

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

SENSORY NEUROGRAPHY, MEDIAN NERVE
DIGI 15mA

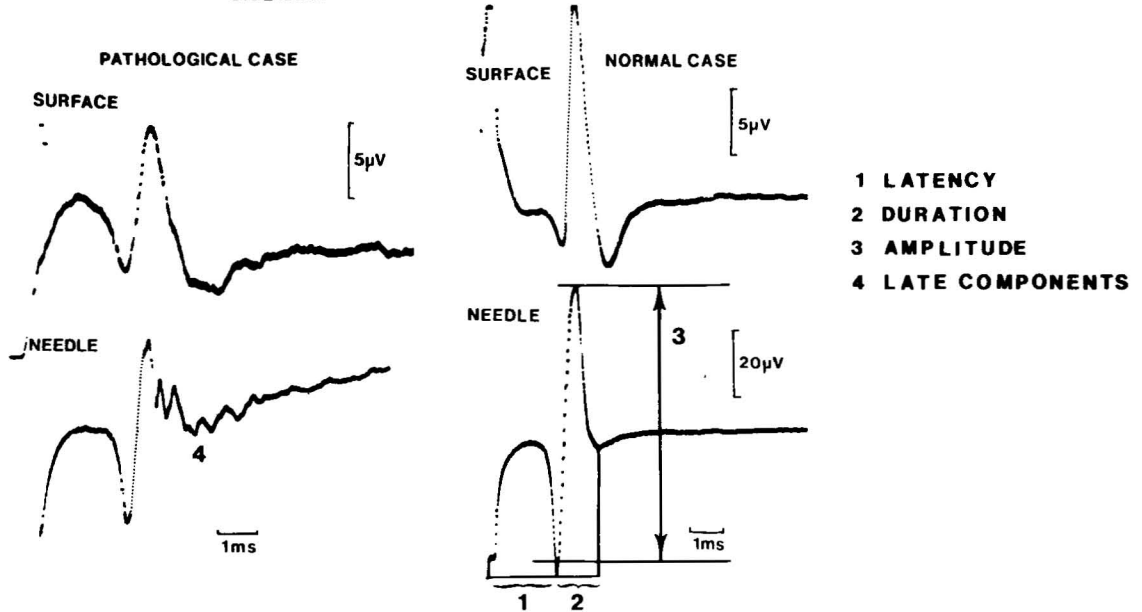


Figure 7. Sensory nerve action potentials recorded with surface and needle electrodes from two subjects, one with normal findings and one with sensory neuropathy. The latency was measured from the stimulus at the start of the sweep to the peak of the initial positive deflection. The duration of the compound nerve action potentials was measured between the two positive peaks. The amplitude was measured from the initial positive peak to the following negative peak. Late components recorded with needle electrodes were quantified and given as the percentage of the amplitude of the main complex.

Table 21. Results of the routine clinical evaluation of the neurographic findings of the exposed and reference groups.

	Exposed group	Reference group
<i>Normal findings</i>		
Whole group	39	46
< 40 years	25	26
40–50 years	11	13
> 50 years	3	7
<i>Slight neuropathy</i>		
Whole group	11	4
< 40 years	2	—
40–50 years	1	2
> 50 years	8	2

Mantel-Haenszel $\chi^2 = 2.96$, $p < 0.1$ (complete table, 3 strata of 2×2 tables).

part of the muscle action potential showed a monophasic negativity. Distal latencies were measured in addition to the motor conduction velocity.

Sensory neurography was performed with surface electrodes from the median and sural nerves. Fingers I and III were stimulated by ring electrodes, and the sensory action potentials were recorded over the median nerve immediately proximal to the wrist (interelectrode distance 30 mm). The stimulus current was adjusted to produce a maximal nerve volley (usually about 15 mA). The sensory action potential of the median nerve was also recorded with a needle electrode positioned close to the median nerve and one needle electrode placed 20 mm more laterally. With needle

electrodes it is possible to define late nerve components which are quantified in proportion to the amplitude of the main nerve action complex (figure 7). Sensory action potentials from the sural nerve were measured antidromically at the lateral malleolus when the nerve at the posterolateral side of the calf was stimulated. Latency, duration, amplitude, and late components were measured after the averaging of 128 individual records.

Thresholds to vibration at 100 Hz were determined at the carpus and pretibially according to the method of Goldberg & Lindblom (34).

Warm-cold difference limens were measured at the chin and at the thenar and lateral edge of the foot according to the method of Fruhstorfer et al (31). The change in temperature was 2°C/s .

Results

Before the statistical evaluation, a routine clinical neurophysiological evaluation was made (table 21). There were slightly more exposed subjects, particularly among the elderly, with slight signs of polyneuropathy (Fisher's exact $p = 0.03$). In addition, neurographic signs of carpal tunnel syndrome were found in one exposed subject and three referents.

The neurographic and psychophysiological variables tended to be slightly better among the exposed workers than among the referents (tables 22 and 23). The only exception was the sensory response of the sural

Table 22. Results of the neurographic examinations of the exposed and reference groups. (N = needle electrodes, S = surface electrodes)

Variable	Exposed group		Reference group		p-Value
	Mean	SD	Mean	SD	
Motor conduction velocity (m/s)					
Median	58.5	4.8	58.7	4.6	0.62
Ulnar	57.6	4.7	57.7	5.5	0.61
Peroneal	47.2	4.2	45.8	3.7	0.03
Posterior tibial	44.6	4.0	44.7	3.5	0.8
Distal motor latency (ms)					
Median	3.8	0.4	3.8	0.4	0.32
Ulnar	3.0	0.4	3.1	0.3	0.25
Peroneal	4.6	0.7	4.8	0.8	0.11
Posterior tibial	5.7	1.4	5.9	1.3	0.18
Sensory conduction velocity (m/s)					
Median digit I N	46.3	4.6	44.8	4.4	0.056
Median digit III N	51.7	6.5	49.6	6.2	0.02
Sural S	43.6	4.1	43.4	3.9	0.94
Sensory action potential amplitude (μ V)					
Median digit I S	22.8	14.9	20.3	13.1	0.32
Median digit III S	15.6	10.1	12.9	10.1	0.10
Sural S	10.9	7.9	12.0	7.6	0.09
Sensory action potential duration (ms)					
Median digit I N	1.17	0.27	1.20	0.32	0.67
Median digit III N	1.25	0.30	1.30	0.32	0.76
Sural S	1.84	0.35	1.69	0.31	0.007
Sensory action potential late components (%)					
Median digit I N	5.7	7.3	6.1	7.4	0.94
Median digit III N	5.6	6.0	7.4	8.2	0.34

nerve. The potential was lower (not significantly so, $p = 0.09$) and showed a significantly larger temporal dispersion among the exposed workers ($p = 0.007$). There was no significant difference between the subgroups with low and high exposure indices. However, the subjects with high exposure had a longer duration of the median sensory action potential as compared with the low exposure subgroup ($p < 0.05$).

Commentary

Although the preliminary survey indicated a slightly increased prevalence of cases with neurographic signs of polyneuropathy, this increase was not confirmed in the quantitative evaluation of the measurements.

However, the significantly increased temporal dispersion of the sensory action potential of the sural nerve is noteworthy and may indicate a sign of mild affection of the most peripheral sensory neurons ex-

Table 23. Results of the psychophysiological tests.

Variable	Exposed group		Reference group		p-Value
	Mean	SD	Mean	SD	
Vibration threshold (μ m)					
Carpal	0.49	0.40	0.56	0.38	0.36
Tibial	1.32	2.14	1.09	1.03	0.28
Warm-cold difference limen ($^{\circ}$ C)					
Chin	1.56	0.86	1.83	0.86	0.097
Hand	2.07	1.06	2.45	1.08	0.047
Foot	6.64	3.14	7.10	3.74	0.51

amined in this study. Among clinical cases of psycho-organic syndromes following many years of house painting the most pronounced changes were seen in this very nerve (73).

Discussion

A problem with a cross-sectional study design like the one used in our study is the selection of "survivors" to the study group. This seems clearly to have been

the case since the subject's accumulated exposures tended to be quite low for more than half of the exposed group. Many highly exposed workers were im-

Table 24. Covariation of the clinical findings of the 50 exposed subjects.

Subject	Exposure index ^a	Actual exposure ^b	Electroencephalography ^c	Electro-neuro-graphy ^c	Psycho-metry ^d	Neuras-thenic score ^e	Regional cerebral blood flow ^c
k05	1	2	—	—	0	3	—
k12	1	1	—	—	0	0	—
776	1	3	—	—	0	0	—
k09	1	1	—	—	0	5	—
k02	1	2	—	—	0	9	—
k00	1	2	—	—	0	2	—
789	1	1	+	—	0	1	—
774	1	3	—	—	1	*	—
787	1	2	+	—	0	7	—
767	1	3	+	—	1	*	—
776	1	2	—	—	0	9	—
k13	1	1	—	—	0	7	—
k14	1	1	—	—	1	2	—
k11	1	1	—	—	1	7	—
k17	1	1	—	—	1	1	—
772	1	1	—	—	0	0	—
782	1	2	—	—	0	0	—
k08 ^f	2	1	+	—	2	11	—
k03	2	2	—	—	1	11	—
761	2	3	+	—	0	5	—
k01	2	1	—	—	0	7	—
794	2	2	—	—	1	1	—
792	2	3	—	—	0	4	—
775	2	2	—	—	0	10	—
k16	2	1	—	—	2	4	—
k15	2	1	—	—	1	3	—
795	2	2	+	—	0	9	—
k04	2	1	—	—	0	9	—
785	2	2	—	—	0	4	+
796	2	2	+	—	1	0	+
k07	2	1	—	—	0	7	—
765	2	2	+	—	0	13	—
788	2	3	—	—	1	6	—
k06	2	1	—	—	1	10	—
k21	2	1	—	—	0	2	+
k10	3	2	—	+	1	5	—
770	3	3	+	—	1	12	—
k18	3	2	—	—	0	9	—
784	3	3	—	+	0	2	—
769	3	3	+	—	0	11	+
783	3	3	+	+	0	3	—
763	3	3	—	—	0	1	—
758 ^f	3	3	—	+	2	*	+
764	3	3	+	+	0	8	—
771 ^g	3	2	—	+	2	7	+
768	3	3	—	+	0	10	—
790	3	2	+	+	1	12	—
759 ^f	3	2	+	+	2	1	+
779 ^f	3	3	+	+	2	*	+
760 ^f	3	3	—	+	2	*	+

^a 1 = low, 2 = medium, and 3 = high exposure; for more specific information on the exposure levels see table 3.

^b 1, 2, and 3 indicate subject's actual exposure according to the hygienic effect values seen in table 4 (1 = <0.1, 2 = 0.1—<0.4, and 3 = 0.4—<0.6).

^c + = suspected pathological finding, — = no suspected pathological finding.

^d 0 = no deviation, 1 = slight deviation, 2 = definite deviation.

^e Score above 8 considered pathological; subjects marked by an asterisk considered by the psychiatrist to be cognitively reduced.

^f Granted compensation.

^g Abstained from seeking compensation.

migrants, and they were examined separately because we considered their matching with referents to be impossible. Instead we examined 19 immigrants clinically, and with the same criteria as in the present study, three of them were diagnosed as suffering from a solvent-induced neurasthenic syndrome.

Selection of a proper reference group is crucial. For the behavioral part of our study we found it very difficult. Pairwise matching and control for possible confounding assured good comparability between the groups, at least for the objective physiological mea-

surements. Including education as a matching criterion, equal performance in the test of general intelligence, and comparable histories of earlier mental problems seems to have validated the group comparisons for the behavioral part of the study too. Different personality characteristics in the study groups is important to keep in mind, especially when the reported symptoms are considered (58). The professional careers of the exposed workers indicate higher levels of ambition among this group in comparison with their referents at the sugar refinery. Personality factors and

recall bias among the exposed subjects, who were well aware of the risks at their workplace, can partly explain the difference in reported symptoms. But the symptoms were more frequent among the more heavily exposed subjects and were reproduced in two independent and very different interview situations. We find reasons to conclude that the neurasthenic and emotional problems experienced by the exposed workers were, to a great extent, solvent induced.

Further proof for the solvent effects can be found in the neuropsychological tests. Admittedly only small differences were found when the group means were considered, but increased distractibility due to organic brain dysfunction can, to some degree, be compensated for in the testing situation, where subjects are allowed to work undisturbed and concentrated. The tests showed disturbances in sustained focused attention capabilities, and there were greater variations in tests that measure memory (Paired Associates and The Revised Visual Retention Test, Benton errors). The variations in the test performances of the exposed subjects are important signs of brain dysfunction and form the basis for the clinical diagnosis of toxic encephalopathy. Thus performance variations are more important to consider than the small differences in group means. Subjects with test performances considered pathological were found among the most heavily exposed subjects, and this result indicates an exposure-effect relationship (table 24). Pathological results in the behavioral interviews and tests seemed to covariate well with the deviations found in the objective physiological measurements of the subjects belonging to the subgroup with the highest exposure (table 24). Statistics did not, however, demonstrate any significant correlation between the measurements, but the power was weak due to the latency time for solvent effects.

The power spectrum analyses of the EEG recordings disclosed a reaction to solvent exposure that differed in the frontal and parietal parts of the brain. The power increase was less pronounced frontally, where also the larger rCBF reductions were found. These ob-

servations of an increased frontal sensitivity to solvent exposure may be a human equivalent to the animal observations made by Haglid et al (41, 75). The decrease in cerebral blood flow was larger, and the reduction of the anteroposterior quotients of the EEG power was more marked in the most highly exposed subjects. These findings might indicate accelerated ageing of the brain as an effect of solvent exposure.

Combined effects on the central and peripheral nervous systems would indicate effects of toxic substances when endogenous intoxication has been excluded, as in the present study. In general we did not find impairment in the peripheral nerves. The exposed group had slightly better nerve function parameters, except for the longest sensory nerve fiber of the body in the sural nerve and a very large dispersion of vibration thresholds on the tibial bone. These observations, and the suspected cases of neuropathy among the most heavily exposed subjects, suggest toxicity to the peripheral nerves as well, but with a longer latency time than for effects on the central nervous system. Our problem with rather low exposure indices may be the reason for the very discrete findings.

The exposure distribution, skewed towards low accumulated exposure indices, generally weakened the strength of our study to demonstrate exposure-effect relationships. Despite this weakness we have found consistent signs of impaired nervous system function in the exposed group. None of the results supported the conclusion that solvents should not be harmful to long-term exposed workers. The most pronounced changes were found among the most heavily exposed subjects. The actual exposure levels were low and can hardly, alone, be the reason for all the differences observed. The group differences possibly caused by long-term exposure to organic solvents indicate that a clinically important neurasthenic syndrome in a patient who has been exposed to solvents for at least one decade should be recognized as work-related when other important diseases have been excluded reasonably well.

Acknowledgments

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