

Psychological examination

The test battery used in the psychological examination was compiled of nine psychometric tests, and the intention was to make a battery for further use as a clinical instrument for examining workers with suspected toxic encephalopathy. To a great extent the battery has been used in earlier studies in the realm of the psychometric assessment of neurotoxicity, with the exception of the tests Paired Associates and the present version of Dots (30, 37, 81). The cognitive functions considered were general intelligence (vocabulary, reasoning, and visuoconstructive intelligence), perceptual accuracy, sustained focused attention, memory, and psychomotor performance. The tests can be described as follows.

Synonyms: a vocabulary test of multiple-choice type (24).

Figure Classification: each item consists of five geometric figures, of which four have something in common. The subject is asked to mark the figure that is not in accordance with the rule. The test is based on Thurstone's primary mental abilities (24, 87). The function measured is reasoning ability.

Block Design: the same version as the Koh's test in the Wechsler Adult Intelligence Scale. The test measures visuoconstructive capabilities, as well as logical-deductive ability. The test comprises seven subtasks, and the score is calculated for accuracy and speed (88).

Paired Associates: the test consists of three subtests, each with 10 paired associates which are read aloud to the subject. After the reading, the first word in each pair is repeated, and the subject is asked to recall the second from memory. The test measures memory function.

The Revised Visual Retention Test (Benton form C): the test consists of 10 designs, each containing one or three geometric figures. Each design is exposed for 10 s, and the subject is asked to do an immediate reproduction from memory. Two scores are calculated from the numbers of correct reproductions and errors. The instrument is intended to assess visual perception, visual memory, and visuoconstructive abilities (10).

Dots: the current version of the test is an elaboration of the test used by Elofsson et al (26). It is a cancellation test of the Bourdon-Wiersma type. Performance is assessed in terms of time for every two rows, thus 10 time fractions are recorded, and the errors for every two rows are noted. The performance is recorded as (i) total time required (speed), (ii) fluctuations in speed (the sum of the three shortest time fractions is subtracted from the sum of the three largest), (iii) total number of errors (accuracy), (iv) fluctuation in errors (the sum of the three smallest error scores is subtracted from the sum of the three largest). The test measures perceptual speed and accuracy, and computations are made to give a measure of the variation in the sustained focused attention in terms of fluctuations in time and errors.

Digit Symbol: the original subtest of the Wechsler Adult Intelligence Scale is used. The subject is required to code a set of random numbers, 1 to 9, according to a code list. The test assesses perceptual speed and, to some extent, general intelligence (88).

Cylinder Board: the test material consists of two wooden plates, each with 60 holes. One plate contains 60 cylinders, and the subject is to move the cylinders, one at a time, to the empty board. The preferred hand is used, and two 40-s trials are recorded. Performance score is the number of cylinders moved during the two trials (43). The test assesses hand dexterity.

Serial Reaction Time: simple reaction time is recorded during a 10-min trial. The subject uses his preferred hand and rests his fingertips on the response plate. Before the main trial there is a 1-min trial for instruction and optimizing motivation. The duration between stimuli is 3.75 s with a maximal variation of ± 1.25 s. Thus, there are 16 stimulations/min and a total of 160 records (83). Means and standard deviations are calculated for each 1-min time fraction. These variables make it possible to investigate more subtle aspects of fluctuation in focused attention over time, as well as changes in absolute reaction time (36, 40, 46). For reviews, see Hänninen (37) and Feldman et al (28).

Results

Of the 14 variables analyzed, only one measure showed statistical significance (table 13). The exposed group had a higher degree of time fluctuation in the Dots test ($p < 0.01$). The overall tendency was for the exposed group to exhibit lower performance scores for 9 of the remaining 13 variables. The four variables that did not follow this trend consisted of tests measuring reasoning ability (Figure Classification) and three measures of perceptual speed and accuracy [Dots (total errors and error fluctuation) and Digit Symbol]. A comparison of the subjects' individual standard deviations in serial reaction time for each of the 10 1-min time fractions disclosed a larger variation for the exposed subjects in all 10 intervals (table 14). The performance differences tended to be greater in the first half of the test.

All the psychometric variables were analyzed for possible exposure-response relationships. Dots was the

only test that showed any significant difference between the three subgroups defined by exposure index. Subjects in the low and medium exposure subgroups tended to have a shorter total time on the Dots test in comparison to their matched referents. For the high exposure subgroup the result was the contrary, ie, the total time was significantly higher ($p < 0.05$), whereas the total error score was significantly lower ($p < 0.001$). Thus the high exposure group used more time to get a more accurate result in test performance. As a consequence the high exposure subgroup had fewer fluctuations in errors compared to the low exposure subgroup ($p < 0.01$). The score for fluctuation in time for the high exposure subgroup was significantly higher than for the low and medium exposure subgroups ($p < 0.01$ and $p < 0.05$, respectively).

Clinical evaluation of individual psychometric profiles

The individual test profiles were evaluated in accordance with current clinical practice at the Psychological Laboratory of the Lund University Hospital. In addition to the value of the general intelligence tests (Synonyms and Figure Classification) as tools to evaluate the comparability of the two investigated groups, there was substantial evidence that vocabulary and, to a somewhat less degree, reasoning ability are resistant to decrement, even in relatively severe encephalopathies (68). Thus the scores of these tests were used as a base line in the clinical evaluation of the individual test profiles. One standard deviation below these expected values was considered a suspect pathological finding. If further support for decrement was found in two or more variables, it was considered substantial support for cognitive dysfunction as a consequence of exposure to organic solvents. Twenty-nine individuals in the exposed group did not show any sign of cognitive dysfunction, whereas a slight deviation from the expected values was found for 14 individuals. Seven exposed workers were considered to be pathologically affected as defined by significant deviation in two or more functions. In the reference group 18 out of 50 had slight deviations in one function, but none had deviations in two or more of the functions tested.

Table 13. Psychometric test results in performance raw points. The poorer performance is indicated by an asterisk.

Test	Exposed group		Reference group		p-Value ^a
	Mean	SD	Mean	SD	
Synonyms	22.1*	5.3	22.2	5.4	NS
Figure Classification	21.4	5.4	20.5*	4.9	NS
Block Design	26.3*	8.0	27.1	8.4	NS
Paired Associates	20.8*	6.0	21.5	4.7	NS
Revised Visual Retention Test (Benton), correct	7.4*	1.7	7.6	1.5	NS
Revised Visual Retention Test (Benton), error	3.8*	3.4	3.6	2.7	NS
Dots, total time	397.8*	98.8	389.2	78.6	NS
Dots, time fluctuation	22.8*	1.5	18.5	0.9	<0.01
Dots, total error	10.1	8.5	13.3*	12.2	NS
Dots, error fluctuation	6.6	0.6	7.0*	0.6	NS
Digit Symbol	53.0	14.2	52.2*	15.6	NS
Cylinder Board	78.0*	9.0	79.3	10.0	NS
Serial Reaction Time					
Time fraction 1	22.3*	0.5	21.8	0.5	NS
Time fraction 10	23.8*	0.8	23.7	0.6	NS

^a NS = not significant.

Table 14. Means and standard deviations of the subjects' individual standard deviations for the 10 consecutive time fractions of the Serial Reaction Time test.

Time fraction	Exposed group		Reference group		p-Value ^a
	Mean	SD	Mean	SD	
1	3.8	1.8	3.0	1.6	<0.02
2	3.4	1.9	2.9	1.2	=0.06
3	3.7	1.7	3.1	1.4	<0.05
4	3.8	2.1	3.4	1.2	NS
5	4.2	2.4	3.3	1.5	=0.01
6	4.0	2.2	3.7	1.8	NS
7	4.1	1.8	3.4	1.2	<0.02
8	3.9	1.8	3.7	1.5	NS
9	4.0	2.1	3.7	1.9	NS
10	4.0	2.6	3.7	1.4	NS

^a NS = not significant.

Commentary

The psychological investigation disclosed very few statistically significant differences between the exposed and reference groups. The general tendency was towards lower performance scores in the exposed group however. The small difference in the more complex tests of general intelligence indicated a high degree of comparability between the two groups. The test battery was almost identical to the one used in a similar study, in which a more pronounced difference was

found between exposed subjects and referents (26). In the present study there were no significant differences in absolute reaction time and hand dexterity, as found by Elofsson et al (26). The main finding in our study was the significant differences in performance fluctuations in tests where sustained focused attention was a substantial factor for stable and fast test performance. A somewhat speculative implication of this is that dysfunction in active, sustained focused attention is an early symptom in encephalopathy caused by long-term exposure to organic solvents. A review of the literature gives some support to the conclusion that, when the differences between exposed and unexposed individuals are not substantial, there seems to be differences at least in tests depending heavily on attentive capability and not on complex, symbolic, intellectual operations (23, 37).

An analysis of psychometrics in relation to exposure data disclosed a deficit in sustained focused attention

in the highest exposed subgroup. The less exposed subgroups did not show any signs of decrement in this function. Of more specific interest were the signs of compensatory behavior in individuals with this attention deficit. Their compensatory mechanism is to work slower to rule out the effects of attentive deficit, and, in doing so, they gain an increased accuracy in performance.

The questions proposed in the present study can thus be tentatively answered. A prolonged exposure to organic solvents seems to cause a deficit in sustained focused attention. The exposed subjects were full-time workers and were nonpatients in the sense that they had not sought medical care for suspected disease or solvent poisoning. This finding suggests that psychometric tests measuring sustained focused attention can be used as sensitive instruments for detecting early signs of cerebral dysfunction caused by exposure to organic solvents.

Electroencephalography

Methods

EEG recording was performed under standardized conditions in the Department of Clinical Neurophysiology of the Lund University Hospital. The record was made on a 16-channel Siemens Elema electroencephalograph at rest and during 3 min of hyperventilation and photoactivation. Periods of drowsiness were counteracted by sound stimulation. During 10 min at rest a quantitative frequency analysis was made on line from two bipolar channels on each side of the skull (F3-C3, P3-O1, F4-C4, P4-O2). Fast Fourier transform analysis was made with the Brainlab program (Digital Equipment AB) on a PDP 11/03 computer. The total power (TP) of the EEG activity within the 0.5–25 Hz range was measured, as well as the relative distribution of power within four frequency ranges (δ 0.5–4 Hz, θ 4–8 Hz, α 8–13 Hz, and β 13–25 Hz) (figure 2). From these values the absolute power within each frequency range was calculated. The peak frequency of the dominant activity for each of the four channels was determined. In order to test the possibility of an altered distribution of activity over the brain, anteroposterior and right-left quotients were calculated for the total power and for each of the four frequency bands. No quotients were constructed with power values less than 1 pW.

Results

Before the statistical evaluation of the fast Fourier transform analyses, a routine inspection of the EEG record was made (table 15).

The results of the quantitative frequency analyses of the EEG recordings are presented in table 16 and figure 3. The peak frequency of the dominant background activity did not differ significantly between the exposed and reference groups, but the frequency was slightly higher in the former. Although there was no significant difference between the groups in terms of relative distribution of activity, the absolute power within each frequency band tended to be higher in the exposed group. This tendency is visualized in figure 3. Particularly the power within the highest frequency (β) range was higher among the exposed subjects. The increase in β power did not differ significantly between subjects with high and low exposure.

The relative distribution of the EEG activity in the anteroposterior direction of the brain was also clearly different in the exposed and unexposed subjects. The exposed group had relatively less power over the anterior parts or, alternatively, more power over the posterior parts (figure 3). These differences were clearer on the left side. Similar, but less pronounced and not statistically significant, differences were seen in the

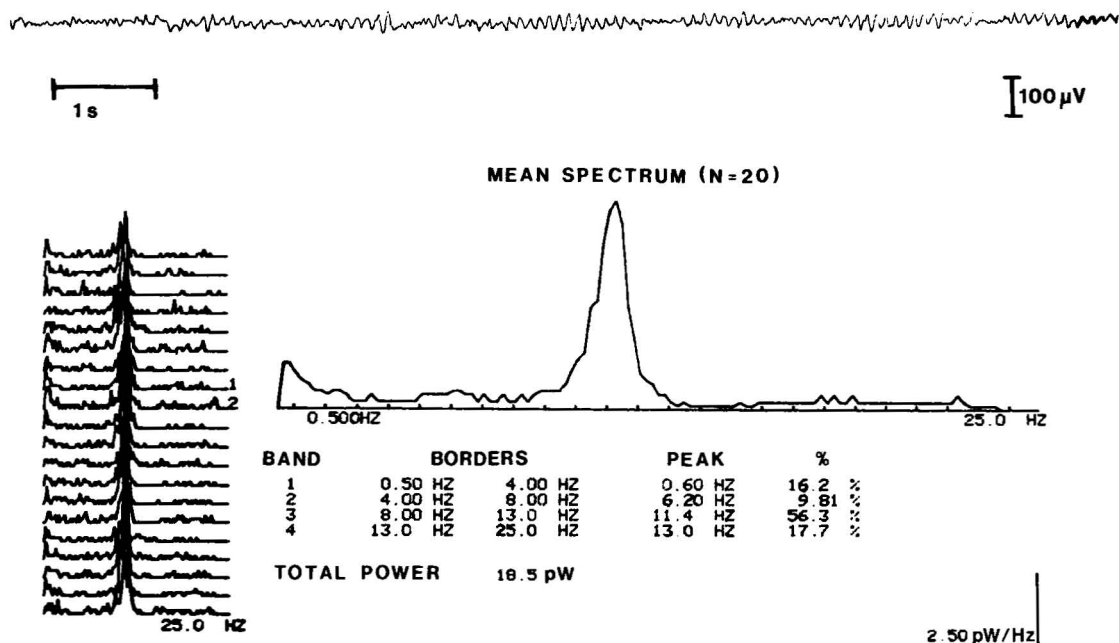


Figure 2. Result of fast Fourier transform analysis of the electroencephalographic recordings as processed on line by computer analysis. Twenty spectra (left row) were averaged, each of which was constructed from 30 s of electroencephalographic recording. Monitoring of the individual spectra makes it possible to check for fluctuations in vigilance and for artifacts. For further details, see the text.

Table 15. Results of the routine evaluation of the electroencephalographic (EEG) records.

	Exposed group	Reference group
Normal EEG	35	47
Increased β activity	9	3*
Increased δ or θ activity	7	0**

$\chi^2 = 10.8$, 2 df, $p = 0.005$ (complete 3×2 table).

* Fisher's exact $p = 0.12$, ** Fisher's exact $p = 0.012$.

Table 16. Results of the quantitative frequency analysis of the electroencephalographic recordings — Dominant frequency and distribution of power in the four electrodes of four frequency bands.

	Exposed group		Reference group		p-Value
	Mean	SD	Mean	SD	
F3—C3					
Dominant frequency (Hz)	9.89	1.28	9.56	1.34	0.23
Total power (pW)	13.81	14.71	12.33	12.36	0.68
δ (%)	46.26	18.29	52.83	20.12	0.12
δ (pW)	5.12	4.09	5.96	6.38	0.28
θ (%)	12.05	5.53	11.52	5.97	0.57
θ (pW)	1.79	2.37	1.42	1.40	0.29
α (%)	31.19	20.30	25.49	18.87	0.20
α (pW)	5.38	9.75	3.57	5.14	0.31
β (%)	13.91	9.35	15.09	12.67	0.51
β (pW)	2.10	2.57	2.16	3.11	0.09
P3—O1					
Dominant frequency (Hz)	9.97	1.11	9.67	1.21	0.19
Total power (pW)	19.64	17.83	14.57	17.98	0.17

(continued)

Table 16. Continued.

	Exposed group		Reference group		p-Value
	Mean	SD	Mean	SD	
δ (%)	37.67	25.89	35.57	24.78	0.50
δ (pW)	5.58	4.49	3.69	4.43	0.03
θ (%)	11.34	10.59	11.52	6.99	0.77
θ (pW)	2.15	2.55	1.53	2.08	0.30
α (%)	47.08	27.18	48.39	28.28	0.66
α (pW)	11.11	14.66	8.82	13.87	0.46
β (%)	7.25	6.92	5.62	6.78	0.24
β (pW)	1.33	1.65	0.63	0.70	0.02
F4—C4					
Dominant frequency (Hz)	9.85	1.20	9.62	1.30	0.36
Total power (pW)	15.66	15.19	12.58	9.55	0.26
δ (%)	44.78	18.93	50.26	18.64	0.17
δ (pW)	5.91	4.31	5.75	3.70	0.86
θ (%)	12.17	5.64	11.92	5.84	0.67
θ (pW)	2.00	2.13	1.55	1.42	0.20
α (%)	31.45	21.24	26.44	18.87	0.36
α (pW)	5.97	10.27	3.92	5.28	0.30
β (%)	14.55	10.81	14.07	9.93	0.10
β (pW)	2.42	2.46	1.75	1.64	0.07
P4—O2					
Dominant frequency (Hz)	10.07	1.10	9.68	1.18	0.07
Total power (pW)	18.48	16.65	15.14	17.08	0.39
δ (%)	32.54	22.03	33.61	24.14	0.94
δ (pW)	4.51	2.85	3.44	4.49	0.19
θ (%)	11.49	9.54	10.75	7.52	0.93
θ (pW)	1.98	2.02	1.53	2.02	0.57
α (%)	49.30	27.19	51.53	27.36	0.70
α (pW)	10.96	13.55	9.77	13.90	0.67
β (%)	8.68	8.64	6.11	6.12	0.07
β (pW)	1.38	1.27	0.68	0.65	0.005

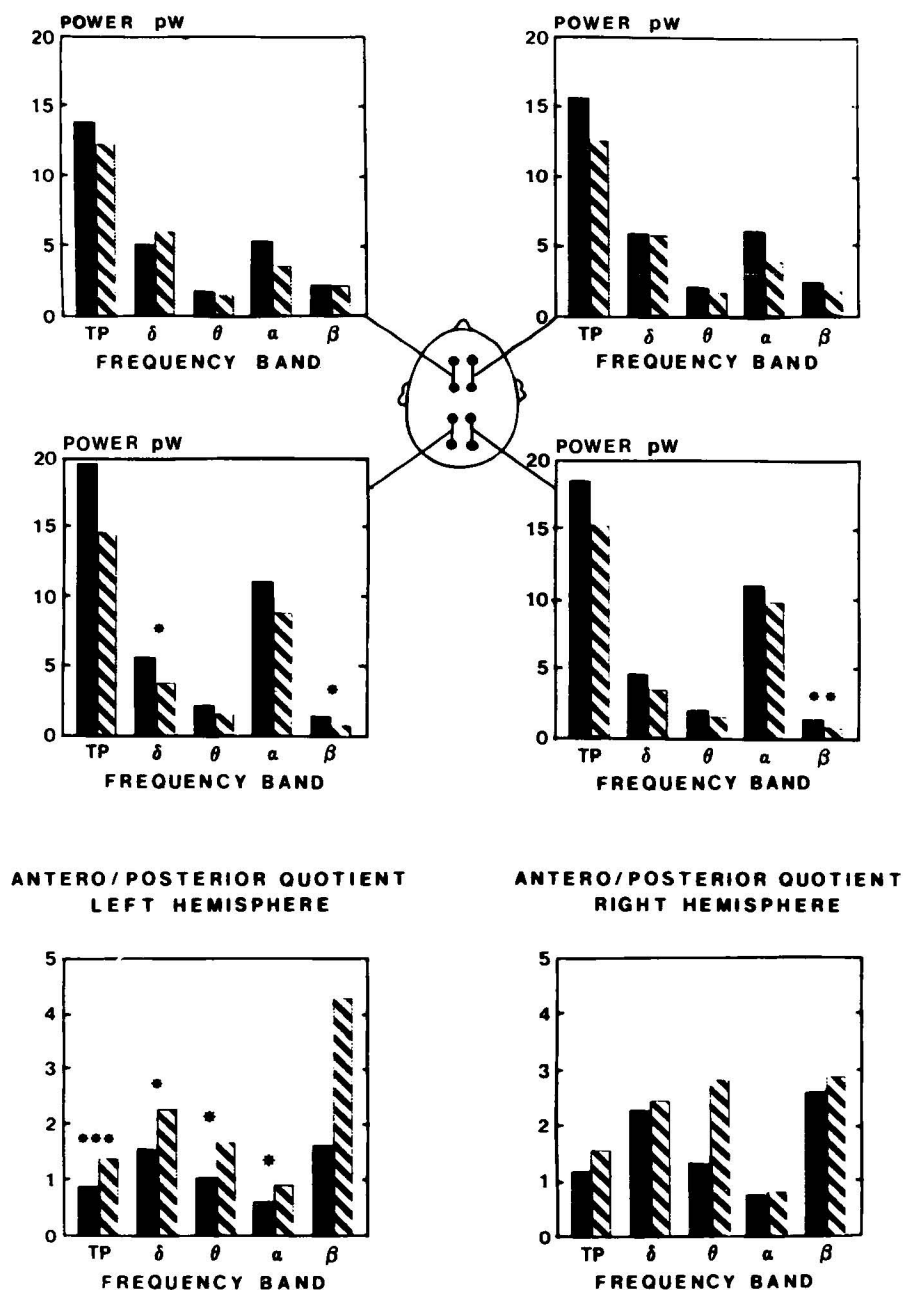


Figure 3. Results of the quantitative electroencephalographic analysis. Comparison of results from the unexposed reference group (striped columns) and the exposed group (black columns). The power in picowatts is plotted for each of the four recording channels and for the whole electroencephalographic spectrum (TP), as well as for the delta, theta, alpha, and beta activity. The two diagrams at the bottom show the anteroposterior quotients of the left and right hemispheres for the same electroencephalographic variables. For further details, see tables 16 and 17 and the text. (* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ in comparisons between the exposed and reference groups)

right hemisphere (table 17). The most highly exposed subgroup showed a greater difference in the total power quotients than the subgroup with the lowest exposure (left hemisphere $p = 0.08$, right hemisphere $p = 0.025$). In the distribution of activity between the right and left halves of the brain no significant dif-

ferences were found between the groups.

Commentary

The quantitative EEG frequency analysis used in our study does not involve any component of subjective

Table 17. Results of the quantitative frequency analysis of the electroencephalographic recordings — Analysis of the antero-posterior (A/P) power distributions calculated as quotients of the anterior and posterior power in each frequency band.

	Exposed group		Reference group		p-Value
	Mean	SD	Mean	SD	
A/P left hemisphere					
Total power	0.85	0.57	1.37	1.02	0.0007
δ	1.59	2.38	2.27	1.51	0.037
θ	1.04	0.71	1.67	1.70	0.017
α	0.59	0.48	0.89	0.92	0.036
β	1.60	1.18	4.28	6.02	0.17
A/P right hemisphere					
Total power	1.16	0.90	1.52	1.89	0.16
δ	2.28	3.29	2.43	1.85	0.78
θ	1.30	1.36	2.80	5.26	0.065
α	0.73	0.64	0.80	0.90	0.47
β	2.59	5.20	2.86	2.53	0.44

estimation of the records apart from excluding epochs of failing vigilance or artifact contamination during the examination. With this technique we were able to demonstrate significant differences in the EEG activity of the exposed and unexposed subjects. The power of the EEG activity within the fast (β) frequencies was greater among the exposed subjects, and the antero-posterior distribution was different. The neurobiological background of these changes is completely unknown. Much more pronounced changes in the same direction have recently been found by us in a parallel study of patients with clinical signs of a psychoorganic syndrome after many years of organic solvent exposure (Rosén et al, in preparation). We tentatively suggest that the EEG changes reflect a neurotoxic effect of long-term organic solvent exposure on the central nervous system.

Regional cerebral blood flow

Methods

rCBF was determined with the noninvasive ^{133}Xe inhalation technique as suggested by Mallet & Veal (60) and further developed by Obrist et al (64) and Risberg et al (70). The technique is based on 1-min inhalation of the freely diffusible, γ -emitting tracer ^{133}Xe , mixed with air (2.5 mCi/l or 111–185 mBq/l). The tracer was administered via a face mask, covering the nose and mouth, and a rebreathing spirometer system. Inhalation was followed by 10 min of normal breathing. During this period, external

detectors continuously monitored the γ radiation emitted by the tracer. In our system, the arrival and washout of the tracer were recorded by 32 scintillation detectors, covering both hemispheres. The average detector location on the cortex of one hemisphere is shown in figure 4. The continuous change of tracer concentration is related to blood flow through the tissue, the tracer disappearing faster with higher blood flow. The rate of isotope washout formed the basis for the calculation of the rCBF.

The following flow measures were calculated: ISI (initial slope index), a flow index dominated by grey

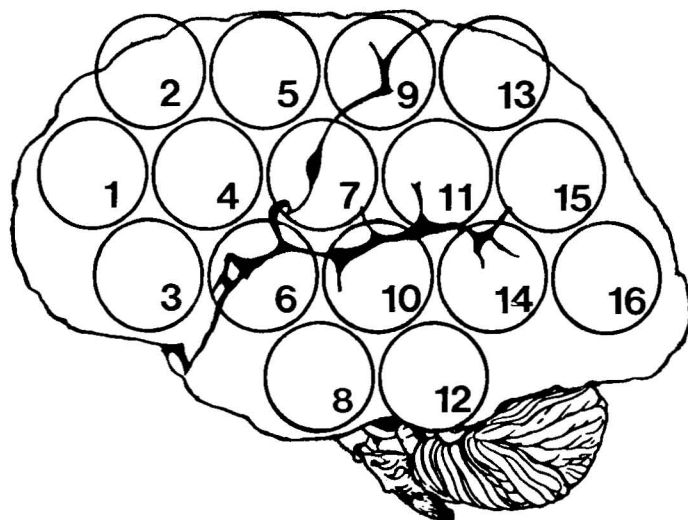


Figure 4. The average detector location over homologous regions of the cerebral hemispheres. The central and lateral fissures are shown for reference.

Table 18. Cerebral blood flow during rest in the exposed and reference groups and in the three subgroups of the exposed group and their matched referents. [ISI = initial slope index, K2 = cerebral white matter flow, Wg = the proportion (relative weight of tissue recorded) which is perfused by the rapid flow expressed as the percentage of total perfused tissue, aPCO₂ = end-expiratory partial pressure of carbon dioxide]

Group or subgroup	N	ISI		K2		Wg		aPCO ₂	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD
Exposed (complete)	50	46.5*	5.5	15.9	1.6	37.8	4.4	40.0	3.1
Reference (complete)	50	48.5	5.6	15.8	1.7	38.5	4.1	39.9	3.4
Low exposure	17	49.4	4.6	16.7	1.6	40.2	3.5	41.2	2.0
Matched referents	17	50.2	5.7	16.1	1.5	40.1	2.7	40.7	2.5
Medium exposure	18	47.4	5.9	16.4	1.7	37.3	4.1	39.8	3.2
Matched referents	18	49.5	7.2	16.1	1.8	38.2	4.3	40.2	3.2
High exposure	15	41.8	4.3	14.7	1.7	35.8	4.4	39.0	3.6
Matched referents	15	44.8	8.2	15.3	1.8	37.0	4.8	38.5	4.0

* $p < 0.05$, in comparison with the reference group (complete).

matter flow (70); K2, cerebral white matter flow; Wg, the proportion (relative weight of tissue recorded) which is perfused by the rapid flow expressed as percentage of total perfused tissue. For an elaborate description of the technique and measurement system, the reader is referred to the report of Risberg (69).

Experimental conditions

Each subject underwent three rCBF measurements, one resting measurement and two measurements during cognitive activation by a verbal memory test and a visuoconstructive spatial task. Under all conditions the subject was lying supine on a comfortable bed, with the detectors placed at right angles to the skull. During the resting measurement, the subject was asked to relax without falling asleep. His eyes were covered with pads, and external stimulation from the laboratory was kept at a minimum. During the second measurement, six slides with 10 word pairs on each were presented to the subject on a clearly visible screen. Each slide was shown for 2 min. The subject's task was to memorize the word combinations. After the measurement, we checked performance by showing the first word in each combination and asking the subject to recall the second word. During the visuoconstructive task (a puzzle test), the subject was required to complete a figure with one or two out of five given alternatives. The completed figure was always a black square. The subject was given such tasks consecutively during the entire measurement. We checked performance after the presentation of each item by asking the subject to report, via a built-in microphone, the number of the alternative(s) chosen.

Results

Mean cerebral blood flow during rest

The mean values for the ISI are shown in table 18. Values are given for the total exposed and reference

groups and for the three subgroups of the exposed group. The main finding was only small differences between the groups. The ISI was, however, significantly lower in the exposed group (4 %, $p < 0.05$). We found a tendency towards increased differences in the cerebral blood flow with higher exposure. For the highest exposed subgroup, the difference in relation to the referents was 7 % lower (95 % confidence limits -17 - +2 %). No major differences in the K2 and Wg values were found between the groups. There was, however, a tendency towards increased differences with higher exposure indices. No group differences in the end-expiratory partial pressure of carbon dioxide were found, so this factor could not have disturbed the results.

Figure 5 demonstrates an age-related decrease in cerebral blood flow with advancing age in both groups. The exposed group had significantly lower values in general ($p < 0.05$), but a considerable overlap was observed in the individual values of the groups at all ages.

Regional cerebral blood flow during rest

Figure 6 shows the differences between the exposed and reference groups for all the regions measured. The regional flow values were generally lower in the exposed group. Statistically significant differences were found in the fronto-orbital region (detector 3) in both hemispheres ($p < 0.01$). In the right hemisphere, flow was significantly lower in the prefrontal area (detector 1) and in one inferior temporal region (detector 8, $p < 0.05$). In the left hemisphere, flow was significantly lower in one superior temporal area and in the parietal lobe (detectors 10 and 13, $p < 0.05$). The regional K2 and Wg values did not show any significant regional differences between the groups.

Responses of the regional cerebral blood flow to mental activation

Table 19 shows the mean cerebral blood flow (ISI) in the resting state and during activation for the exposed and reference groups and for the subgroups of the exposed group. Only the highest exposed subgroup

rCBF - AGE REGRESSION

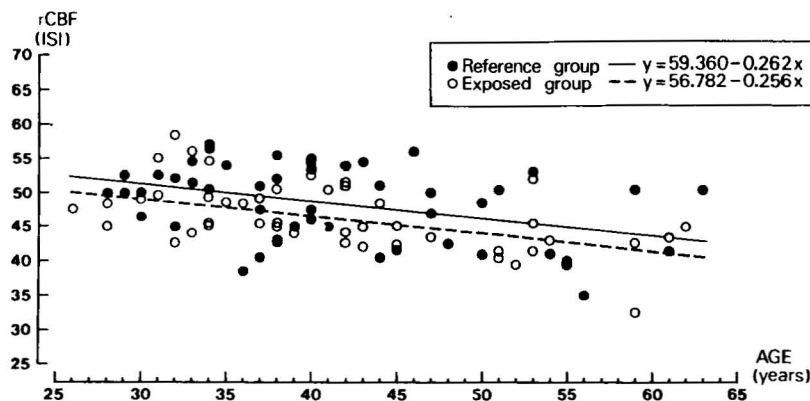


Figure 5. The relationship between the initial slope index (ISI) of the regional cerebral blood flow (rCBF) at rest and age for the exposed subjects and the referents. The rCBF values were corrected for variations in end-expiratory partial pressure of carbon dioxide.

Table 19. Cerebral blood flow (as indicated by the initial slope index) during rest and functional activations in the exposed and reference groups and in the three subgroups of the exposed group and their matched referents.

Group or subgroup	N	Rest		Verbal test		Spatial test	
		Mean	SD	Mean	SD	Mean	SD
Exposed (complete)	50	46.5	5.5	47.1	5.9	50.8	6.8
Reference (complete)	50	48.5	5.6	47.4	6.8	50.8	7.0
Low exposure	17	49.4	4.6	48.7	5.8	53.9	6.4
Matched referents	17	50.2	5.7	50.5	6.2	53.4	6.6
Medium exposure	18	47.4	5.9	46.2	5.0	51.4	6.8
Matched referents	18	49.5	7.2	47.4	6.8	50.4	6.6
High exposure	15	41.8	4.3	44.4*	5.3	47.9**	6.0
Matched referents	15	44.8	8.2	44.4	6.8	48.2	7.4

* $p < 0.05$, ** $p < 0.01$, comparison of rest values of the high-exposure subgroup with their respective verbal test and spatial test values.

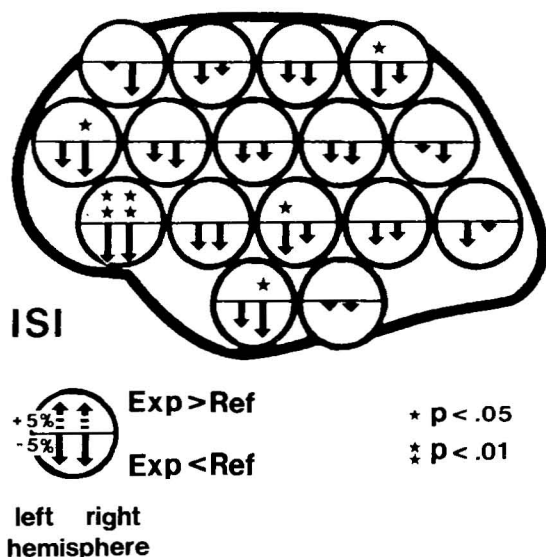


Figure 6. Differences in the regional cerebral blood flow (rCBF) of the exposed (exp) and reference (ref) groups. (ISI = initial slope index)

showed a significant increase in cerebral blood flow from rest to activation ($p < 0.05$), while their age-matched referents showed a weaker activation re-

sponse. There was a tendency towards a higher activation response with increased exposure and, likewise, a tendency towards increased differences in the magnitude of the activation response between the exposed subjects and the referents at higher exposure levels. These differences between the subgroups were, however, not statistically significant.

The test performance score of the two activation tests decreased with increasing exposure (table 20). In addition the performance of the referents decreased with increasing age. Performance was somewhat lower in all three exposure subgroups in comparison to that of their matched referents. These differences were not statistically significant. Regionally, increases in cerebral blood flow were seen in expected areas, according to previous research and neuropsychological theory. The regional changes were, as expected, highest in the group showing the highest mean flow increases, namely, the group with the highest exposure level.

Clinical evaluation of individual results

Each individual rCBF result was clinically evaluated as to its normality, according to clinical experience and studies of normal subjects (71). In the exposed group, a normal rCBF pattern and level was found for 42 sub-

jects. Three subjects showed cerebral blood flow levels that were slightly below normal. Five subjects showed slight regional deviations. Four of them had lower than normal flows in frontal areas and one parietally. In none of these cases did the rCBF deviations indicate primary organic brain disease. An evaluation of the individual rCBF results in the reference group showed that three subjects had slight deviations from normal standards. These deviations were not considered to indicate pathology.

Commentary

We found that the cerebral blood flow was 4 % ($p < 0.05$) lower in the exposed group than in the reference group. This finding is in agreement with the results of a pilot study showing 6 % lower cerebral blood flow in patients with symptoms likely to be solvent-induced, in comparison to the corresponding levels of normal persons of similar age (61). A more marked decrease in the cerebral blood flow has been reported in a study of nine house painters (7). These painters had intellectual impairment as revealed by psychological testing, and they were referred for examination due to suspicion of chronic solvent intoxication. These factors may account for the larger mean decrease in cerebral blood flow observed, in comparison to the results in the present study. The reduction observed in the present study may indicate cerebral dysfunction due to long-term exposure to organic solvents. The regional accentuation of the decrease in frontal and frontotemporal areas may indicate a specific sensitivity to toxic solvents in these areas. This assumption is supported by our EEG results showing relatively lower activity in frontal than in posterior cerebral areas. It is also of interest to note that similar regional decreases in cerebral blood flow have been found in old chronic alcohol abusers (11). It is possible that the

Table 20. Test performance scores of subgroups of the exposed group and their matched referents during activation of the regional cerebral blood flow.

Subgroup	N	Verbal test		Spatial test	
		Mean	SD	Mean	SD
Low exposure	17	10.3	19.7	11.2	3.6
Matched referents	17	12.4	14.1	10.9	4.9
Medium exposure	18	7.3	10.2	10.8	4.8
Matched referents	18	12.9	12.1	12.6	4.2
High exposure	15	1.9	3.2	6.4	3.5
Matched referents	15	3.9	6.4	7.3	2.3

frontotemporal decrease in flow seen in our exposed group reflects a process similar to that observed in chronic alcoholics.

The difference in activation response between the exposed subjects and referents was generally small and not statistically significant. The response was found to increase with increased exposure both globally and regionally, while test performance decreased. This tendency may indicate compensatory mechanisms due to cerebral dysfunction. However the present results do not agree with the findings from our pilot study, which showed a lower activation response in highly exposed subjects when they were compared to less exposed subjects (61). Thus the activation results must be interpreted cautiously.

The differences in the rCBF of the exposed subjects and referents of the present study are only evident from group data. The overlap between the groups demonstrated in figure 5 is far too large to allow differentiation on an individual basis. The exclusion of other possible causes of neurasthenic syndrome, such as organic dementia or vascular brain disease, appears to be the primary role for the measurement of rCBF in the evaluation of single cases examined because of a suspicion of solvent-induced encephalopathy.

Peripheral nervous system

Methods

Peripheral nervous functions were extensively investigated with the objective in mind of revealing a peripheral neuropathy not necessarily expressed as a slowing of nerve conduction velocities. Disa 1500 equipment with a constant current stimulator was used. The subjects were warmed if necessary, to obtain skin surface temperatures exceeding 30°C in the hands or feet.

Conduction velocities of the fast motor fibers were determined for the median, ulnar, peroneal, and posterior tibial nerves. Compound muscle action potentials were recorded with surface electrodes from the thenar, hypothenar, extensor digitorum brevis, and abductor hallucis muscles, and the nerves were stimulated at the wrist, elbow, ankle, and knee levels. The active recording electrode was placed so that the initial