Hypothalamic-pituitary stress axis in female patients with bulimia nervosa
-Neuroendocrine diurnal regulation of hunger and satiety in women with bulimia nervosa-

5th year paper in Medisin Embetsstudie, University of Tromsø

by

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Summary

In this paper we try to examine differences in hormonal diurnal biorhythms in women with bulimia nervosa compared to healthy controls with matching BMI. Our research has focused on investigating the circadian rhythm of the three hormones leptin, cortisol and melatonin. Blood samples from 8 women with bulimia nervosa and 8 healthy controls were drawn every 2nd hour for 24 hours while they were admitted to a clinical research ward at the University Hospital of Nord-Norge in Tromsø.

We found that patients suffering from bulimia nervosa have a higher than normal secretion of melatonin at night. They had an increase in plasma cortisol levels after dinner while healthy controls experienced a decrease in cortisol levels. The subjects with bulimia nervosa had decreased leptin secretion throughout the day and night compared to healthy controls.

These differences in hormonal secretion may to some extent explain the eating habits seen in subjects suffering from bulimia nervosa.
Introduction

Disturbances in hormonal biorythms have been reported in numerous studies in bulimia nervosa. We designed a study to test two hypotheses.

Hypothesis number one is that neuroendocrine hormones play an important role in mediating the feeling of hunger and satiety in bulimia nervosa. The effect of neuroendocrine hormones differ depending on the stage of the disease.

The hypothalamic-pituitary axis regulates different metabolic processes in the body. Hypothesis number two is that in patients suffering from bulimia nervosa there is an increased activity in this axis when the disease is non active, meaning there is no overeating and no compensatory behaviour such as purging or excessive exercising.

Our patients were all examined during a non active phase of their disease. We decided to focus on the hormones, leptin, cortisol and melatonin, but we are well aware of the fact that many hormones and nutritive substances are important in this aspect. Our main purpose was thus to describe the 24 hour biorythm of leptin, melatonin and cortisol in bulimia nervosa.

People suffering from bulimia nervosa have severe compensatory behaviour such as volunteer vomiting or extreme exercising, which prevents them from gaining weight. They often feel hungry and can not stop eating when first started. This may result in overeating. Patients with bulimia nervosa often have a normal body weight. Their disease may thus go undetected for
years. People with bulimia nervosa may feel guilty about their behaviour, this may also prevent them from informing their family, friends and doctor about their disease.

Biological factors such as genetic factors, neurotransmitter imbalances and hormonal imbalances may lead to different eating disorders. Several studies have shown that some people are more predisposed than others in suffering from an eating disorder, for example people with disturbances in the serotonin metabolism in the central nervous system\(^2\) or disturbances in the cortisol- and prolactin metabolism.\(^3\) But there are several conditions required for bulimia nervosa to manifest in an individual, and these conditions might be of psychological, psychosocial and/or biological nature.
Method

Eight women with bulimia nervosa were recruited to our project via information posters describing the study during the fall of 2002 (Enclosure 1: Information poster). The women were all examined during a non active phase of their disease and psychologically tested. All the subjects met DSM-III-R criteria for bulimia nervosa (American Psychiatric Association 1987. Dignostical and statistical manual of mental disorders, ed 3, revised. Washington DC: American Psychiatric Press) with additional criteria of binge eating and purging, on the average, at least three times per week over the proceeding 6 months. Diagnostic evaluation was also based on a modified version of the Schedule for Affective Disorders and Schizophrenia-Life version (Enclosure 2: Questionnaire for women with bulimia nervosa).

Eight control women were also recruited. They were healthy women of normal weight with similar BMI compared with the women with bulimia nervosa.

During fall 2001 controls and women with bulimia nervosa were admitted to a clinical research ward for a 24-hour registration of circadian rhythms of leptin, melatonin and cortisol analysed from blood samples. Blood samples were drawn every two hours, from 8AM day 1 to 7.59AM day 2. The women were admitted fasting at 8 AM. They ate breakfast at 8:30 AM, dinner at 1:00 AM, afternoon meal at 5:00 PM and a light snack at 8:00 PM.

Leptin values differ with BMI or amount of fat in the human body as leptin is secreted from the adipocytes. High BMI normally leads to high leptin secretion and low BMI leads to low
leptin secretion. To be able to compare the mean values of leptin secreted at the different hours we adjusted all the leptin values to a BMI equal 22. According to Lissner et al\textsuperscript{4}

\[ \text{Leptin10 (leptin)} = -0.22 + 0.054 \times \text{BMI} \quad (r=0.74, p=0.0001). \]

By using this equation we were able to find expected leptin values for healthy women with specific BMI. According to the same equation healthy women with BMI equal 22 should have leptin values of 9.3. The difference between the expected leptin value from healthy women with a given BMI and 9.3 was subtracted from the measured leptin values in both control group and the women with bulimia nervosa. These adjusted leptin values are lower than those measured in women with BMI above 22, and contrary adjusted leptin values will be higher than measured in those women with BMI lower than 22.
Background

Hunger and Satiety

When full, cholecystokinin (CCK) from the intestine, leptin from the adipocytes and nutritive substances such as glucose in the blood, reach the brain giving a feeling of satiety. These signals are called satiety signals and they reach the satiety centre in the hypothalamus via the blood brain barrier or via afferent neurons. The satiety center is placed in the ventro medial nucleus. The signals of hunger are neuropeptid Y and orexin. When the hunger centres are stimulated, the persons feel hungry. The hunger centre is located in the lateral nucleus in the lateral part of the hypothalamus. These signals affect the hypothalamic-pituitary axis, which controls the metabolism of the body.

Tryptophan is a precursor of serotonin and thus regulates the concentration of serotonin in the brain. Serotonin stimulates the satiety center. People with low levels of tryptophan and consequently serotonin will thus experience lack of satiety regardless of how many calories they have ingested. Other nutritive stimuli of hunger and satiety centres are plasma levels of insulin and glucagon. Activation of stretch receptors and chemoreceptors in the stomach and a rise in body temperature give a feeling of satiety. Stress can lead to both hunger and satiety.
Bulimia nervosa

There are several different types of eating disorder; anorexia nervosa, bulimia nervosa, binge eating and night eating syndrome are some. Anorexia nervosa and bulimia nervosa are the most common diseases and the oldest known eating disorders. Latin writings of Aulus Gellius ans Sextus Pompeius Festus described conditions compatible with bulimia nervosa as early as the 2\textsuperscript{nd} and 4\textsuperscript{th} cenuary A.D respectively. This was noted by Smith, in 1866.

Vandereycken and Van Deth suggested in 1995 that voluntary self-starvation similar to anorexia nervosa has occurred for many centuries.\textsuperscript{5}

In 1996 Ziolko reported that there are no reports of anorexia from classical Greece.\textsuperscript{6}

\textit{Definition}

Bulimia nervosa is recurrent episodes of binge eating followed by compensatory behaviour in order to prevent weight gain, such as self-induced vomiting, misuse of laxatives, diuretics, enemas or other medications, fasting or excessive exercise. Both binge eating and inappropriate behaviours have to occur, on average, at last twice a week for three months in order for the full diagnose to be made.\textsuperscript{7} Bulimia nervosa is more common than anorexia nervosa. Some patients with anorexia nervosa also manifest bulimia. Many patients with bulimia, however are of normal weight or overweight.

The \textit{Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)}, gives diagnostic criteria for bulimia nervosa, including the following:
- Recurrent episodes of binge eating. An episode of binge eating is characterised by both of the following:

  * Eating in a discrete period of time (for example within any 2-h period), an amount of food that is definitely larger than most people would eat during a similar period of time under similar circumstances.

  * A perceived lack of control over eating during the episode, for example feeling that one cannot stop eating or cannot control what or how much one is eating.

- Recurrent inappropriate compensatory behaviour is used to prevent weight gain (for example, self-induced vomiting; misuse of laxatives, diuretics, enemas, or other medication; fasting; excessive exercise).

- Binge eating and inappropriate compensatory behaviours each occur, on average, at least twice a week for 3 months.

- Self-evaluation is influenced unduly by body shape and weight.

- The disturbance does not occur exclusively during episodes of anorexia nervosa.

Bulimia nervosa may be categorised as purging type if, during the current episode, the person has engaged regularly in self-induced vomiting or the misuse of laxatives, diuretics, or
enemas. If other inappropriate compensatory behaviours, such as fasting or excessive exercise, have been used without self-induced vomiting or misuse of laxatives, diuretics, or enemas, the diagnosis is bulimia nervosa, non-purging type. Individuals who binge eat without the regular use of characteristic inappropriate compensatory behaviours of bulimia nervosa are included under the category of eating disorders not otherwise specified (NOS).  

Bulimia nervosa may begin early in adolescence when young women and men attempt restrictive diets, fail and react by binge eating. People with bulimia nervosa who do not progress to anorexia, have a normal to high-normal body weight, but the weight may vary more than 10 pounds because of the binge-purge cycle. People with eating disorders are more vulnerable to stress, have reduced self-esteem and are less confident when faced with challenges.

**Symptoms**

The induced vomiting can cause enlarged parotid glands, inflammation in the oesophagus, dental caries and injuries to the mouth. Vomiting may also cause broken blood vessels in the eyes. Repeated self-induced vomiting in which the person thrust the hand down the throat, can produce small cuts and calluses across the tops of the finger joints. Vomiting can also lead to electrolyte imbalance. Low potassium may cause urinary tract infections, kidney failure and heart irregularities. The laxative abuse can cause muscular weakness, thirst, abdominal pain, diarrhoea, as well as low potassium, calcium and magnesium level. Diuretic drugs can cause dehydration and low potassium. A bulimic person may complain of chronic indigestion, facial puffiness, sore throats, constipation, muscle weakness, irregular
menses and fatigue. Other symptoms of bulimia may be oedema, loss of hair, restlessness, bad breath, extreme weakness and dizziness.\textsuperscript{11}

\textbf{Mortality}

One study of patients suffering from bulimia nervosa and undergoing therapy reported a 1\% mortality rate after six years.\textsuperscript{1} Patients suffering from bulimia nervosa have a better diagnosis than subjects suffering from anorexia nervosa.\textsuperscript{1}

\textbf{Familial risk}

Among the female relatives of bulimia nervosa patients, the rate of anorexia nervosa was 3.7\% and of bulimia nervosa 4\%.\textsuperscript{12} One report recently estimated that 80\% of the hereditability of bulimia nervosa is due to genetic factors, whereas shared environment does not seem to be a significant contributor.\textsuperscript{13}

\textbf{Prevalence}

It is estimated that 3\% to 5\% of young women are affected by bulimia nervosa.\textsuperscript{14}

\textbf{Hormones involved in hunger and satiety}

\textbf{Leptin}

Leptin is a protein that inhibits the feeling of hunger and is produced in fat cells and deposited in the bloodstream. The blood concentration of leptin is an indicator of the total amount of
triglyceride fat stored in adipose tissue. Leptin reduces production and release of neuropeptide Y in hypothalamus.\textsuperscript{15} Neuropeptide Y stimulates the centre of hunger in the hypothalamus.\textsuperscript{16} Leptin transfers signals of amount of body fat and is a blood-borne signal between fat stores and the areas of the brain controlling food intake.\textsuperscript{17}

Leptin has an important role in the pathogenesis of obesity and eating disorders and it may mediate the neuroendocrine responses to a shortage of food.\textsuperscript{18} There appears to be a peripubertal surge in plasma leptin levels and a postmenopausal decline. Leptin is responsive to hormonal manipulation. Insulin, glucocorticoids, estradiol and growth hormone can increase leptin levels.\textsuperscript{19} Leptin binds to leptin receptors in the ventro-medial hypothalamus and reduces caloric intake.\textsuperscript{20}

\textbf{Melatonin}

Melatonin is a hormone secreted by the pineal stalk. The synthesis and secretion of melatonin is increased during darkness and decreased during the day. This is controlled by sympathetic nerve activity that is itself regulated by light signals from the retina. It has been assumed that this enables the pineal gland to synchronise the various biological clocks with the day-night cycle.\textsuperscript{21} Melatonin reaches the organ it affects by the bloodstream.

\textbf{Cortisol}

The glucocorticoid cortisol is a steroid secreted from the Zona Fasciculata and Zona Reticularis of the adrenal cortex. Corticotropin releasing hormone (CRH) is secreted from the
paraventricular nucleus of the hypothalamus and induces secretion of Adrenocorticotropic hormone (ACTH) from the anterior pituitary gland. ACTH controls secretion of cortisol.

Almost any kind of psychological and physical stress can lead to increased ACTH and thus cortisol. Cortisol negatively inhibits CRH in the hypothalamus and ACTH in the anterior pituitary gland when blood cortisol concentration becomes too high.

The cortisol blood concentration differs between individuals and follows a circadian rhythm where blood concentration of cortisol varies between a high of 20 mg/dl one hour before arising in the morning and a low of about 5 mg/dl around midnight.\textsuperscript{22}

**Serotonin**

Serotonin exists in many different tissues in the body and is realised from trombocytes. It leads to contraction of the arteries, inhibits disposal of stomach acid and is a neurotransmitter in the CNS. Serotonin is made of tryptophan and is a precursor of melatonin.\textsuperscript{15}

**Cholecystokinin (CCK)**

Cholecystokinin (CCK) is a hormone realised from the mucosa of intestine after eating a fatty meal. Cholecystokinin is a neuroactive peptide that exists in various forms and exhibits a variety of both peripheral and central nervous system actions. There are several different CCK.\textsuperscript{23}
Orexin

Orexin are peptides found exclusively in the lateral hypothalamus. The concentration of orexin rises with starvation and with decreasing levels of leptin.\textsuperscript{24}

Neurotransmitter imbalances

Serotonin

Disturbances of the serotonin activity may create vulnerability for the expression of a cluster of symptoms that are common to both anorexia nervosa and bulimia nervosa.\textsuperscript{25} It seems that increased serotonin activity in the brain may be responsible for anorectic behaviour, while deceased serotonin activity may be responsible for bulimic behaviour.\textsuperscript{26}

Compared with healthy controls, studies have shown that subjects with a history of bulimia nervosa had significant lowering of mood, increases in ratings of body concern, and subjective loss of control of eating following a tryptophan-free mixture given. The results suggest that diminished serotonin activity may trigger some of the cognitive and mood disturbances associated with bulimia nervosa. Findings support suggestions that chronic depletion of plasma tryptophan may be one of the mechanisms whereby persistent dieting can lead to the development of eating disorders in vulnerable individuals.\textsuperscript{27} Abnormalities of the serotonin system have been reported in both anorexia nervosa and bulimia nervosa. For example patients who have recovered from the acute phase of illness have increased cerebrospinal fluid (CSF) 5-hydroxyindoleacetic acid.\textsuperscript{28}

At the Western Psychiatric Institute and Clinic, University of Pittsburgh Medical Centre, the reaction of 22 healthy women suffering from bulimia nervosa and 16 healthy control women
who were given tryptophan depleted mixture of aminoacids, was studied. Their mood and appetite were rated and blood samples were taken. After 420 minutes all the women were presented with foods and allowed to binge and vomit if they wanted to. The result was that all “women had similar and significant reduction in plasma tryptophan levels. After ATD (Acute Tryptophan Depletion), the BN women had a significantly greater increase in peak (minus baseline) depression, mood lability, sadness and desire to binge compared to the CW.”

The researchers concluded that the women with bulimia nervosa are more vulnerable to the mood lowering effects of acute tryptophan depletion. This may suggest that they have altered modulation of central 5-HT neuronal systems.²⁹

In one research an amino acid mixture lacking the serotonin precursor tryptophan and a balanced mixture were given to 10 women with a history of Bulimia Nervosa. The women were not told what mixture they got when. Eleven healthy female subjects with no history of any psychiatric disorder were also given the two different amino acid mixtures. The results showed that subjects with a history of bulimia nervosa had significant lowering of mood, were more concerned about their body image and lost control of eating when they got the tryptophan-free mixture, compared to the healthy controls. The study concluded that diminished serotonin activity may lead to some of the cognitive and mood disturbances associated with bulimia nervosa. In other words; persistent dieting lead to a chronic depletion of plasma tryptophan and this may lead to the development of eating disorders in vulnerable individuals.²⁷
Neuropeptid Y

One study has shown that patients with anorexia and bulimia nervosa have significantly elevated levels of plasma neuropeptid Y (NPY) concentration compared with healthy controls. The elevated NPY in bulimia nervosa was not related to BMI because both the controls and the people with bulimia nervosa had the same BMI. 26

Nutritive imbalances

Bulimia Nervosa and leptin

At the Department of Psychiatry and Behavioral Sciences, Medical University of South Carolina, researchers have indicated that plasma leptin levels are significantly correlated to body mass index (BMI) (P<0.002) and weight (P<0.001) and that women with bulimia nervosa do have significantly reduced plasma levels of leptin compared with healthy control women with comparable BMI (P<0.001). 30

Researchers at Massachusetts General hospital, Boston, USA has conducted a study of seven lean, healthy women without a history of eating disorder, investigating the effect of binge eating on metabolic and leptin dynamics. The women were investigated on two occasions. During one admission they ate three regular meals plus a snack every day. On the other admission, they ate the same number of calories in a single meal. Glucose, insulin, and leptin
were measured frequently for 12 h beginning at 0800 h on the third day of each diet, and an insulin tolerance test was performed while the subjects were fasting on the fourth day.

The researchers concluded with the following:

1) Ingestion of a large number of calories at one time (binge eating) impacts metabolic parameters even when total calories and macronutrients are appropriate for weight.

2) The timing of energy intake is an independent determinant of the diurnal rhythm of leptin secretion.

3) The mechanism of exaggerated insulin secretion after a binge meal remains to be determined, but may be related to the altered diurnal pattern of leptin secretion.

4) As most binge eating episodes in the population is associated with the ingestion of excess calories, it is hypothesised that binge eating behaviour is associated with even greater metabolic dysfunction than that described herein.  

In Italy, researchers measured plasma levels of leptin, glucose and other hormones in three groups of eating disorder patients with different body weight, 21 with anorexia nervosa (AN), 32 with bulimia nervosa (BN), 14 with binge-eating disorder (BED) and 25 healthy females volunteered for the study. In AN patients, plasma glucose was reduced and plasma cortisol was enhanced. In all three groups, women with low body weight had reduced leptin levels. No definite correlation between leptin and “psychopathological measures, plasma glucose [and] cortisol was found.” Their conclusion was that other factors “than body weight may play a role in the determination of leptin changes in eating disorders.”

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In Warsaw, Polen a resent study also shows that leptin levels in women suffering from anorexia nervosa or bulimia nervosa are significantly lower than in healthy women of the control group with the same BMI. Women with bulimia nervosa had significantly higher leptin levels than women with anorexia nervosa. Several studies have concluded that it appears leptin has an important role in the pathogenesis of obesity and eating disorders.

**Anorexi nervosa and Leptin**

Underweight anorexia nervosa patients have low serum leptin, plasma and CSF concentrations of leptin.

**Night-eaters and leptin**

For comparison, leptin levels in night eaters were higher among the overweight subjects than among the normal-weight subjects (both night-eaters and controls) (P<0.001). When compared with their respective control group, the rise in the nocturnal (12 PM to 6 AM) plasma leptin levels, were lower in both normal-weight and overweight night eaters (P<0.001).

**Hormone imbalances**

**Bulimia Nervosa and Melatonin**

In a review on the melatonin involvement in psychiatry, Pacchierotti et al concluded that the characteristic rhythm of melatonin secretion seems to be altered in various psychiatric disorders. The authors meant that further investigation is necessary to decide if this alteration has etiological importance, and in which psychiatric disorder this is significant.
Another study concluded that women with eating disorders, but are not depressed, have normal pineal gland melatonin secretion. The study compared cycling and amenorrhoeic women with normal weight with eight bulimia nervosa and seven women with anorexia nervosa to 21 normal cycling controls and measured. Every twenty minutes blood samples for melatonin measurements were obtained in a controlled light-dark environment. Cycling women were studied in the early follicular phase of the menstrual cycle. Mean melatonin levels were similar in all three groups. Even the time of melatonin peak, the time of onset and offset of the nocturnal serum melatonin excursion and the duration of the nocturnal elevation were similar.\textsuperscript{37}

\textit{Orexin A, Orexin B}

These hormones are in one study connected with feeding behaviour in rats. An injection of these hormones into the lateral hypothalamus in rats, were found to immediately stimulate eating eight to ten times more than normal. The research also showed elevated levels of these hormones when the rats were starved.\textsuperscript{24}
Results

Cortisol

Figur 1: Circadian cortisol levels in patients suffering from bulimia nervosa

In our study the diurnal cortisol secretion showed a peak at 8AM in both groups. The maximum and minimum levels did not differ between the groups. However, at 4-6 PM there was a significant increase in the plasma concentrations of cortisol in the bulimic subjects compared to the controls (p<0.05) who experienced a decrease in plasma concentration of cortisol. This represents a time of 210 min after ingestion of dinner. (Fig 1).
Melatonin

Figur 2: Circadian melatonin levels in patients suffering from bulimia nervosa

In our study significantly increases in nocturnal levels of plasma melatonin concentrations were observed in the bulimic women when compared to the controls (fig 2) at times 12 PM, 2 AM, 4 AM, 6 AM and 8 AM ($p<0.05$). The time of the maximal increase in melatonin was approximately the same in both groups, at 2 AM. In the control group, melatonin secretion reached the maximal daily inhibition point at 8 AM, in bulimia nervosa, however, the maximal daily inhibition point was reached first at 2 PM.
Leptin

Figur 3: Circadian leptin levels in patients suffering from bulimia nervosa

Patients with bulimia nervosa have lower leptin blood concentration values throughout the day and night than the healthy control group when the leptin levels were corrected for BMI (p<0.05). (Fig 3).
Discussion

Melatonin

In our study the bulimic patients had increased nocturnal levels of melatonin compared to the control subjects. The timing for the maximal peak was the same in both groups, whereas the melatonin secretion reached the maximal daily inhibition point first at time 2PM. Compared to the controls this was 6 hours later. It is hard to explain the association between the dysregulation of melatonin and bulimia nervosa. There are few documentations of a role of melatonin in regulation of eating. In birds cyclic melatonin synchronizes the circadian rhythm of feeding\textsuperscript{38}, whereas in fish exogenous melatonin suppresses food intake\textsuperscript{39}. We have experienced that the remissed bulimics registered satiety in the morning and increasing hunger during afternoon and evening (personal observation). Therefore, we may speculate if the nocturnal hypermelatoninemia postpones the time with maximal inhibition of its secretion which may be crucial for initiating hunger feeling in the morning. Another explanation may be that the high melatonin in the morning induces tiredness that in return may depress the feeling of hunger. However, further studies are needed to determine the exact role of melatonin in regulation of feeding patterns.

Cortisol

There are no significant differences between the time, level of maximum (8 AM) or nadir (12PM) levels in the diurnal secretion of cortisol between the bulimics and the control group. This profile of cortisol secretion represents a characteristic diurnal secretion and is described
as the hypothalamic-pituitary-adrenal (HPA) axis. The protein rich dinner eaten at 1 PM is a physiological challenge to the HPA axis. The measurement of free cortisol in saliva during a meal has been proposed as an ideal psychological stress-free and reliable technique to assess the HPA axis. As expected the decrease of cortisol in the controls was slightly attenuated during afternoon and early evening due to responses to food intake. The significant increase in the plasma concentrations of cortisol in the bulimic subjects seen at 4-6 PM, may indicate a hyperreactive hypothalamic CRH and/or pituitary ACTH release in response to a physiological stimuli. This is a unique response pattern in a phase of the disease where the bulimics were all in a non active period of the disease with no purging or overeating, and the stress factor should be as in normal subjects. This may indicate that one of the primary defects of bulimia nervosa is a neuroendocrine state of hyperreactive hypothalamic-pituitary axis. These patients seem to be highly vulnerable to stress. Several diseases have been associated with increased HPA axis such as melancholic depression and chronic anxiety. It would be of interest to test these diseases in a remissed state and study if a primary defect of hyperreactive ACTH-cortisol response to a physiological, and/or an exogenous CRH stimuli, can be found. Furthermore it may be interesting to investigate the plasma cortisol levels of bulimics when they are in an active phase of the disease.

People suffering from bulimia nervosa have a stressed hypothalamic-pituitary axis according to unpublished studies by Birkevedt et al (to be submitted). The significant difference in cortisol value seen at 4 pm is the result of a higher than normal increase in CRH after dinner. CRH increases cortisol levels.
Leptin

The bulimic patients had lower circadian leptin levels (corrected for BMI). Based on our knowledge of leptin it is reasonable to assume that the reduced levels of leptin experienced in bulimia nervosa leads to reduced inhibition of hunger, thus increased feeling of hunger and increased food intake. But this needs further investigation.

Conclusion

The circadian levels of cortisol, melatonin and leptin in patients with bulimia nervosa exhibit great deviations from healthy control subjects. These neuroendocrine abnormalities may to some extent explain the clinical phenotype of bulimia nervosa, but are too complex to give a comprehensible understanding of the pathophysiology of the disease.
References

1. www.noah-health.org/english/wellcomp/eatdisorders.htm


Enclosure 1: Information poster

Do you have bulimia nervosa and want to participate in a research project?

We are doing a research project where we are trying to learn more about how our body regulates hunger and satiety. In this regard we want to come in contact with people with bulimia nervosa who may be interested in participating. People who are seriously ill, smoke or use medication that may affect hormones or your body’s metabolism (e.g. contraceptive pills) are unfortunately excluded from the project. The project consists of an evaluation conversation lasting approximately one hour, a somatic examination and admittance to a clinical research ward for 24 hours. Those who participate will receive 500 NOK.

For further information please contact

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Enclosure 2:

**Questionnaire for women with bulimia nervosa**

*Developed by Grethe Støe Birketvedt*

**Name:**

**Address:**

**Phone:**

1. During a two hour period, do you often eat what most people would consider an unusually large amount of food?

   **YES**  **NO**

2. Do you feel loosing control over what you eat and how much you eat?

   **YES**  **NO**

3. Has this happened twice or more the last 3 months?

   **YES**  **NO**

4. After eating episodes, do you ever loose your food by throwing up or use laxatives?

   **YES**  **NO**

5. Does this happen more than twice a week?

   **YES**  **NO**

6. After an eating episode, do you ever avoid eating for 24 hours or more?

   **YES**  **NO**

7. Or do you exercise for an hour or more afterwards to keep from gaining weight?

   **YES**  **NO**
8. Does this occur more than twice a week?
YES     NO

9. Are you hungry in the morning?
YES     NO

10. Do you eat more than half of your daily calorie intake after 8 pm?
YES     NO

11. Do you eat after your last meal in the evening?
YES     NO

12. Do you get up at night to eat?
YES     NO

13. Do you wake up at night more than once with an urge to eat?
YES     NO

14. Does this happen three times or more during a week?
YES     NO

15. Do you have problems sleeping after having gone to bed at night?
YES     NO

16. Do you wake up and eat if you can not sleep?
YES     NO

17. Do other members of your family have the same problems?
YES     NO

If so, which problems?
18. Do you use any regular medication? (Birth control pills?)

YES       NO

What kind?

---

19. Do you smoke?

YES       NO

20. How much alcohol do you drink per week? (Name amount and type)

---

21. Do you have any diseases?.................................

YES       NO

What kind of disease?

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