Pain Perception in Depression: Relationships to Symptomatology and Naloxone-Sensitive Mechanisms

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A decrease in pain sensitivity during acute depression has been observed in several studies, apparently related to the severity of symptomatology. However, the question remains whether this relationship can be found only in heterogeneous groups of depressive patients or also in a single diagnostic group, such as major depression. In the present study, pain thresholds were assessed in 20 patients with major depression (DSM-III-R) and in 20 healthy controls. Two threshold methods with a differing impact of reaction time on the results were used. Contact heat was applied as a natural source of pain. With both methods the pain thresholds were significantly increased in the depressive patients. No relationship was found to the various symptoms of depression assessed by psychopathometric scales. In contrast to the pain thresholds, the thresholds of skin sensitivity for nonnoxious stimuli (warmth, cold, vibration) were only slightly increased. In subsamples (N = 10 in each group), naloxone (5 mg IV) and placebo were administered in a double-blind design. No systematic changes in pain thresholds occurred under either treatment. Our findings suggest that the decrease in skin sensitivity in major depression is specific to pain and not due to an increased reaction time. Moreover, the decrease appears to be related neither to a naloxone-sensitive mechanism nor to symptomatology.

Key words: major depression, pain perception, somatosensation, naloxone.

INTRODUCTION

Depression and pain appear to be closely related. This view stems mainly from research that investigates the mutual influences of depression and chronic pain (1). On the one hand, depression constitutes a state of increased vulnerability to pain problems and changes the way one deals with them (2, 3). On the other hand, chronic pain is frequently accompanied by depressive symptoms, and it sometimes leads to a full-blown depressive disorder (4, 5).

But, depression also has another relationship to the pain system: It seems to reduce pain sensitivity. (Previous studies of this relationship are cited later on.) Hence, the influence of depression on the pain system appears to be somewhat paradoxical because both an increase in clinical pain problems and a decrease in experimental pain sensitivity have been observed.

Hall and Stride (6) reported as early as 1954 on an increased pain threshold for radiation heat in depressive patients. This phenomenon was especially distinct in patients with endogenous depression. The authors considered two types of causation. First, depression might represent a general state of perceptual unresponsiveness, with diminished pain perception being only one example. Second, depression might produce an affective indifference to aversive stimulation that is not based on a truly sensory deficit.

It now seems unlikely that there is a generalized perceptual unresponsiveness; von Knorring (7, 8) found no difference between depressive patients and healthy controls for the electrical detection threshold but did find a significant difference for the pain threshold, suggesting that the effect of depression is specific to pain. In support of an affective indifference as the cause, Ben-Tovim and Schwartz (9) observed that in a group of depressive patients only those with the symptom "emotional indifference" had increased electrical pain thresholds. Furthermore, Davis et al. (10), using electrical stimulation and signal detection analysis of the results, provided some evidence that stoic responses, rather than a sensory deficit, underlies the pain insensitivity in depression. Their results seem to corroborate the "emotional indifference" hypothesis. However, there have also been other outcomes with the signal detection approach (11, 12), and a too straightforward interpretation of the signal detection parameters as reflecting the sensory and affective components of the pain response may be misleading (13).

Currently, it has seemed highly likely that the

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Received for publication March 19, 1993; revision received July 27, 1993.

degree of illness severity and the type of symptomatology are major influences, as suggested by the findings of Hall and Stride (6). Von Knorring (8) demonstrated that patients with psychotic symptoms had higher electrical pain and tolerance thresholds than those without. He and other authors found that patients with psychomotor retardation were less pain sensitive than agitated patients (7, 14). Otto et al. (15) did not find a change in experimental pain parameters in their study of mild forms of depression. Furthermore, Hall and Stride (6) and von Knorring (16) reported normalized pain sensitivity in individuals who had recovered from depression.

The perceptual deficit has appeared to be specific to pain and dependent on symptomatology. One shortcoming of the studies conducted so far has been that the diagnostic procedures either were not described explicitly or did not correspond to contemporary norms. Therefore, one aim of the present investigation was to study the relationship between pain sensitivity and illness severity in a clearly defined group, in this case patients diagnosed as having major depression according to DSM-III-R (17).

Another problem with past studies has been the choice of the stimulation methods used. Electrocutaneous stimulation was applied in most of the studies (7–10, 14, 16), which leads to artificial pain sensations and therefore might not be fully suitable for the study of psychiatric patients. The importance of this methodological issue is especially evident if we look at a study done by Merskey (18). Merskey used a pressure algometer and found, in contrast to the authors just cited, that healthy controls had higher pain and tolerance thresholds than depressive patients. Therefore, a study of depressive patients seemed in order, using a stimulation method that produces natural pain sensations with state-of-the-art methodology. This led us to apply contact heat with a Peltier thermode (19, 20).

An additional aim of our study was to consider the possible role of the perceptual processing speed. For this reason we used two methods to assess heat pain thresholds, one that is dependent on the reaction time and another that is not. Moreover, some of the findings reported suggest that the decrease in pain sensitivity is not due to a generalized deficit in somatosensory perception. To broaden the basis for this conclusion, we assessed several somatosensory modalities (warmth, cold, vibration).

Finally, and perhaps most important, we wanted to shed some light on the mechanisms of causation. Davis et al. (10) proposed "studies with narcotic antagonists in depressed pain-tolerant patients." However, none of the subsequent studies has included this or any other pharmacological strategy of investigation. Although an opioidergic causation of depression is now, after a phase of enthusiastic speculation, considered unlikely, the possibility of opioid dysfunctions in certain spinal or cerebral systems has not yet been dismissed (21, 22). Considering the great importance of opiates and opioids for analgesic changes, an attempt that follows this line of reasoning seemed worthwhile, at least as a first step. Therefore, we decided to study pain sensitivity before and after the administration of the opiate antagonist naloxone in a subsample of the depressive patients.

METHODS

Subjects

The subjects were 20 patients (8 women and 12 men) with the DSM-III-R diagnosis of a major depression (17) and 20 healthy controls matched for age and sex. The patients' diagnoses were confirmed by the Structured Clinical Interview for DSM-III-R (23). In addition, a score of more than 18 on the Hamilton Depression Scale (24) was required. Subjects were excluded from the study if they suffered from an additional psychiatric disorder, an organic mood syndrome (e.g. due to an endocrine disorder), if there was evidence of a psychoactive substance use disorder, or if there were clinical signs of disk disease, neuropathy, hypertension, or dermatosis at the site of somatosensory stimulation. The patients were studied in the first 2 weeks after admission and before initiation of any pharmacological treatment. Six patients were on antidepressant medication at admission (fluvoxamine, doxepin, dibenzepin, clomipramine, and two on maprotiline). These patients underwent a 7- to 12-day washout period, the duration of which was at least three times the half-life of the respective drug and its active metabolite. Table 1 gives a descrip-

TABLE 1. Basic and Psychopathometric Description and Local Skin Temperature at the Site of Threshold Assessment of Depressive Patients and Healthy Controls (mean ± SD)

	Depressive Patients (N = 20/8 W, 12 M)	Healthy Controls (N = 20/8 W, 12 M)
Age	36.9 ± 12.0	36.2 ± 11.0
Hamilton Depression Scale	25.1 ± 5.0	
IMPS-PHS	0.0 ± 0.0	
IMPS-OPS	6.1 ± 3.6	
IMPS-DS	32.2 ± 8.0	
IMPS-MS	1.6 ± 2.5	
Depression Scale*	31.1 ± 8.9	2.2 ± 2.3
Complaint List*	34.5 ± 15.0	5.6 ± 7.3
STAI-X1*	57.7 ± 13.3	31.7 ± 5.9
Skin Temperature (°C)**	27.7 ± 2.5	29.9 ± 2.7

* $p < 0.001$, t test (one-tailed); ** $p < 0.01$, t test (two-tailed). IMPS-PHS = IMPS-Paranoid-Hallucinatory Syndrome; IMPS-OPS = IMPS-Other Psychotic Symptoms; IMPS-DS = IMPS-Depressive Syndrome; IMPS-MS = IMPS-Manic Syndrome.

tion of the samples. The protocol was approved by an ethics commission; all subjects gave written informed consent.

Apparatus and Procedure

The physical examination and one part of the psychopathometric assessment took place 1 or 2 days before the first test session. The assessment included observer ratings on the Hamilton Depression Scale (HDS) (21-item version) (24) and on the Inpatient Multidimensional Psychiatric Scale (IMPS) (25). The IMPS measures 12 basic psychopathological dimensions, which can be grouped into four categories to describe psychiatric syndromes (paranoid-hallucinatory syndrome, other psychotic symptoms, depressive syndrome, manic syndrome).

All patients and controls took part in a first test session (day 1), at the beginning of which pain sensitivity and somatosensation were tested under baseline conditions. Ten patients of each group were also subjects in a second test session on another day (day 2), with a maximum interval of 3 days. Two test sessions were necessary to evaluate the effect of the opiate antagonist naloxone. Only a subsample was studied under pharmacological treatment because some patients refused to take part in two sessions, and for other patients a further delay in antidepressant treatment seemed inappropriate.

In the subgroups with two sessions, naloxone and placebo were administered in a double-blind design as used in an earlier study (26), with neither the subjects nor the investigator knowing which treatment was being used. To control for order effects, the order of naloxone and placebo was randomized for the first half of the subjects in each group and then the second half were treated in the reverse order.

To control for any influences of "needle stress" and the expectation of receiving a pharmacological treatment, the subjects with only one session were given a placebo infusion after the baseline evaluation and took part in a "posttreatment" measurement. Thus, in the first session (day 1), the procedures were identical for all subjects.

The sessions always started at 3:30 PM. On day 1, the following scales were given at the beginning of the session: Depression Scale (DS) (27) for the assessment of anxious-depressive mood; Complaint List (CL) (27) for the assessment of somatic and general complaints as reported in particular by psychiatric patients; and the state version of the State-Trait Anxiety Inventory (STAI-X1) (28).

Then two identical blocks of measurements followed, one before and one after the treatment. Each block took approximately 25 minutes. After the first block, 100 ml of saline either with or without 5 mg of naloxone (Narcanti^{R}) was administered IV. A dose of 5 mg was chosen to block the effects of all endogenous opioids; opioids binding on kappa- and delta-receptors can be antagonized only by considerably larger doses than required for opioids binding on mu-receptors, where amounts below 1 mg seem to be sufficient (29). The second block of measurements followed 30 minutes later.

Each block started with the administration of eight visual analog scales for assessment of subjective state. The scales measured tiredness, headache, dryness of mouth, nausea, physical discomfort, bad mood, sensation of warmth, and drowsiness.

The device used for the subsequent tests was the computer-controlled stimulation unit PATH-Tester MPI 100 (Phywe GmbH, Göttingen, Germany) which produces thermal stimuli by a Peltier thermode (stimulation area: 6 cm^2; contact pressure: 0.4 N/cm^2). The long edge of the thermode was attached to the right lateral dorsum pedis at a distance of about 1 cm from the toes.

First, the heat pain threshold was assessed by a method that is to some degree dependent on reaction time (Pain Threshold 1). The pain threshold was determined by having the subject stop a temperature rise of 0.7°C/sec, starting from 38°C, as soon as s/he felt pain. There were eight trials. The threshold was computed as the mean of the peak temperatures of the last five trials.

As indicators of thermal skin sensitivity, warmth and cold thresholds were measured by applying seven warm stimuli and then seven cold stimuli, starting from 32°C. The rate of the temperature change was again 0.7°C/sec. The subject had to press a button as soon as s/he noticed a change in temperature. 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.

Then a second measurement of heat pain threshold was conducted, using a method developed for the present study (Pain Threshold 2). This threshold measure was designed to be free of reaction time influences. The subject had to adjust the temperature to the level of her/his pain threshold with heating and cooling buttons, starting from 38°C. The change in temperature stopped when the subject released the buttons. Therefore, the rate of stimulation was dependent on the subject's speed of adjustment. Seven trials were conducted. The threshold was computed as the mean of the last six trials.

Finally, as an indicator of skin sensitivity to mechanical stimuli, the vibration threshold was assessed by a VIBRA-Tester (Phywe GmbH) (30). The site of threshold determination was the dorsomedial aspect of the first metatarsal bone, where the stimulator was fixed with a contact pressure of 3.7 N/cm^2. The vibration amplitude was increased from zero at a rate of change of 0.2 μm/sec until the subject felt the vibration and pressed a button. There were three trials. Then, in another three trials, the vibration amplitude was decreased at the same rate of change from a clearly supra-threshold value until the sensation disappeared. As Claus (30) suggested, the logarithm of the average of the six trials multiplied by 10 was taken as the vibration threshold.

During each block skin temperature was assessed four times on the dorsal side of the same foot with a PT-100 sensor, and the average was taken.

Evaluation

Inspection of the measures assessed under baseline conditions (psychopathological and psychological measures, pain and somatosensory sensitivity, and skin temperature before the treatment on day 1) led to the conclusion that the use of parametric statistical methods (multivariate (MANOVA), univariate (ANOVA) analyses of variance t test, and Pearson correlation) was justified.

The difference between the measures before and after the treatment was computed to evaluate the treatment effect. The sign of the difference was reversed so that a positive value of this change score indicates an increase of thresholds and a negative value a decrease. These change scores differed clearly in variance between the groups and the treatments. Therefore, nonparametric statistics were used (Wilcoxon signed-ranks test).

One-tailed significance tests were used when directed hypotheses were available, such as "higher pain and somatosensory thresholds as well as more psychopathology in depression," "positive relationship between disease severity and both pain and somatosensory thresholds," and "decrease in pain and somatosen-

sory thresholds under naloxone compared to placebo." In all other cases, two-tailed tests were applied. The alpha-level was 0.05 throughout.

RESULTS

Psychopathology

Of the 20 patients studied, all diagnosed as having a major depression according to DSM-III-R, two had mood-congruent psychotic features. The psychopathology, assessed multidimensionally, is presented in Table 1.

The patients differed highly significantly from the control subjects on those scales administered to both groups (DS, CL, and STAI-X1). With reference to the normal values (25, 27, 28, 31), the patients' high scores on the scales HDS, IMPS-Depressive Syndrome, DS, CL, and STAI-X1 and their low scores on the IMPS scales paranoid-hallucinatory syndrome, other psychotic symptoms, and manic syndrome indicate the presence of a moderate to severe depressive core syndrome but the absence of additional psychopathology. Furthermore, the patients appeared to be suffering from considerable levels of anxious-depressive mood, anxiety, and psychosomatic complaints.

Group Comparisons of Pain and Somatosensory Thresholds

The possible group difference in pain sensitivity between the depressive patients and the healthy controls was evaluated by a multivariate analysis of variance (MANOVA) with the two pain thresholds (Pain Threshold 1 and Pain Threshold 2) as dependent variables. The group effect was significant (Hotelling's test, $F(2, 37) = 3.2$, p (one-tailed) = 0.026). The corresponding mean threshold values are shown in Figure 1.

The univariate tests (ANOVA) conducted subsequently revealed that the difference was based almost equally on the two pain thresholds: Pain Threshold 1, $F(1,38) = 3.0$, p (one-tailed) = 0.047; Pain Threshold 2, $F(1,38) = 6.6$, p (one-tailed) = 0.007. The contribution of Pain Threshold 2 to the overall difference appeared to be slightly greater, suggesting that the increase in pain thresholds in the depressive patients was definitely not due to a prolongation of reaction time.

To test for a group difference in skin sensitivity for nonnoxious stimulation, we computed a second MANOVA with the warmth, cold, and vibration thresholds as dependent variables. No significant group effect resulted (Hotelling's test, $F(3, 35) = 1.6$, p (one-tailed) = 0.102). Figure 2 shows the corresponding mean threshold values and reveals just a trend toward higher thresholds in the depressive patients.

Local skin temperature, a variable of interest when skin sensitivity is under investigation, differed highly significantly between the groups, with lower values for the patients (Table 1). It is unlikely that this effect was caused by the room temperature during testing, because the temperature was about the same on the average in both groups (patients, 22.1°C; controls, 21.6°C).

For none of the variables discussed in this section was there a significant group difference between the

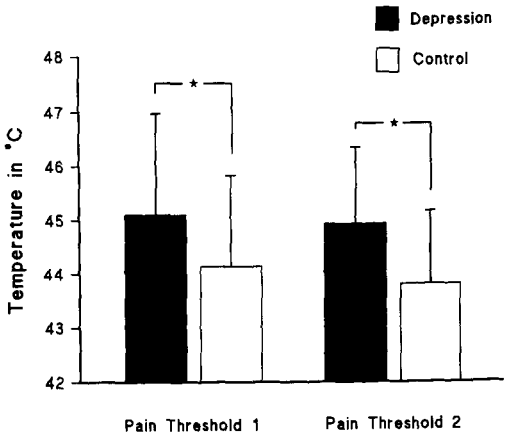

Fig. 1. Mean and standard deviation of Pain Thresholds 1 and 2 in the depressive patients and the healthy controls; $N = 20$ in each group; asterisks indicate significant differences ($p \leq 0.05$) between the pain thresholds of the patients and the control subjects.

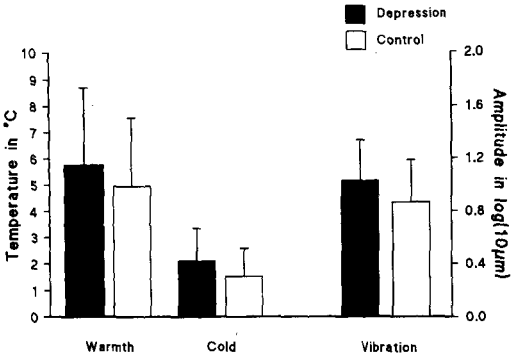

Fig. 2. Mean and standard deviation of the warmth and cold thresholds (*left ordinate*) and the vibration thresholds (*right ordinate*) in the depressive patients and the healthy controls; $N = 20$ in each group.

patients who had not been on medication at admission and those who had been on antidepressant medication and had experienced a washout period.

Correlations of the Pain Thresholds With Other Measures (Patients Only)

The only associations that were evaluated were between the two pain thresholds and (a) the measures of psychopathology and (b) the local skin temperature, because the pain thresholds alone were elevated in the patients. Of the four IMPS syndrome scales, only the depressive syndrome scale had enough variance to allow a correlation computation. The three primary scales contributing to this syndrome scale, anxious depression (mean = 11.0, SD = 4.3), retardation and apathy (mean = 6.0, SD = 3.6), and impaired functioning (mean = 15.2, SD = 2.8), could also be included. The results are given in Table 2. None of the psychopathological measures nor the local skin temperature correlated significantly with either of the two pain thresholds (Table 2).

In the patients with major depression, the severity of depressive symptoms appeared to have no influence on the degree of pain threshold elevation. This is especially noteworthy with respect to the IMPS-retardation and apathy scale because reduced pain sensitivity has been claimed to be associated with psychomotor retardation in depression (see "Introduction"). Although the patients had both elevated pain thresholds and decreased local skin temperature, the relationship between these two measures was not strong.

Effects of Naloxone

The effects of naloxone and placebo were investigated in subgroups of 10 patients and 10 healthy controls. These subgroups did not differ from the other subjects with regard to the pain and somatosensory thresholds under baseline conditions (MANOVA, depressives, pain thresholds: Hotelling's test, $F(2, 17) = 0.5$, p (two-tailed) = 0.642; depressives, somatosensory thresholds: Hotelling's test, $F(3,15) = 0.8$, p (two-tailed) = 0.526; controls, pain thresholds: Hotelling's test, $F(2,17) = 2.2$, p (two-tailed) = 0.142; controls, somatosensory thresholds: Hotelling's test, $F(3,16) = 0.9$, p (two-tailed) = 0.471). This suggests that representative subsamples were obtained.

Treatment effects were evaluated by comparing the change scores for the naloxone and placebo sessions using the Wilcoxon signed-ranks test. The change scores for the pain and somatosensory thresholds are shown in Figure 3, *A* and *B*. It is obvious from the figures that the only substantial

TABLE 2. Pearson Correlations (*R*) Between Pain Thresholds 1 and 2 and the Measures of Psychopathology and the Local Skin Temperature in the Depressive Patients ($N = 20$)

	Pain Threshold 1	Pain Threshold 2
HDS	−0.021	0.329
IMPS-DS	−0.143	0.207
IMPS-ANX	−0.250	0.197
IMPS-RTD	0.041	0.066
IMPS-IMP	−0.074	0.199
DS	0.191	0.267
CL	0.218	0.192
STAI-X1	−0.148	−0.137
Skin Temperature	−0.027	−0.251

IMPS-DS = IMPS-Depressive Syndrome; IMPS-ANX = IMPS-Anxious Depression; IMPS-RTD = IMPS-Retardation and Apathy; IMPS-IMP = IMPS-Impaired Functioning.

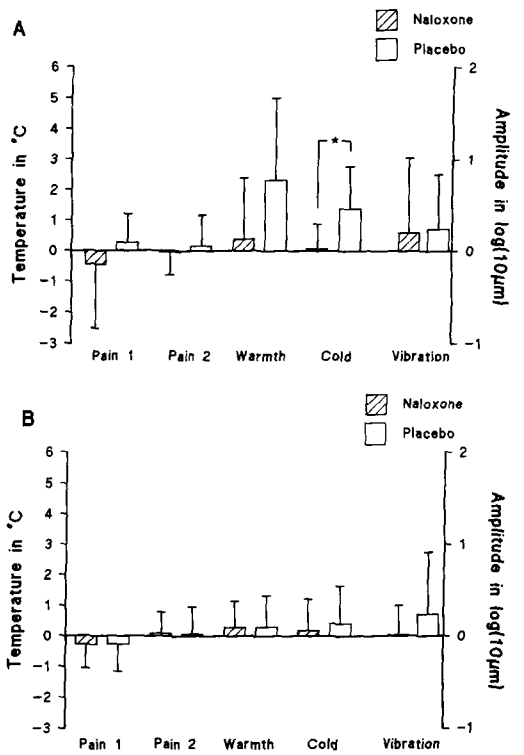

Fig. 3. Mean change scores and standard deviation of Pain Thresholds 1 and 2 and the warmth and cold thresholds (*left ordinate*) and of the vibration thresholds (*right ordinate*) in the depressive patients (*A*) and the healthy controls (*B*); $N = 10$ in each group; the asterisk indicates a significant difference ($p \leq 0.05$) between the change scores with naloxone and placebo.

differences between naloxone and placebo occurred in the depressive patients. The change scores for the warmth and cold thresholds were clearly higher under placebo than under naloxone, which resulted in a significant difference for the cold threshold (p (one-tailed) = 0.003) and an almost significant one for the warmth threshold (p (one-tailed) = 0.057). For none of the other somatosensory thresholds (patients: vibration threshold; control subjects: warmth, cold, and vibration thresholds) was there a significant difference (p (one-tailed) > 0.05). Furthermore, naloxone did not affect the pain thresholds differently from placebo in either the patients or the controls (p (one-tailed) > 0.05, for all comparisons).

None of the change scores for the eight visual analog scales measuring subjective state nor for the local skin temperature showed significant differences between naloxone and placebo in either group (p (two-tailed) > 0.05, for all comparisons). These variables did not seem to be the cause of the change in thermal thresholds.

DISCUSSION

The present study corroborates the findings of other investigators that depression produces a decrease in pain sensitivity. The novel aspect of our study is that the subjects were patients diagnosed as having a major depression according to the contemporary definition of DSM-III-R. Earlier studies observed the decrease in pain sensitivity mainly in patients who were described as having endogenous depression or psychotic symptoms, and less often in patients with neurotic depression (6, 8, 14, 15). Thus, the current diagnosis of major depression, which is based on the duration and severity of the depressive symptoms and abandons the idea of a dichotomy between neurotic and endogenous depression, still identifies a group of patients with hypalgesic changes.

The increase in pain thresholds was found with a method that uses contact heat stimulation. Therefore, the notion that in the majority of the earlier studies, in which electrical skin stimulation was applied (7–10, 14, 16), the results were because of the artificial quality of the pain sensation, does not appear to be substantiated. Furthermore, the fact that similar results were obtained with two pain threshold measurement procedures, one in which the rate of stimulation was pre-set and the other in which the subject determined the rate, rules out the reaction time or, in general, the speed of perceptual processing as a major influence.

The lack of similar increases in the thresholds for nonnoxious skin sensitivity (warmth, cold, vibration) proves that the perceptual change is specific to pain. This finding is in agreement with those obtained by Ben-Tovim and Schwartz (9) and by von Knorring (7, 8), who observed elevated electrical pain thresholds but almost normal electrical detection thresholds. Therefore, somatosensation seems to be intact, whereas pain perception is disturbed. This does not exclude the possibility that perceptual deficits exist in other sensory modalities or that attention is impaired.

We used a variety of instruments measuring psychopathology, including self-ratings and observer ratings, to assess numerous aspects of depression (depressive mood, functional impairment, anxiety, cognitive and psychomotor changes, etc.). None of these variables showed any relationship to the pain thresholds in the depressive patients. The idea, derived from earlier studies (7, 8, 14), that the severity of depressive symptoms, and especially the degree of psychomotor retardation, influences the amount of change in pain perception is not supported. One reason for this discrepancy might be that these relationships appear only when different diagnostic subgroups of depression are grouped together. In the present study, only patients with the diagnosis of major depression and a considerable degree of depressive symptomatology were investigated. Taken together, these findings suggest that, from a certain degree of disease severity on, pain perception is affected in an all-or-nothing fashion.

Naloxone did not differ from placebo in its effect on the pain thresholds either in the depressive patients or in the healthy controls. Therefore, the elevated thresholds of the patients were probably not caused by a naloxone-sensitive analgesic mechanism or, as far as this can be proven by the application of an antagonist, by an excess activity of endogenous opioids. In this respect, the finding in the present study is similar to our earlier finding in patients with anorexia nervosa and bulimia nervosa, where the elevated pain thresholds also could not be normalized by the same dosage of naloxone (26, 32). Whether this constitutes a neurobiological similarity between these disorders, especially between depression and bulimia nervosa, remains to be clarified. Several neurotransmitter and neurohormone systems are involved in forms of analgesia that are not reversible by naloxone; in this context, these systems represent potential candidates for causation (33).

Some comments on the effect of naloxone on pain perception in nonclinical samples are in order. Nal-

oxone (5 mg IV) had no effect on the pain thresholds of the healthy controls. We and several other authors had made similar observations in earlier studies (26, 34–36). Buchsbaum et al. (37) presented some tentative data showing an increased pain sensitivity after a dose of 2 mg, but only in healthy controls classified as pain-insensitive. With respect to pain-evoked cerebral potentials, Bromm et al. (35) observed an amplitude increase after an oral dose of 32 mg, and Davis et al. (36) observed a shortening of latencies after 2 mg IV. Hence, the evidence for systematic changes in pain perception in humans after naloxone administration has been weak.

Whereas naloxone had no impact on pain perception, it seemed to affect the thermal thresholds (the cold threshold strongly and the warmth threshold slightly) in the depressive patients. Under placebo the patients showed a reduction in thermal sensitivity during repeated testing. We think that a decrease in sustained attention or vigilance, which is more likely to occur in depressives than in healthy persons (38–40), might have been responsible for this effect. (The thermal thresholds were determined by applying weak, affectively neutral stimuli, which always started from sub-threshold levels and were therefore most susceptible to changes in attention or vigilance.) Naloxone, which has been found to have beneficial short-term effects on some attentional processes (41, 42), might have counteracted the reduction in thermal sensitivity during repeated testing. However, a replication is necessary before any definite conclusions can be drawn.

In summary, the pain threshold was elevated in our depressive patients, and this was not due to a generalized somatosensory deficit. Thus, the diagnosis of major depression according to DSM-III-R appeared to identify a group of patients with hypalgesic changes. There were no relationships between various aspects of depression (depressive mood, functional impairment, anxiety, cognitive and psychomotor changes, etc.) and pain thresholds in this distinct group of patients. Naloxone did not differ from placebo in its effect on pain thresholds in either the depressive patients or the healthy controls. Therefore, an opioidergic causation of the pain threshold elevation is unlikely.

We thank Prof. H. Merskey for his helpful comments on an earlier version of this manuscript. This study is part of D. Strian's doctoral dissertation. It was supported, in part, by the Wilhelm Sander-Stiftung (92.040.1).

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