Modulation of thermal pain perception by stress and sweet taste in women with bulimia nervosa

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Abstract

OBJECTIVES: To investigate if the increased pain threshold in women with bulimia nervosa (BN) may be due to chronic stress-induced analgesia.
METHODS: We measured thermal pain threshold latency, blood pressure and heart rate in 21 women with BN and 21 healthy women (HW) under six consecutive conditions: rest I, mental arithmetic task, rest II, eating sweet food, rest III, cold-pressor test.
RESULTS: Thermal pain threshold latency was longer in BN than in HW in all six conditions. It increased during mental arithmetic test and remained increased during the rest of the experiment in both groups. In the BN group, the increase of pain threshold during mental arithmetic was positively correlated with illness duration. The differential modulation of pain threshold by stress in BN and HW could not be explained by autonomic system reactivity. In HW, the pain threshold increased more during eating and blood pressure increased more during mental stress; in BN, the pain threshold was highest in the mental stress condition and blood pressure was most increased during eating. During the cold pressor test, women with BN showed smaller blood pressure increase and tolerated the cold for shorter time than HW.
CONCLUSION: The observed marked modulation of pain threshold by experimental stress suggests that stress-induced analgesia is unlikely to account for baseline pain insensitivity in BN. Increased pain threshold in BN is a stable yet incompletely understood phenomenon, which may be related to the predisposition to or maintenance of the disorder.

1. INTRODUCTION

Bulimia nervosa (BN) is a mental illness commonly affecting young women. The core features of BN are restrained eating motivated by dissatisfaction with own body weight and shape and episodes of overeating with compensatory behaviours, such as self-induced vomiting (Russell, 1979). The dissatisfaction with own body is associated with distorted perception of the body. It has been suggested that a general insensitivity to bodily stimuli, including pain, hunger and fatigue, underlies the distorted body shape perception (Bruch, 1962; Uher *et al.*, 2002; Uher *et al.*, 2004).

ORIGINAL ARTICLE

Elevation of pain threshold in individuals with BN is a consistent yet unexplained finding (Lautenbacher *et al.*, 1991; Faris *et al.*, 1992; de Zwaan *et al.*, 1996a). Previous investigations indicated, that pain insensitivity in BN develops dynamically in concert with pathological eating behaviour and changes in the tone of autonomic nervous system (Faris *et al.*, 1998; Raymond *et al.*, 1999). This may be explained as stress-induced analgesia (Lewis *et al.*, 1980), waxing with increasing psychopathology-related distress and waning with its temporary resolution in purging behaviour (Faris *et al.*, 1998; Raymond *et al.*, 1999). However, the relationship between stress, autonomic system reactivity and analgesia is unclear.

In healthy individuals, sensitivity to pain is diminished during mental and physical stress (Lewis *et al.*, 1980; Terkelsen *et al.*, 2004), heterotopic painful stimulation (Plaghki *et al.*, 1994) or sweet food intake (Mercer & Holder 1997; Lewkowski *et al.*, 2003). However, the pain modulating effect of these factors disappears in the context of chronic stress, suggesting that their effect is not cumulative with chronic stress-related analgesia (Willer *et al.*, 1981; Torres *et al.*, 2001; Lewkowski *et al.*, 2003; Torres *et al.*, 2003; Fontella *et al.*, 2004). We therefore hypothesised that if chronic stress and autonomic arousal are responsible for increased pain tolerance, then moderate experimental challenges will not cause further decrease in pain sensitivity in BN.

The concept of sweet-taste analgesia is relevant to BN. While individuals with BN show strong preference for sweet taste, they find it also aversive by association with calories and fatness (Sunday and Halmi 1990; Franko *et al.*, 1994; Eiber *et al.*, 2002). We hypothesized that the effect of sweet food on pain threshold and autonomic system will be less in BN than in healthy controls.

Sympathetic and parasympathetic systems affect pain perception (Cepeda 1995). High blood pressure is associated with lower pain sensitivity (France & Stewart, 1995; Janssen *et al.*, 2001; al'Absi & Petersen 2003). It has been suggested that vagal hyperactivity (Faris *et al.*, 1998; Raymond *et al.*, 1999) or blood pressure (Girdler *et al.*, 1998) account for the analgesia in BN. Here we examine this relationship over several experimental challenge conditions including mental arithmetic, sweet taste and heterotopic cold. We hypothesise that differences in pain threshold modulation across these conditions will be independent of autonomic nervous function as indexed by blood pressure and heart rate.

2. METHODS

2.1. Participants

Inclusion criteria were: female, age 18–40, no use of analgesic medication in the past week, not pregnant, no history of neurological illness or diabetes, no psychotic illness or substance dependence on structured psychiatric interview (Sheehan *et al.*, 1998).

Twenty-one women fulfilling inclusion criteria and DSM-IV diagnostic criteria for bulimia nervosa (BN) were recruited as consecutive admissions to the outpatients and inpatients departments at the Specialized Unit for Eating Disorders, Psychiatric Department of the 1st Medical School of the Charles University in Prague. Their average age was 23.2 (S.D. = 4.5) years and their mean body mass index (BMI; kg/m^2) was 20.1 (S.D. = 1.7). At the time of the study, they were engaging in self-induced vomiting on average 23 times per week (S.D. = 12, range 7–40); three abused laxatives, one used diuretics, and one used over-the-counter slimming tablets. Fifteen were medication-free and six used SSRI antidepressants. In addition to bulimia nervosa, two fulfilled the criteria for unipolar depression, two for an anxiety disorder (phobia, generalised anxiety), and two for substance abuse without dependence (alcohol). Axis II diagnoses were not assessed.

As a comparison group, 21 healthy women (HW) of similar age (23.1 ± 3.8 years) and body mass index (20.7 ± 1.4 kg/m^2) were recruited by advertisement from the local community. They were screened to exclude eating disorder or other psychiatric disorder (Sheehan *et al.*, 1998). There were no significant differences in age or BMI between BN and HW ($t_{(1,40)} < 1$, $p > 0.1$).

All subjects signed an informed consent as approved by the Ethical Committee of Charles University, Prague.

2.2. Apparatus and materials

The pain threshold was measured at rest and under stress conditions using the Analgesia Meter (IITC Life Science USA Model 33), which applies radiant heat of constant intensity to an area of 1cm^2 (Papezova *et al.*, 2005). In each experimental condition the pain threshold was measured three times on the dorsal side of index, middle and ring finger of the right hand. Average of the three measurements was used in the analysis. Participants were instructed to withdraw their finger when the heat becomes painful. The time from start of the radiant heat to the finger withdrawal was measured as thermal pain threshold latency. To prevent tissue damage, the maximum duration of the heat exposure was 40 s.

Blood pressure and heart rate were recorded using oscillometric digital monitor Omron (Model HEM-703C, Omron, Tokyo, Japan). To obtain a single index of blood pressure, mean arterial pressure (MAP) was calculated as diastolic blood pressure plus one third of the difference between the diastolic and systolic pressure (Caceres & Burns 1997).

2.3. Procedure

The experiments were carried out in the afternoon (2 to 5 PM), starting 2–3 hours after lunch. Testing was performed at an ambient temperature 20–22°C after 15 minutes adaptation in the experimental room. First, the female experimenter explained the procedures to

the participants: she described these in a practical way, generally avoiding words like 'painful', 'noxious' and 'unpleasant' and instead using descriptive terms such as 'heat' and 'cold'. The purpose of the study was explained in very general fashion 'exploring the perception of various sensations' and no specific hypotheses were given. Then, participants were weighted, measured, and interviewed by a female experimenter. Then, initial resting measurements of pain threshold, blood pressure and heart rate were taken simultaneously, while the participants were instructed to relax.

The same measurements were repeated 6 times in total (3 times at rest and once under each of the experimental challenge conditions). As the cold pressor may have stronger and longer lasting effects on autonomic system than mental arithmetic (Oshima *et al.*, 2001), the experimental stress conditions were introduced in a fixed order with the cold pressor performed last (Rest I, Mental arithmetic, Rest II, Eating, Rest III, Cold pressor). Each active or rest condition lasted five minutes.

Mental arithmetic task was used as a mental stressor (Jern *et al.*, 1991). Subjects were instructed to perform serial subtraction of 7s from 700. The lowest number reached was taken as an approximate measure of engagement and performance. Errors were not corrected.

In the eating condition, participants were encouraged to eat sweet butter biscuits. The instruction was "eat as much as you wish and hold one biscuit in your mouth even if you do not want to eat any more." Number of consumed pieces of biscuit was recorded. Each biscuit contained 1.5 g of sugar, 0.2 g of protein and 0.1 g of vegetable fat and had nutritional value of 0.33 kJ.

During the cold pressor condition (Lovallo, 1975), participants were asked to keep their non-dominant hand immersed in ice-water mixture maintained at 1–3°C while the thermal pain threshold was measured on the dominant hand. They were instructed to remove the hand if the cold pain becomes intolerable. Time from immersion to hand withdrawal was recorded as a measure of tolerance. Intensity of cold pain at the time of hand removal was assessed by a 10 cm visual analogue scale (VAS) with the left extreme labelled as 'no pain' and the right extreme as 'maximum possible pain'.

2.4. Analysis

The distributions of thermal pain threshold latencies, blood pressure and heart rate did not significantly deviate from normality in any group or condition (Kolmogorov-Smirnov test; all $p > 0.05$); hence parametric analysis of variance (ANOVA) was used with within-subject factor *condition* (6 levels: rest 1, mental arithmetic, rest 2, eating, rest 3, cold pressor) and between-subject factor *group* (2 levels: HW and BN). The assumption of sphericity was tested for each analysis with more than 2 levels of any within subject factor using the Mauchly test. The Greenhouse-Geisser correction was used where the assumption of sphericity was not met. For the between subject factor *group* (HW vs. BN), simple planned contrasts were specified with HW as the reference group. For the within subject factor *condition*, repeated planned contrasts were specified to identify significant change between any two consecutive conditions.

We further explored the effect of each challenge condition on pain threshold by contrasting it to the immediately preceding resting measurement in 3 separate mixed design 2×2 ANOVAs. As each of the analyses only included one active challenge condition, the inclusion of challenge-specific covariates was possible (performance in mental arithmetic, number of biscuits eaten, tolerance and subjective algosity of CPT). The second of these analyses is of interest, as it is relevant to our hypothesis on the effect of sweet food intake.

To explore the effects of baseline blood pressure and heart rate on changes in pain perception, we repeated the 2x2 mixed design ANOVA comparing pain threshold during the mental arithmetic challenge to the initial resting condition and using initial resting mean arterial pressure and heart rate as covariates.

3. RESULTS

3.1. Thermal pain threshold latency

The results of pain threshold measurements are given in Figure 1A. ANOVA revealed a significant main effect of *group* ($F_{(1,40)} = 16.1$, $p < 0.001$), a significant main effect of *condition* ($F_{(5,36)} = 18.0$, corrected d.f. = 3.76; $p < 0.001$) and a significant *condition* x *group* interaction ($F_{(5,36)} = 3.4$, corrected d.f. = 3.76, $p = 0.012$).

The main effect of *group* was due to higher pain threshold in BN than in HW on all six measurements (all six $t > 25.0$, d.f .= 1,40; $p < 0.002$).

As for the main effect of *condition*, the repeated planned contrasts indicated that there was significant increase in pain threshold from the initial resting state to mental arithmetic ($F_{(1,40)} = 53.5$; $p < 0.001$).

The significant *condition* x *group* interaction occurred between the first two measurements, where there was greater increase in pain threshold from the initial rest to the mental arithmetic condition in BN than in HW ($F_{(1,40)} = 9.6$, $p < 0.004$).

In summary, the BN group had significantly higher pain threshold under all the experimental conditions. Compared to the initial resting condition, pain threshold significantly increased with mental stress in both groups and remained increased during all subsequent measurements. Contrary to our prediction, the increase in pain threshold was significantly steeper in the BN group than in healthy control women.

3.2. Blood pressure

This analysis showed a significant main effect of *condition* ($F_{(5,36)} = 9.3$, corrected d.f. = 3.68; $p < 0.001$) and a significant *condition* x *group* interaction ($F_{(5,36)} = 3.5$,

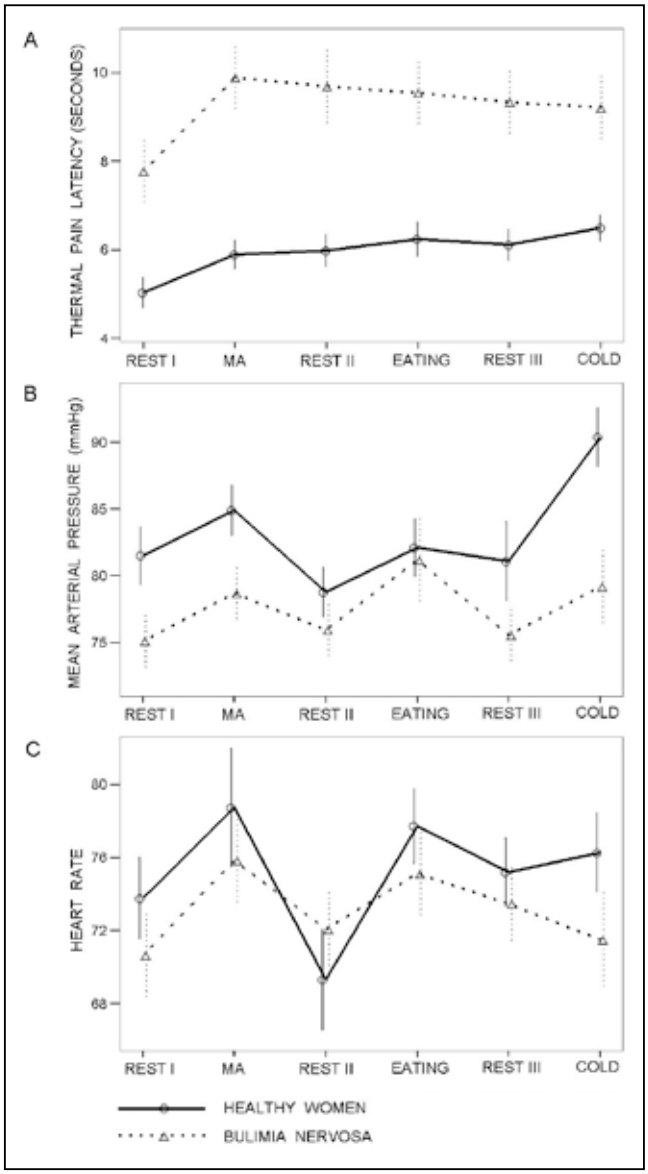

Figure 1: **Time course of thermal pain, mean arterial pressure and heart rate.** The mean values of thermal pain threshold latency (A), mean arterial blood pressure (B) and heart rate (C) are given separately for the group of healthy women (n=21, full line) and women with bulimia nervosa (n=21, dotted line) under the six experimental conditions (REST = resting condition, MA = mental arithmetic task, EATING = sweet food ingestion, COLD = cold pressor test). The error bars represent one standard error of the mean.

corrected d.f. = 3.76, $p = 0.011$); the main effect of *group* just missed the significance criterion ($F_{(1,40)} = 3.9$, $p = 0.056$).

The planned repeated contrasts indicated that the mean arterial pressure changed significantly between each two subsequent conditions (Figure 1B) indicating that in both groups the blood pressure increased in all three active conditions and decreased during rest. The *condition* x *group* interaction occurred between the third resting condition and the cold-pressor challenge, reflecting a steeper increase in blood pressure during cold pressor in HW than in BN.

3.3. Heart rate

This analysis showed a significant main effect of *condition* ($F_{(5,36)} = 6.0$, $p < 0.001$); the main effect of *group* ($F_{(1,40)} = 0.5$, $p > 0.1$) and *condition* x *group* interaction ($F_{(5,36)} = 1.6$, $p > 0.1$) were non-significant.

The planned repeated contrasts indicated that heart rate changed significantly at three points: between initial rest and mental arithmetic, between mental arithmetic and second rest and between second rest and eating (Figure 1C). This analysis showed that heart rate reactivity to various challenges is similar in BN and HW.

3.4. Performance

In the mental arithmetic task, HW performed on average 22.5 (S.D. = 12.4) and BN 19.9 (S.D. = 11.3) subtractions; the group difference in performance was not significant ($t_{(1,40)} = 0.7$, $p > 0.1$).

In the eating condition, HW ate significantly more biscuits than BN (7.0 ± 3.5 vs. 4.6 ± 3.7; $t_{(1,40)} = 2.1$, $p = 0.04$).

In the cold pressor test, HW tolerated the icy water for significantly longer than BN (102.6 ± 61.8 seconds vs. 66.9 ± 46.2 seconds; $t_{(1,40)} = 2.1$, $p = 0.04$). The pain intensity at discontinuation of the cold pressor did not differ between the groups (57.8 ± 24.9 vs. 57.3 ± 26.1; $t_{(1,40)} = 0.05$, $p > 0.1$).

3.5. Covariate analyses

3.5.1. Effects of specific challenge conditions on thermal pain threshold latency

The first 2×2 mixed design ANOVA compared pain threshold latency during the mental arithmetic challenge with the initial resting condition, using performance in mental arithmetic (number of subtractions) as a covariate. This showed significant main effect of *group* ($F_{(1,40)} = 19.9$, $p < 0.001$), main effect of *condition* ($F_{(1,40)} = 19.9$, $p < 0.001$), and *group* x *condition* interaction ($F_{(1,40)} = 8.8$, $p = 0.005$); the effect of the covariate was non-significant ($F_{(1,40)} < 1$, $p > 0.1$) This analysis confirmed that during the mental arithmetic challenge there was a steeper increase in thermal pain threshold latency in BN than in HW and this was independent of performance in the task.

The second 2×2 ANOVA compared pain threshold latency during eating challenge to the immediately preceding second rest condition with number of biscuits eaten as a covariate. It found a strong main effect of *group* ($F_{(1,40)} = 20.3$, $p < 0.001$). The main effect of *condition* ($F_{(1,40)} = 0.2$; $p > 0.1$), the *group* x *condition* interaction ($F_{[1,40]} = 2.3$, $p > 0.1$) were non-significant. The main effect of covariate just missed significance ($F_{(1,40)} = 4.0$, $p = 0.054$) and its interaction with condition was non-significant ($F_{(1,40)} = 0.1$, $p > 0.1$). These results did not support our hypothesis, as the effect of eating on pain threshold was not different in BN compared to HW.

The third 2×2 mixed design ANOVA compared pain threshold latency during the cold pressor to the imme-

diately preceding third resting condition including the tolerance and subjective algosity as covariates. Apart from the main effect of group ($F_{(1,40)} = 13.0$, $p = 0.001$) all effects and interactions were non-significant ($F < 1$, $p > 0.1$).

3.5.2. Relationship between pain threshold and cardiovascular indices of autonomic reactivity

Analysis using initial resting mean arterial pressure and heart rate as covariates showed significant main effect of group ($F_{(1,40)} = 17.2$, $p < 0.001$), significant main effect of condition ($F_{(1,40)} = 5.5$, $p = 0.024$), and significant group by condition interaction ($F_{(1,40)} = 6.4$, $p = 0.015$); the main effects of baseline resting mean arterial pressure ($F_{(1,40)} = 0.5$, $p > 0.1$) and heart rate ($F_{(1,40)} = 0.05$, $p > 0.1$) were non-significant; the interaction between condition and baseline mean blood pressure was non-significant ($F_{(1,40)} = 0.3$, $p > 0.1$) and the interaction between condition and baseline heart rate showed a trend ($F_{(1,40)} = 3.6$, $p = 0.066$). This analysis indicates that the group difference in pain sensitivity modulation by mental stress is independent of baseline heart rate and blood pressure.

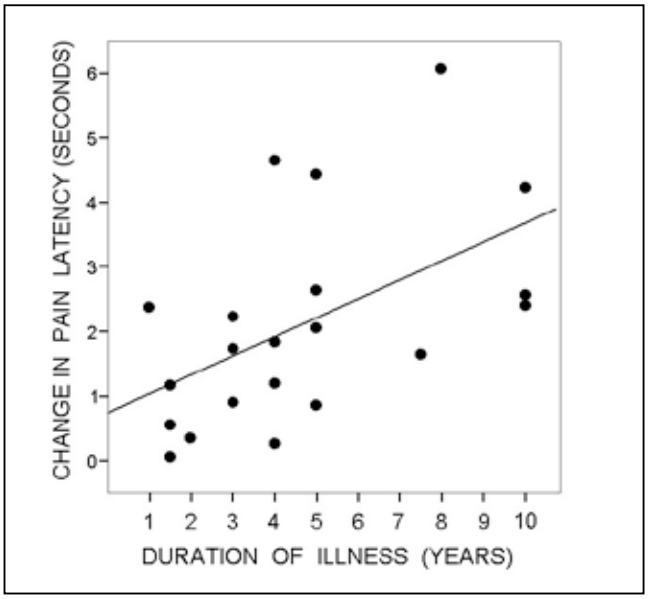

Figure 2: Correlation between duration of illness and change of thermal pain threshold latency with mental stress in the group of women with bulimia nervosa (n=21).

3.6. Relative changes in pain threshold, blood pressure and heart rate

To make the data from the different measurements comparable and to partial out baseline differences, we used relative values obtained by dividing the measured value by the relevant baseline (initial resting condition). The results revealed a significant main effect of *measure* ($F_{(2,39)} = 26.4$, corrected d.f. = 1.33, $p < 0.001$), significant *condition* × *group* interaction ($F_{(2,39)} = 6.6$, corrected d.f. = 1.91, $p = 0.003$) and significant three-way *measure* × *condition* × *group* interaction ($F_{(4,37)} = 4.1$, corrected d.f. = 2.84, $p = 0.010$). All other effects and interactions were non-significant ($p < 0.1$).

Exploring the main effect of *measure*, planned simple contrast showed that the pain threshold was significantly more modulated by challenge conditions than blood pressure and heart rate. The *condition* x *group* interaction was between eating and cold pressor conditions due to greater reactivity to cold pressor in HW compared to BN. The *measure* x *condition* x *group* interaction occurred between measures pain and blood pressure and between mental arithmetic and eating. In HW, the pain threshold increased more during eating and blood pressure increased more during mental stress; in BN, the pain threshold was highest in the mental stress condition and blood pressure was most increased during eating.

3.7. Relationship between pain threshold modulation and disease characteristics in bulimia nervosa

To investigate the relationship between pain modulation and pathology of bulimia nervosa, we run the repeated measure analysis of variance in the BN group with frequency of self-induced vomiting and illness duration as covariates. The main effect of these covariates and their interactions with the factor condition were non-significant (all $p > 0.05$). However, when the duration of illness was used as a covariate, there was a trend for *covariate* × *condition* interaction ($F_{(5,15)} = 2.0$, $p = 0.08$) and the main effect of *condition* became non-significant. To further explore the influence of illness duration on pain threshold modulation, we performed a correlation between illness duration and the change of pain threshold with mental arithmetic (difference between baseline resting latency and latency during mental arithmetic test); this showed a positive correlation (Pearson's r = 0.53, $p = 0.014$) suggesting that pain threshold modulation by mental stress is stronger in those with long-standing illness (Figure 2).

3.8. Exclusion of medication and comorbidity

Finally, to address the potential effects of medication or comorbidity we repeated the primary analysis with the 14 BN medication-free patients without axis I comorbidity. In spite of the loss of power associated with this diminished sample, the results were identical: a significant main effect of *group* ($F_{(1,33)} = 14.5$, $p = 0.001$), a significant main effect of *condition* ($F_{(5,29)} = 15.4$, corrected d.f. = 3.65; $p < 0.001$) and a significant *condition* x *group* interaction ($F_{(5,29)} = 3.79$, corrected d.f. = 3.76, $p = 0.009$). This analysis confirmed that the higher pain threshold and greater increase in pain threshold with mental stress are associated with bulimia nervosa per se rather than medication or comorbidity.

4. DISCUSSION

4.1. The chronic stress-induced analgesia hypothesis

In has been suggested that pain sensitivity in bulimia nervosa is dynamically determined by the state of distress and autonomic arousal (Faris *et al.*, 1998; Girdler *et al.*, 1998; Raymond *et al.*, 1999) and we hypothesised that stress-induced analgesia may account for the consistent finding of increased pain threshold in BN compared to healthy controls (Lautenbacher *et al.*, 1991; Papezova *et al.*, 2005). To test this hypothesis, we used several experimental challenges to modulate the level of autonomic arousal. Observed changes in blood pressure and heart rate indicated that this modulation was effective. Contrary to our expectation, the difference in pain sensitivity between BN and HW did not diminish with this modulation. Indeed the opposite occurred and, during mental stress challenge, the pain threshold increased more in BN than in HW. This differential modulation of pain sensitivity was independent of medication, comorbidity, baseline autonomic function and performance in the challenge task.

The analgesic effects of chronic stress and acute factors are generally not cumulative. For example, after 45 minutes, there is no further decrease in pain sensitivity with stress repetition and there is no summation of analgesic effects across sessions (Willer *et al.*, 1981); chronically stressed animals show tolerance to the analgesic effects of morphine (Torres *et al.*, 2003) and novel stimuli (Torres *et al.*, 2001), and the analgesic effect of sweet taste does not occur in chronically stressed animals (Fontella *et al.*, 2004) or in humans with high pain threshold associated with hypertension (Lewkowski *et al.*, 2003). Therefore, the finding of prompt modulation of pain threshold by experimental stressor in BN is not consistent with stress-induced analgesia being operational at the baseline. Instead, the low sensitivity to pain in BN appears to be a stable phenomenon, which persists under various experimental conditions. This is similar to findings in women with borderline personality disorder, who show decreased sensitivity to pain across states of subjective distress and calmness (Bohus *et al.*, 2000). It is also consistent with the finding that pain sensitivity remains low in women long-term recovered from BN (Stein *et al.*, 2003). Taken together, these data suggest that decreased pain sensitivity is a trait marker which may be associated with the predisposition to BN.

4.2. Correlation with illness duration

An unexpected finding was that the degree of pain threshold modulation by mental stress correlated with the duration of BN. It is possible that this increased stress analgesia is a cumulative 'scar' effect of past bulimic behaviour or that it is a moderating factor that predisposes to longer duration of illness. From the present cross-sectional investigation, it is impossible to determine which of these explanations is valid and longitudinal study would be required to allow a less conjectural interpretation.

4.3. Modulation of pain sensitivity by sweet taste

We further hypothesised that ingestion of sweet food would have different effect on pain threshold in BN compared to HW. The primary analysis of pain threshold data alone did not find support for this hypothesis. However, when different indices of reactivity to the three challenges were compared, it was found that the relative modulation of blood pressure and pain threshold differed between BN and HW. While in BN the pain threshold peaked during the mental stress task, in HW it further increased with eating; the blood pressure showed the opposite pattern leading to a significant three-way interaction. This may suggest that the sweet-taste related analgesia (Mercer & Holder 1997; Lewkowski *et al.*, 2003) is not operational in BN. The interpretation of this finding is however complex: while sweet-taste analgesia in normal subjects is not stress-related, it is likely that ingestion of sweets was perceived as aversive and threatening in those with BN and these emotional associations explain the differential effects on pain perception and autonomic system function (Meagher *et al.*, 2001).

Participants with BN ate fewer biscuits that HW during the eating condition. However, the amount eaten did not contribute significantly to pain threshold changes. Also, as all participants were holding a biscuit in the mouth even when not eating, the sweet taste element was delivered throughout the condition in all participants.

4.4. The cold pressor test

In the cold pressor test, women with BN tolerated the icy water for a shorter time than did HW. Furthermore, blood pressure during cold pressor increased more in HW than in BN. These are unexpected results, inconsistent with previous and current findings of decreased sensitivity to various modalities of pain in BN. People with BN are less sensitive to thermal, mechanical and ischemic pain (Faris *et al.*, 1992; de Zwaan *et al.*, 1996b; Girdler *et al.*, 1998; Papezova *et al.*, 2005). However, sensitivity to pain in different modalities is to a large extent independent (Janal, 1994) and, to our knowledge, cold pain threshold and tolerability have not been previously investigated in BN. This is surprising as the cold-pressor test is one of the most commonly used experimental pain paradigms (Lovallo, 1975) and has been widely used in other conditions (Nishith *et al.*, 2002). Sensitivity to cold pain is decreased in women with borderline personality disorder, a condition often comorbid with BN (Bohus *et al.*, 2000).

4.5. Relationship between pain perception and autonomic system function

Finally, we have hypothesised that the group differences in pain perception will be independent of changes in autonomic function, as indexed by blood pressure and heart rate. This hypothesis was confirmed: the group differences in pain threshold and its modulation by experimental challenges in the present study were independent of heart rate and blood pressure. The heart rate and blood pressure reactivity across the conditions were similar in BN and HW with the exception of smaller blood pressure reactivity to cold in BN.

4.6. Limitations

Because the cold pressor test has long-standing effects on autonomic system function and pain perception (Talbot *et al.*, 1987; Oshima *et al.*, 2001), we presented the challenges in a fixed order, with mental arithmetic first. While this set up optimised the sensitivity to detect pain threshold modulation by mental stress, the sensitivity to the effects of the other two conditions may have been compromised. While heart rate and blood pressure normalised during the resting conditions in both group, the elevation of pain threshold largely persisted throughout the experiment.

4.7. Conclusion

Compared to healthy age-matched controls, women with bulimia nervosa are less sensitive to thermal pain across a variety of experimental conditions. This difference further increased during stress and cannot be explained by stress-related analgesia mechanism or by differences in the function of autonomous nervous system. Further study is needed to determine the mechanism of this robust finding and its relevance as a predisposing or prognostic factor.

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