of earlier studies. Thus, there was a greater interindividual variation of performance among the present workers than among previously studied groups. The fact that a statistically significant performance decrement among the exposed subjects only appears for some of the tests may to some extent be attributed to the circumstances and possibly to the differential sensitivity of different tests.

Neurophysiological examinations

Electroencephalograms. The appearance of abnormal EEGs in this material was 15 %, which is not remarkable in a clinically healthy population (11).

A ranking of the mainly normal EEGs of the control and exposed subjects yielded, however, a significant ($p < 0.05$) difference. The exposed group showed, on the average, a lower amplitude and a less observable rhythmic activity than the control group, which was more concentrated in the direction of the most "normal" end of the ranking scale.

Also the SPA yielded statistically significant differences between the two groups for some parameters. The results (significant or trends) were essentially in agreement with the visual ranking. It should be noted, however, that the SPA analysis concerned only the two single EEG leads which gave detailed information, while the visual inspection covered the whole EEG record.

The SPA changes essentially agree with what can be seen in an EEG of increasing degree of "abnormality" (27). It is, however, remarkable that the alpha peak frequency appears to be higher for the exposed subjects than for the controls. The physiological reason is unclear, but to some extent it is contradictory to an EEG change acutely induced. From studies of, for example, alcoholic intoxications, it is known that the frequency of the basic rhythm decreases due to the acute in-

fluence of alcohol (21). The chronic effect of organic solvents on the EEG is little known even if many authors report an increased amount of abnormal EEGs among subjects chronically exposed to organic solvents (42).

The SPA findings imply that the exposed group showed a lower degree of frequency stability of the EEG, as can be seen both from the model-fit parameter and the bandwidth (σ_α) of the alpha component, as well as from the comparison of the interindividual variability of the parameters. The alpha activity is regarded as a result of a thalamic control of the cortical activity (2). The harder the control, the larger the effect on the alpha activity, i.e., a higher value of the power G_α and a narrower banded (σ_α) alpha peak in the power spectrum. On the other hand, if the control vanishes completely, the whole signal acquires the character of low-pass filtered noise, i.e., only a delta component, $G = 100$ %. A small value of the bandwidth reflects a frequency-stable thalamic control. Therefore, the signal essentially has time-invariant spectral properties which yield a good model adaptation to the signal, i.e., a low value of the model-fit parameter. The SPA results might indicate that the effect of jet fuel is, among other things, an influence on the thalamic control of the cortical activity with an increased time variability, decreased frequency stability, and a less widespread control of the cortical neurons, i.e., an instability in the thalamocortical system.

Peripheral nervous system examinations. The results of the examination of the peripheral nerve functions with ENeG methods and vibration threshold determinations indicated differences between the groups in terms of (a) smaller NAPs of sensory nerves and an overrepresentation of higher vibration thresholds of the extremities in the exposed group and (b) slower SCVs and an overrepresentation of slower MCVs in the nonexposed group.

Clinical practice gives support to the view that measuring the NAPs of the peripheral part of sensory nerves is one of the most sensitive ENeG methods to detect early nerve function impairment of

light degree. The method of measuring vibration thresholds is also considered sensitive for the diagnosis of such functional disturbance. With these facts in mind, one should recall the findings of smaller NAPs of sensory nerves in the exposed group and, on the average, a higher vibration threshold of the extremities. These findings agree with the results of the quantitative neurological examination. The slow conduction velocities in the ulnar (SCV) and median (MCV) nerves of the controls is an intriguing finding. The difference observed is probably not due to nerve damage however. The SCVs in these nerves are considered a late indicator of polyneuropathy, when compared to the NAP amplitudes, which were larger among the controls. The paradox may be explained by an occasional sampling of individuals with excellent peripheral nerve function in the exposed group. If so, the difference in NAP amplitude between the examined groups is an underestimate of the true impairment of nerve function in the exposed subjects.

GENERAL DISCUSSION

The present and the first study (32) on jet fuel exposed industrial workers show many similarities, e.g., more than two-thirds of the exposed subjects in both investigations stated acute symptoms repeatedly to occur in association with exposure to jet fuel vapors and about three-fourths had an incidence of neuropsychiatric ill health during the years of exposure. Also as to type of symptoms, there are similarities, dizziness being prominent among the acute symptoms and depressed mood, lack of initiative, dizziness, palpitations, chest oppression, sleep disturbances, and headache being frequent in a non-acute "syndrome" of neuropsychiatric health disturbance.

In the psychiatric interviews made independently of the aforementioned investigations, the exposed subjects showed an increased prevalence of neurasthenic symptoms when compared with the controls. The results of the psychiatric interviews thus are consistent with the evaluations on mental health made by non-psychiatrists and also with earlier descrip-

tions of chronic fuel intoxications, and the results of the first jet fuel study. The results also agree with those of a study on Swedish Air Force personnel exposed to jet fuel during aircraft servicing. The fuel exposure in this group was considerably less than that of the exposed group in the present study. Many subjects were exposed outdoors when refueling jet planes or at work with the planes in hangars. Only a slight fraction of the examined service men were exposed in the same order of magnitude as the exposed workers of the present study. All the service men were examined by psychiatrists, and the results showed that symptoms indicative of minor brain damage were more frequent among 142 highly exposed persons than among 105 persons with a low exposure to jet fuel (Jansson, Siwers and Antoniew, personal communication). Since the 247 examined were selected on the basis of exposure as well as subjective symptoms (Strandberg, personal communication), the result is probably an underestimate of the difference between the groups.

Petroleum-distilled fuels chemically consist of different organic hydrocarbons. Also the industrial solvents and some of the components in plastics and paints are hydrocarbons. In recent epidemiologic studies on house painters (4, 5, 6, 8) and car painters (25) occupationally exposed to such solvents, the results strongly indicated an increased risk for neuropsychiatric illness to result from long-term solvent exposure. In a case referent study using a regional register of disability pensions, a relative risk of 1.8 was found for the contraction of neuropsychiatric disease among workers exposed to solvents, e.g., painters, varnishers and carpetlayers, when compared to building workers without such exposure (6). In one of the previously mentioned studies (5), case reports were given on ten heavily exposed painters, who were found to have symptoms such as deterioration of memory, personality changes of asthenic or depressive-aggressive types and abnormal fatigue. The results led the authors to suggest a chronic psycho-organic syndrome in these patients.

The symptoms recorded among the jet fuel exposed workers fit well into such a syndrome. This is not surprising since the solvents and the fuels are both com-

posed of organic hydrocarbons. It is sobering to realize, however, that neuropsychiatric ill health may develop at concentration levels well below that which, until recently, has been considered safe for exposed workers.

The reported effects on mental health cannot, furthermore, be disregarded as marginal or unimportant. In view of both risk source prevalence and the impact of disease in terms of personal suffering and social burden, exposure to organic hydrocarbons should be recognized as a cause of serious concern. We feel that it is advisable to reevaluate the basis of threshold limit values set for organic solvent products and — in so doing — give greater consideration than hitherto to the risk for long-term effects on the nervous system.

SUMMARY

Thirty jet fuel exposed workers selected according to exposure criteria and thirty nonexposed controls from a jet motor factory were examined with special reference to the nervous system by occupational hygiene physicians, psychiatrists, psychologists, and neurophysiologists. The controls were matched with respect to age, employment duration, and education. Among the exposed subjects the mean exposure duration was 17 years, and 300 mg/m³ was calculated as a rough time-weighted average exposure level.

All but four subjects in the exposed group reported recurrent acute symptoms upon exposure to jet fuel vapors during work (dizziness, fatigue, headache, nausea, respiratory tract symptoms, palpitations, and thoracic oppression). The incidence of neurasthenia, anxiety and/or mental depression during employment at the factory was significantly higher in the exposed than in the nonexposed groups, as recorded in (a) the medical history and a standardized interview and (b) notations in the medical records of the factory health department. Among the neurasthenic symptoms fatigue, depressed mood, lack of initiative, and dizziness dominated, but significant differences were also found for palpitations and thoracic oppression, sleep disturbances, and headache.

The prevalence of mental symptoms in the exposed and nonexposed groups was assessed from psychiatric interviews and ratings. The interviews were taped and later evaluated, with the use of rating scales, independently by the interviewing psychiatrist and another psychiatrist, who had no prior knowledge of the subject and did not know whether the subject was exposed or not. The correlation was found to be good between the ratings made by the interviewer and by the second psychiatrist. The evaluation of the interviews resulted in a score estimating the amount of symptoms in the individuals. Comparisons showed the score of the exposed workers to be larger than that of the controls in 20 of 30 pairs. In two pairs the scores were equal, and in eight pairs the control score was larger than that of the exposed worker. The average score of the exposed group exceeded that of the control group. The results show that exposed individuals have more psychiatric symptoms than the controls. Neurasthenic symptoms showed the largest differentiation between the groups, followed by neurotic disturbances.

As to occurrence of symptoms and signs possibly indicative of polyneuropathy, trends towards higher prevalences were found in the exposed group. The results of the examination of the peripheral nerve functions with electroneurographic methods and vibration threshold determinations indicated differences between the groups in terms of (a) smaller nerve action potentials of sensory nerves and a tendency toward higher vibration thresholds of the extremities in the exposed group and (b) slower sensory nerve conduction velocities and a tendency toward slower motor nerve conduction velocities in the nonexposed group.

In the psychological examination behavioral performance tests indicated a difference in performance capability between the groups. The exposed subjects had a greater irregularity of performance on a test of complex reaction time, a greater performance decrement over time in a simple reaction time task, and a poorer performance in a task of perceptual speed than the nonexposed subjects.

The EEGs recorded were considered clinically normal in almost all of the cases.

However, this normality concept includes many EEG varieties. Thus, when the EEGs were ranked as to configuration of alpha activity, significant differences were obtained between the two groups. The exposed group showed, on the average, a lower amplitude and a less observable rhythmic activity than the control group, the EEGs of which were clustered in the most "normal" end of the ranking scale. Also a computer assisted spectral parameter analysis of the EEGs resulted in significant differences between the groups.

To summarize, the present investigation revealed significant differences between the exposed and nonexposed groups for (a) incidence and prevalence of psychiatric symptoms, (b) psychological tests with load on attention and sensorimotor speed and (c) EEGs. In the selection of the control group it was ensured that the two groups were essentially equivalent except for exposure to jet fuel. It is concluded, therefore, that the differences found between the groups are probably related to exposure to jet fuel.

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APPENDIX

Contents of the interview and the items used for rating the liability for mental symptoms (A), the items used for rating different mental symptoms (B), and the principal steps of the scale used for rating the two sets of items (C)

A.

1. Hereditary factors
 2. Factors in previous mental health
 3. Factors in previous physical health
 4. Way of life
 5. Miscellaneous
-

B.

- | | |
|--------------------------|-----------------------------------|
| 1. Sadness | 20. Reduced sexual interest |
| 2. Elation | 21. Increased sexual interest |
| 3. Inner tension | 22. Aches and pains |
| 4. Hostile feelings | 23. Muscular tension |
| 5. Inability to feel | 24. Recent memory |
| 6. Pessimistic thoughts | 25. Long-term memory |
| 7. Suicidal thoughts | 26. Headache |
| 8. Hypochondriasis | 27. Learning |
| 9. Worrying over trifles | 28. Vertigo and dizziness |
| 10. Compulsive thoughts | 29. Chest oppression |
| 11. Phobias | 30. Heart symptoms |
| 12. Rituals | 31. Nausea |
| 13. Indecision | 32. Gastrointestinal disturbances |
| 14. Inertia | 33. Tics |
| 15. Fatigability | 34. Stimulus sensitivity |
| 16. Concentration | 35. Mood lability |
| 17. Reduced appetite | 36. Impulsivity |
| 18. Reduced sleep | 37. Precision movements |
| 19. Increased sleep | |
-

C.

0. None: Absence of symptoms (load)
 - 0.5
 1. Minimal symptoms (load)
 - 1.5
 2. Moderate and definite symptoms (load)
 - 2.5
 3. Severe or incapacitating symptoms (load)
-