Pain Sensitivity in Anorexia Nervosa and Bulimia Nervosa

Stefan Lautenbacher, Andrejs Michaels Pauls, Friedrich Strian, Karl-Martin Pirke, and Jürgen-Christian Krieg

Pain threshold was measured with short heat stimuli using a contact thermode in 19 patients with anorexia nervosa, 20 patients with bulimia nervosa, and 21 control subjects. Both patient groups had significantly elevated pain thresholds compared with the control subjects. In the total sample, no substantial covariation could be demonstrated among pain threshold and clinical, physiological, metabolic, or psychological data. However, in separate regression analyses pain threshold correlated significantly (negatively) with local skin temperature in the anorectic patients and almost significantly (positively) with body weight in the bulimic patients. This finding suggests that the reduced pain sensitivity in the two kinds of eating disorders might have different causes.

Introduction

In a previous study we reported on reduced heat pain sensitivity in patients with bulimia nervosa and in some patients with anorexia nervosa (Lautenbacher et al 1990). Because of accounts of increased plasma and cerebrospinal fluid levels of β-endorphin in eating disorder patients (Brambilla et al 1985; Fullerton et al 1986; Pickar et al 1982), we had hypothesized that an opioid mechanism might be responsible for the reduced pain sensitivity. However, an application of naloxone (5 mg, IV; double blind with naloxone and saline) did not reverse the elevated pain thresholds (Lautenbacher et al 1990). Moreover, the activity of the hypothalamic–pituitary–adrenal axis did not seem to be involved in the development of reduced pain sensitivity, as was indicated by a lack of correlation between plasma cortisol and pain threshold. Therefore, our findings were not comparable to those of Abraham and Joseph (1987) who, in a single case study of bulimia nervosa, reported a naloxone reversible and cortisol correlated change of pain sensitivity immediately after vomiting.

The aim of the present study was twofold: (1) to study pain sensitivity in an enlarged sample of eating-disorder patients especially in order to determine whether patients with anorexia nervosa indeed display a reduced pain sensitivity; (2) to conduct a systematic search for covariates, as the cause of the reduced pain sensitivity is still completely

From the Department of Psychiatry, Max Planck Institute for Psychiatry, Clinical Institute, Munich, Federal Republic of Germany.
Address reprint requests to PD Dr. med. Jürgen-Christian Krieg, Max Planck Institute for Psychiatry, Kraepelinstr. 10, D-8000 Munich 40, Federal Republic of Germany.
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unclear. Variables included were anamnestic data, body measures, and β-hydroxybutyric acid and triiodothyronine as indicators of intermittent and prolonged dieting (Pirke et al 1985). In addition, the local skin temperature at the site of pain stimulation was measured to evaluate a possible influence of changes in peripheral thermoregulation. Finally, state anxiety, which is often increased in psychiatric patients, was assessed because of its well-known impact on pain perception.

Method

Subjects

Nineteen inpatients with anorexia nervosa, 20 inpatients with bulimia nervosa, and 21 healthy controls (all Caucasian females) took part in the study. The diagnosis of the eating disorder was made according to the DSM-III-R criteria (American Psychiatric Association 1987). Subjects with other psychiatric and somatic disorders, substance abuse, or long-term medication use were excluded. Table 1 gives the clinical description of the three groups. The age distribution was similar in all three groups of subjects, but the bulimic patients had a slightly longer duration of illness than the anorectic patients. The anorectic patients were not only severely underweight but also slightly shorter than the bulimic patients and the controls. Twelve of the bulimic patients had a history of anorexia nervosa and five of the anorectic patients had had bulimic episodes. In the bulimia nervosa group the number of binges ranged from 1 to 28 per week with a median of 6.5.

All patients were studied at the beginning of a behavior therapy program that generally begins in the first week after hospital admission (some of the anorectic patients had had a preceeding short refeeding program to overcome severe malnutrition). No patient received drug treatment during the study or in the course of therapy. The protocol was approved by an ethics commission; all subjects gave written informed consent.

Apparatus and Procedure

Sessions started at 7:30 AM with the collection of a blood sample for the biochemical analyses. Triiodothyronine (T3) was measured by radioimmunoassay (SERONO, Freiburg) as described earlier (Heufelder et al 1985). Interassay variability was 5.6% at an average concentration of 1.1 ng/ml T3. β-hydroxybutyric acid (β-HBA) was measured according to Williamson and Mellonby (1974). Interassay variability was 5.1% at 0.53 μmol/ml.

At about 8:00 AM state anxiety was measured with the STAI-X1 (Spielberger et al 1970). Then pain thresholds were assessed with heat stimuli applied to the lateral dorsum pedis of the right leg by a Peltier thermode (stimulation area: 6 cm^2; contact pressure: 0.4 N/cm^2). The subjects had to stop a temperature rise of 0.7°C/sec starting from 38°C as soon as they felt pain. Eight trials were completed. The threshold was computed as the mean of the peak temperatures of the last five trials. The apparatus used was the pain and thermal sensitivity diagnosis unit PATH-Tester MPI 100 (Phywe Systeme GmbH). Due to a high degree of standardization (instructions to the subject, guidelines for the investigator, etc.) retest reliability coefficients of about 0.80 were repeatedly achieved with this unit (Galfe et al 1990). Skin temperature near the thermode placement was assessed by a PT100 sensor in three readings during pain threshold assessment.

Menstrual variations in pain sensitivity and opioid activity (Hapidou and De Catanzaro

Table 1. Descriptive Statistics (Mean ± SD) of the Clinical Data, Endocrine and Metabolic Variables, Anxiety, Local Skin Temperature, and Pain Threshold for the Anorectic (A, n = 19) and the Bulimic (B, n = 20) Patients and the Control Subjects (C, n = 21) As Well As the Results of the Analysis of Variance (One-Way ANOVA) and Duncan Tests (for Post-Hoc Comparisons)

	Anorexia nervosa	Bulimia nervosa	Control subjects	Test	
Parameter	A	B	C	Comparison	p value
Age (years)	22.9 ± 4.3	22.2 ± 3.4	22.7 ± 3.3		
Duration of illness (years)	3.4 ± 2.7	5.8 ± 3.9	—	A vs B[a]	$p \leq 0.05$
Height (cm)	164.7 ± 4.9	169.0 ± 7.2	168.4 ± 6.0		
Weight (kg)	38.3 ± 3.5	58.5 ± 7.0	56.9 ± 4.2	A vs B vs C	$p \leq 0.01$
				A vs B	$p \leq 0.01$
				A vs C	$p \leq 0.01$
Ideal weight (%)[b]	68.5 ± 6.6	97.8 ± 11.7	98.0 ± 4.9	A vs B vs C	$p \leq 0.01$
				A vs B	$p \leq 0.01$
				A vs C	$p \leq 0.01$
T3 (ng/ml)	0.92 ± 0.18	1.11 ± 0.26	1.48 ± 0.31	A vs B vs C	$p \leq 0.01$
				A vs B	$p \leq 0.05$
				A vs C	$p \leq 0.01$
				B vs C	$p \leq 0.01$
β-HBA (μmol/ml)	0.25 ± 0.64	0.25 ± 0.32	0.04 ± 0.05		
Skin temperature (°C)	25.3 ± 2.8	25.2 ± 1.5	25.7 ± 2.1		
Anxiety (STAI-X1)	48.7 ± 13.4	45.9 ± 11.9	34.0 ± 7.8	A vs B vs C	$p \leq 0.01$
				A vs C	$p \leq 0.01$
				B vs C	$p \leq 0.01$
Pain (°C)	44.5 ± 2.4	44.4 ± 1.5	42.2 ± 1.6	A vs B vs C	$p \leq 0.01$
				A vs C	$p \leq 0.01$
				B vs C	$p \leq 0.01$

[a]t-test used.
[b]Computed according to the tables of the Metropolitan Life Insurance Company (1959).

1988; Veith et al 1984) were controlled by studying the control subjects only during the first 14 days of their menstrual cycle. This type of control was impossible in the patients because of oligomenorrhea or amenorrhea. Due to procedural and technical problems not all measures could be assessed in all subjects.

Results

The analysis of variance (One-way ANOVA) showed that the groups differed significantly regarding pain thresholds (see Table 1). This was caused by significantly higher pain thresholds of the anorectic as well as the bulimic patients compared to the controls as evidenced by the results of the Duncan test for differences between the respective two groups.

In order to find the best predictors of the pain threshold, a multiple regression analysis (STEPWISE FORWARD) was conducted with all variables of Table 1 (in computations including the control subjects the duration of illness was excluded). This approach was chosen because the predictors could not be assumed to be uncorrelated. Only the three predictors with the lowest probability of their respective F value were admitted to enter

Table 2. Multiple Regression Analysis With Partial and Multiple Correlations Between the Pain Threshold (Dependent) and the Set of Best Predictors (All Variables of Table 1 Included With the Exception of Duration of Illness in Computations With Control Subjects); See Results Section for Further Explantation

Group	Partial correlation			Multiple correlation
	Skin temperature	Age	T3	
Anorexia nervosa	$r = -0.60$	$r = 0.38$	$r = 0.32$	$r = 0.67$
($n = 19$)	$p = 0.014$	$p = 0.149$	$p = 0.220$	$p = 0.037$
	Weight	Skin temperature	Age	
Bulimia nervosa	$r = 0.48$	$r = 0.31$	$r = -0.28$	$r = 0.63$
($n = 20$)	$p = 0.060$	$p = 0.249$	$p = 0.295$	$p = 0.062$
	Skin temperature	T3	β-HBA	
Anorexia and bulimia	$r = -0.21$	$r = 0.21$	$r = -0.14$	$r = 0.35$
combined ($n = 39$)	$p = 0.230$	$p = 0.232$	$p = 0.420$	$p = 0.229$
	Height	T3	Skin temperature	
Control subjects	$r = 0.28$	$r = -0.28$	$r = 0.22$	$r = 0.51$
($n = 21$)	$p = 0.268$	$p = 0.275$	$p = 0.395$	$p = 0.206$

the regression equation; computation was done separately for each group and for the combined group of patients. The result is given in Table 2. The resulting predictor sets showed substantial multiple correlations with the pain threshold only, with the patients' groups analyzed separately (significant for the anorectic patients and near significant for the bulimic patients). However, the variables in the set of the best predictors differed between these two groups. The highest partial correlations were found in the anorectic group for local skin temperature (negative) and in the bulimic group for body weight (positive). Admitting two or four predictors to enter the regression equation did not change the results for these two variables (partial correlations with 2 or 4 predictors; local skin temperature in the anorectic group: $r = -0.55$ or $r = -0.58$; body weight in the bulimic group: $r = 0.50$ or $r = 0.51$).

Discussion

The findings of the present study clearly demonstrate that not only bulimic patients but also anorectic patients have a reduced pain sensitivity. The validity of these results, especially with regard to the anorectic patients has not yet become clear, because in our former study (Lautenbacher et al 1990) using a smaller sample, we gained only tendentious results. The finding of reduced pain sensitivity despite significantly higher anxiety levels in both patients' groups (see Table 1) appears even more valid, as anxiety is known to increase pain sensitivity in most cases (Kleinknecht 1986).

The single case study of Abraham and Joseph (1987) and our studies have been the first attempts to study pain sensitivity in anorexia and bulimia nervosa. The computation of a regression analysis was initiated to generate plausible hypotheses about the causation of the reduced pain sensitivity because an experimentally validated explanation cannot be offered at the moment. These limitations must be kept in mind when discussing the following: It appears that different mechanisms in the anorectic and bulimic patients are responsible for the phenomenon of reduced pain sensitivity. The best predictor of the pain threshold was the body weight in the group of patients with bulimia nervosa with a positive partial correlation of 0.48 (nearing significance because of the small sample). This finding allows one to assume that overweight predisposes bulimic patients to reduced pain sensitivity. Reduced pain sensitivity has also been observed in obese subjects (Zahorska-Markiewicz et al 1983, 1988), although contrary findings on this topic do exist (McKendall and Haier 1983; Pradalier et al 1981). Nevertheless, with regard to pain sensitivity, it seems more appropriate to relate bulimia nervosa to obesity than to anorexia nervosa. Our finding that the increased pain threshold in bulimic patients could not be reversed to normal by naloxone (Lautenbacher et al 1990) might also be of interest with respect to obese subjects, as hyperendorphinemia was hypothesized as the cause of reduced pain sensitivity in these patients. This assumption, however, has not yet been experimentally proven (Zahorska-Markiewicz et al 1983, 1988).

The significant negative partial correlation of pain threshold and local skin temperature in the anorectic patients points to an association between the changes of thermoregulatory capacities found in anorexia nervosa patients and the reduction of pain sensitivity. Normally, the local skin temperature does not influence pain sensitivity to a great degree, as seen in our control subjects and in other studies (Croze et al 1977; Kojo and Pertovaara 1987). The complexity of thermoregulatory changes in anorectic patients (Freyschuss et al 1978) makes it difficult to explain why anorectic patients with low skin temperature had high pain thresholds. Merely that a reduced blood supply of the peripheral afferents was the underlying mechanism of reduced pain sensitivity in the anorectics is not likely because they did not differ in local skin temperature from the control subjects as a group, and we did not observe a comparable alteration of sensitivity in other somatosensory modalities (warmth, cold, vibration; unpublished data). One may speculate that central or peripheral sympathetic functions that are altered in anorectic patients (Freyschuss et al 1978; Nudel et al 1987, Pirke et al 1985) are the links influencing both pain sensitivity and skin temperature. But the influence of sympathetic activity on pain sensitivity under nonneuropathological conditions is still a matter of controversy (Jänig 1985; Lovick 1986). An interesting finding, in this context, was reported in a study on thermoregulatory behavior by Luck and Wakeling (1982): Some patients with anorexia nervosa choose temperatures of 44°C and more when putting their hands in a water bath and being asked to rate the most pleasant temperature. Such temperatures are normally felt as very hot or even painful. The authors interpreted this as a sign that a centrally mediated displacement of the set-point for the preferred temperature was not sufficiently limited in the upper range due to disturbed pain sensitivity. However, pain sensitivity was not tested in this experiment. It must be stressed that a relationship between thermoregulation and heat pain sensitivity would be characteristic for patients with anorexia nervosa as Croze and co-workers (1977) convincingly showed that the heat pain threshold is not affected by variations of the skin and the core temperature in normal subjects.

Future research should be guided by the hypothesis that reduced pain sensitivity in anorexia nervosa patients is linked with disturbances in thermoregulation. Therefore, measures of both skin and core temperature should be used and experimentally manipulated, and the association with neuroendocrine indicators of thermoregulation should be studied.

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