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Assessment of Somatosensory Indicators of Polyneuropathy in Patients with Eating Disorders

A. M. Pauls, S. Lautenbacher, F. Strian, K.-M. Pirke, and J.-C. Krieg

Max-Planck-Institut für Psychiatrie, Klinisches Institut, Kraepelinstrasse 10, W-8000 Munich 40, Federal Republic of Germany

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Summary. The somatosensory functions of small-diameter nerve fibres were tested on the lower and upper extremities in nine patients with anorexia nervosa, ten patients with bulimia nervosa and ten control subjects, by analysing warmth, cold, and pain thresholds. To test large-diameter nerve fibres, the vibration threshold was also measured. Both patient groups had markedly elevated pain thresholds compared with the control subjects. In contrast, warmth and cold thresholds were only suggestively elevated while vibration thresholds were not at all increased in the patients. A distal-proximal pattern of somatosensory deficits, suggestive of peripheral polyneuropathy, was not observed. Hence, a peripheral polyneuropathy affecting small or large afferent fibres as a consequence of an eating disorder seems to be a rare event.

Key words: Somatosensory thresholds – Peripheral polyneuropathy – Anorexia nervosa – Bulimia nervosa – Eating disorder

Introduction

Patients with eating disorders – i.e. anorexia nervosa and bulimia nervosa – frequently complain of peripheral neuropathic symptoms in the course of their disease. In 33 of 51 patients with anorexia nervosa, MacKenzie et al. (1989) found subjective symptoms of a peripheral neuropathy, namely paraesthesias in the distal extremities, muscle weakness and diminished position sense. But only 4 of 51 patients showed electrodiagnostic evidence of a sensorimotor peripheral neuropathy. Slettebo and colleagues (1984) reported a denervation type atrophy in all muscle biopsies of ten patients with anorexia nervosa. Five had clinical findings suggestive of a mild peripheral neuropathy; however, electrodiagnostic testing was normal in all cases. Alloway and coworkers (1985) recently described two electrodiagnostically confirmed cases of neuromyopathy in patients with a severe form of anorexia nervosa and bulimia nervosa, respectively. These findings suggest that electrodiagnostic measurements (nerve conduction velocity, somatosensory evoked potentials) may not be sensitive enough to detect early stages of a peripheral neuropathy in eating disorder patients. One reason for this might be that, in the course of an eating disorder, large-diameter nerve fibres (Aα, Aβ), which are tested in electrodiagnostic procedures, are affected later than small-diameter nerve fibres (Aδ, C).

This hypothesis is also plausible with respect to the possible causation: MacKenzie and coworkers (1989) considered that a chronic protein malnutrition is responsible for the neuropathic symptoms. Reports on frequent alcohol and drug abuse in bulimic patients (Mitchell et al. 1985; Bulik 1987) point to a toxic causation. In deficiency, metabolic, and toxic polyneuropathies, the small fibres are frequently affected early (Lindblom and Tegnér 1985; Claus 1987; Ziegler et al. 1988b; Strian 1990). Our recent findings of reduced pain sensitivity in anorexia and bulimia nervosa (Lautenbacher et al. 1991), which could not be explained by an increased opioid activity (Lautenbacher et al. 1990), also correspond with the assumption of a small fibre neuropathy.

As polyneuropathies often produce a distal-proximal pattern of deficits, we decided to test small fibre functions at distal and proximal sites in eating disorder patients and expected to find stronger deficits at the distal site. Thermal sensitivity measurement has become a standard diagnostic approach in testing small fibre functions (Lindblom and Tegnér 1985; Claus et al. 1987; Ziegler et al. 1988a, b; Strian 1990); we therefore assessed warmth and cold thresholds in addition to the pain threshold. Finally, to have a comparable somatosensory test for large fibre functions, the threshold for vibration sensitivity was also measured.

Offprint requests to: J.-C. Krieg

Table 1. Descriptive statistics (mean, SD) of the clinical, endocrine and metabolic data and local skin temperature for the anorectic (AN, $n = 9$) and the bulimic (BN, $n = 10$) patients and the control subjects (CO, $n = 10$) as well as the results of the analysis of variance and *t*-tests

	Anorexia nervosa	Bulimia nervosa	Control subjects	Test
Age (years)	23.1, 5.2	21.9, 3.6	22.3, 3.6	
Duration of illness (years)	2.3, 2.1	6.3, 4.7	–	B
Height (cm)	167.0, 4.2	165.1, 5.9	166.2, 5.9	
Weight (kg)	40.3, 3.2	56.7, 4.2	55.4, 5.0	A, B, C
Percentage of ideal body weight[a] (%)	70.3, 7.0	100.1, 10.8	98.0, 6.1	A, B, C
T3 (ng/ml)	0.91, 0.18	1.03, 0.21	1.53, 0.38	A, C, D
β-HBA (μmol/ml)	0.07, 0.16	0.29, 0.34	0.04, 0.03	a, d
Skin temp. (°C)				
Hand	27.0, 2.3	28.5, 2.9	29.5, 1.0	c
Foot	23.7, 2.3	24.0, 0.98	24.4, 1.6	

One-way analysis of variance (a, A): AN, BN, and CO; *t*-tests (B): AN vs BN; (c, C): AN vs CO; (d, D): BN vs CO; Significance levels: (a, c, d): $P \leq 0.05$; (A, B, C, D): $P \leq 0.01$

[a] Computed according to the tables of the Metropolitan Life Insurance Company (1959)

To ensure the assessment of early stages of a peripheral polyneuropathy, only patients without manifest symptoms were studied.

Patients and Methods

The subjects were nine patients with anorexia nervosa, ten patients with bulimia nervosa, and ten healthy controls (all females). All patients fulfilled the respective DSM-III-R criteria (American Psychiatric Association 1987). Subjects with other additional psychiatric or somatic disorders, substance abuse or long-term medication were excluded. A thorough clinical neurological examination was performed on all subjects by a trained neurologist; no patient had manifest peripheral neurological symptoms, which would have resulted in exclusion from the study. Table 1 gives details of the three groups. The age distribution was similar in all three groups, but the bulimic patients had a longer duration of illness than the anorectic patients. The anorectic patients were, in contrast to the bulimic patients and the control group, severely underweight. Eight of the anorectic patients controlled their weight only by fasting and one also by occasional vomiting. Two of the anorectic patients had had bulimic episodes. In the bulimic group the number of binges ranged from 1 to 28 per week with a median of 6 (binge frequency was assessed in the 1st week of hospitalization).

Owing to possible menstrual variations in pain sensitivity (Hapidou and DeCatanzaro 1988) the control subjects were studied only during the first 14 days of their menstrual cycle to control for this factor. This type of control was impossible in the eating disorder patients because of amenorrhoea or oligomenorrhoea.

All patients were studied at the beginning of the behaviour therapy program which is generally started in the 1st week after hospital admission and which concentrates on weight gain and normalization of the disturbed eating behaviour. No patient received any drug treatment. All subjects gave written informed consent.

Examination sessions for patients and controls started at 7.30 a.m. with collection of a blood sample for the biochemical analyses. Triiodothyronine (T3) was assessed as an indicator for prolonged fasting, and β-hydroxybutyric acid (β-HBA) to gain information about the patients' fasting state at the time of the investigation (Pirke et al. 1985). T3 was measured by radioimmunoassay (Serono, Freiburg, FRG) as described earlier (Heufelder et al. 1985); interassay variability was 6.2% at an average concentration of 1.1 ng/ml T3. β-HBA was measured according to Williamson and Mellonby (1974); interassay variability was 3.6% at 0.150 μmol/ml.

From 8.15 a.m. on, thresholds for pain, warmth, cold and vibration were measured in this sequence on the hand and foot. Thermal and pain thresholds were obtained with a PATH-Tester MPI 100 [Phywe Systeme, Göttingen, FRG; for details, see Galfe et al. (1990)]. For measurement on the hand (proximal site), subjects placed the thenar of the right hand on the thermode. For measurement on the foot (distal site), the thermode was attached to the right lateral dorsum pedis with the long edge at a distance of about 1 cm from the toes. Vibratory thresholds were assessed by a vibrameter [Somedic, Stockholm, Sweden; for details, see Goldberg and Lindblom (1979)]. The two sites for threshold determination were proximally the dorsum of the metacarpal bone of the first index finger and distally the dorsomedial aspect of the first metatarsal bone.

For determination of the pain threshold, eight heat stimuli were applied with a rate of temperature change of 0.7°C/s, beginning at 38°C. The subjects were instructed to press a button as soon as they felt pain. Each time they pressed the button, the temperature returned to the base value at a cooling rate of 1.5°C/s. The pain threshold was calculated as the mean of the peak temperatures of the last five stimuli. The start of each trial was announced visually and acoustically, but the stimulus was presented with a pseudo-randomized delay between 1 and 3 s.

To measure the warmth and cold threshold, seven warm stimuli and then seven cold stimuli were administered, starting at a temperature of 32°C. The rate of the temperature change was again 0.7°C/s. The subjects had to press a button as soon as they noticed a change in temperature. Thereupon, the temperature returned to the base value (cooling rate: 1.5°C/s). The mean differences between the base temperature and the peak temperature in the two sets of seven trials were the measures of the warmth and cold thresholds.

The vibration thresholds were determined by increasing the vibration amplitude from zero until the subjects felt the vibration for the first time (vibration perception threshold, VPT), and then, by decreasing the stimulus strength from a slightly supraliminal level until the sensation disappeared (vibration disappearance threshold, VDT). The average of VPT and VDT – measured in three trials – was taken as the vibration threshold.

As somatosensory thresholds partially depend on the basal skin temperature, skin temperature near the thermode placement was assessed by a PT-100 sensor.

A two-way analysis of variance was computed to determine (a) group differences (factor "group"), (b) site of measurement (factor "site") differences and (c) "group" × "site" interaction effects for pain, warmth, cold and vibration thresholds. Interaction effects were expected to be significant if there were more pronounced sensory deficits at the distal sites in the eating disorder patients than in the controls. For all other data a one-way analysis of variance was performed. When only two groups were compared, *t*-tests were used. All *P*-values were computed for a two-sided testing.

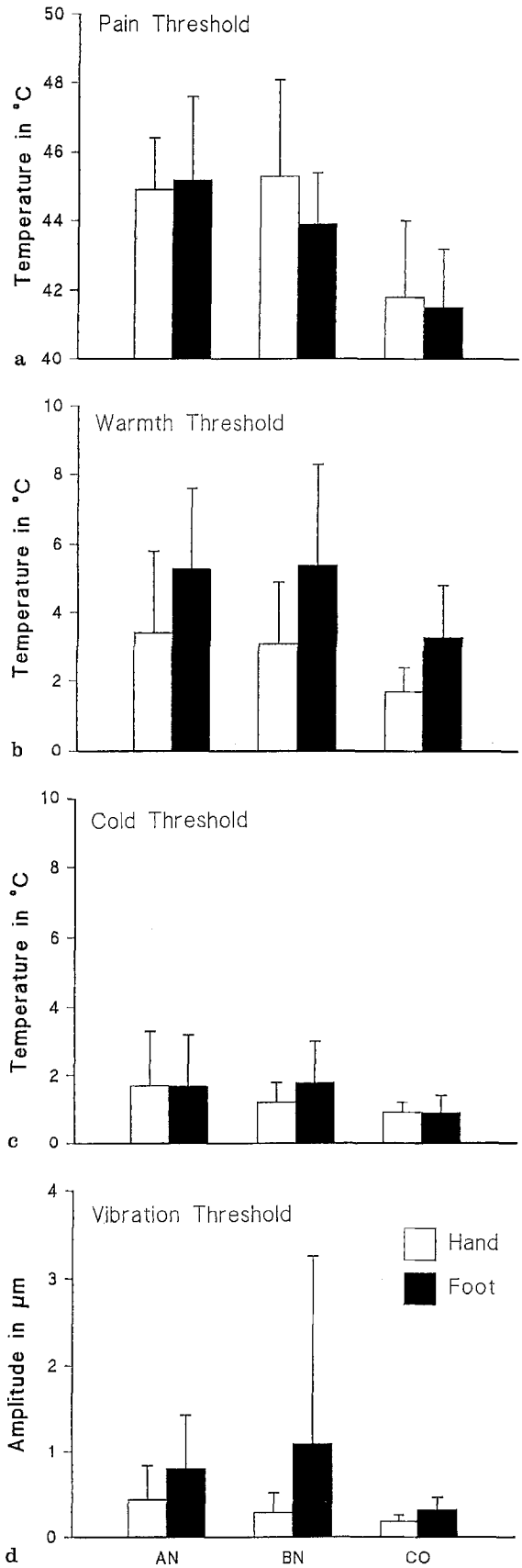

Fig. 1a–d. Mean and standard deviations of (**a**) pain threshold, (**b**) warmth threshold, (**c**) cold threshold and (**d**) vibration threshold at hand (*open bar*) and at foot (*solid bar*) for the patients with anorexia nervosa (AN, $n = 9$), and bulimia nervosa (BN, $n = 10$) and for the control subjects (CO, $n = 10$)

Results

The very significantly lower T3 values of the patient groups compared with the controls and the significantly increased β-HBA values in the bulimic group suggest that both anorectic and bulimic patients had a period of prolonged fasting prior to our study, but that only the bulimic patients were in an acute fasting state at the time of the investigation (Table 1; Pirke et al. 1985).

Analysis of variance showed that the groups differed significantly in pain thresholds (Table 2, Fig. 1a). This was due to significantly higher pain thresholds of the anorectic and the bulimic patients compared with the controls, as evidenced by the results of the *t*-test ($P \leq 0.01$ for the two groups comparisons on the hand and foot, respectively). There were no significant differences among the three groups when comparing warmth, cold and vibration thresholds (Table 2, Fig. 1b–d).

Furthermore, there were no significant "group" × "site" interactions (Table 2). Therefore, there is no convincing evidence for a stronger affection on distal sites in the patient groups compared with the control group. (Site differences between hand and foot in the warmth threshold – as observed – are a well-known phenomenon; Table 2).

The anorectic patients had elevated warmth thresholds on the foot and bulimic patients had elevated warmth thresholds on the hand and increased cold thresholds on the foot, compared with the control subjects (*t*-test, $P \leq 0.05$ for the reported group comparisons, respectively). But these results seem to be rather tendentious, because they are due to only a few patients in each group.

Significant group differences in skin temperature (with the exception of a small difference between the anorectic and control subjects on the hand) were not found (Table 1).

Discussion

Our results on warmth, cold and vibration thresholds suggest that in anorectic and bulimic patients without clinical neuropathic symptoms small- and large-diameter nerve fibre functions are unimpaired in most cases. Furthermore, we did not observe a distal-proximal pattern of somatosensory deficits with a greater involvement of the lower than of the upper extremities – a pattern which is well known in a variety of peripheral polyneuropathies (Neundörfer et al. 1987; Strian 1990;). The finding of reduced pain sensitivity as the outstanding somatosensory deficit in eating disorder patients also contradicts the assumption of a peripheral polyneuropathy. For example, in peripheral polyneuropathy due to diabetes mellitus, thermal thresholds are much more affected than pain thresholds (Ziegler et al. 1988a, b; Levy et al. 1989). Whether the few patients with elevated thermal thresholds really had small fibre dysfunctions or whether the threshold elevations in these cases were due to a more general perceptual deficit remains to be clarified. Taken together, our results do not support our hypothesis of a subclinical polyneuropathy in anorexia

Table 2. Results of the two-way analysis of variance for the factor "group" with anorectic patients ($n = 9$), bulimic patients ($n = 10$) and control subjects ($n = 10$), for the factor "site" with hand and foot and for the interactions between both factors

Effects	Group			Site			Group × site		
	df	*F*	*P*	*df*	*F*	*P*	*df*	*F*	*P*
Thresholds									
Pain threshold	26,2	8.9	0.001	26,1	2.2	0.148	26,2	2.7	0.086
Warmth threshold	26,2	3.1	0.063	26,1	32.0	< 0.001	26,2	0.3	0.744
Cold threshold	26,2	1.7	0.206	26,1	2.6	0.119	26,2	2.1	0.139
Vibration threshold	26,2	1.0	0.376	26,1	3.9	0.059	26,2	0.8	0.445

and bulimia nervosa, which mainly affects small-diameter nerve fibres, and which may be a first step towards a manifest neuropathy.

The cause of the reduced pain sensitivity, which we have now observed in repeated experimental trials performed on different samples of eating disorder patients, is still totally unclear. The possibility that a mere starvation effect is responsible for the reduced pain perception is also unlikely because the results of a subsequent study on fasting healthy women do not support such an explanation (Lautenbacher et al., in press).

The trend for there to be a lower skin temperature in the patients with anorexia nervosa deserves some comments. In healthy subjects the thresholds of warmth, cold, vibration and heat pain depend only to a small degree on the skin temperature of the site of stimulation when the physiological temperature range is not exceeded (Croze et al. 1977; Halonen 1986; Verrilo and Bolanowksi 1986; Kojo and Pertovaara 1987; Sosenko et al. 1989). From this point of view, the tendency towards a decreased skin temperature in the anorectic patients can hardly explain the markedly increased pain thresholds in these patients. In our earlier study, however, we found a strong inverse relationship between skin temperature and heat pain threshold in the anorectic patients (Lautenbacher et al. 1991). This relationship has not been observed in the control subjects, which points to the possibility that disturbances of thermoregulation and pain sensitivity may be linked in anorectic patients and to the need for parallel investigations in future studies.

From another point of view, the reduced pain sensitivity in most of the patients and the reduced thermal sensitivity in a few of them is also remarkable. Regardless of the underlying mechanism, disturbances of the somaesthetic sensitivity in eating disorder patients – also demonstrated for tactile perception by Florin and coworkers (1988) – have to be related to the well-known phenomenon of body image distortion. The close association between cognitive, affective and sensory factors in the pathogenesis of body image distortion has recently been stressed by Cutting (1989). Therefore, a consideration of "neurological" deficits may help to understand so-called "genuine psychiatric" symptoms such as "distorted body image" in eating disorder patients.

In conclusion, a peripheral polyneuropathy affecting small or large afferent fibres due to an eating disorder seems to be a rare event. As has been demonstrated, subclinical deficits may occur in some patients. Hence, the results of this study were in good agreement with those of other authors (Slettebo et al. 1984; Alloway et al. 1985; MacKenzie et al. 1989) which showed that objective findings of a neuropathy seem to be confined to long-standing and severely ill cases. In contrast, a reduced pain sensitivity again proved to be a valid feature of patients with anorexia and bulimia nervosa, irrespective of the occurrence of neuropathic deficits.

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