Neuroendocrinology Letters ISSN 0172–780X

CLINICAL ORIGINAL ARTICLE

Plasma Leptin, Neuropeptide Y (NPY) and Galanin Concentrations in Bulimia Nervosa and in Anorexia Nervosa

Bogusława Baranowska, Ewa Wolinska-Witort, Elzbieta Wasilewska-Dziubinska, Krzysztof Roguski & Magdalena Chmielowska

Neuroendocrinology Department, Medical Centre of Postgraduate Education, Fieldorfa 40, 04-158 Warsaw, Poland.

Correspondence to: Professor Bogusława Baranowska, M.D., Ph.D.
Neuroendocrinology Dpt. Fieldorfa 40, 04-158 Warsaw Poland.
TEL/FAX +48 22 610 31 59
E-MAIL zncmkp@free.polbox.pl
E-MAIL zncmkp@polbox.com

Submitted: *July 9, 2001*
Accepted: *July 29, 2001*

Key words: **leptin, NPY, bulimia nervosa, anorexia nervosa**

*Neuroendocrinology Letters 2001; **22**:356–358 pii: NEL220501A05 Copyright © Neuroendocrinology Letters 2001*

Abstract

OBJECTIVES: It has been reported that leptin and neuropeptide Y (NPY) play a role in the control of appetite and in the regulation of hormonal secretion.
METHODS: Plasma leptin, neuropeptide Y (NPY) and galanin concentrations were estimated in 13 women with bulimia nervosa (BN) 19 women with anorexia nervosa (AN) and in 19 healthy women of the control group (CG).
RESULTS: Plasma leptin concentration in BN was significantly higher than that in AN and it was lower as compared with the control group, despite the same BMI (body mass index) in both the groups. Plasma leptin level in AN was significantly lower as compared with the controls. Plasma galanin concentrations in AN and BN did not differ significantly from the control group.
Plasma NPY concentration in AN was lower than that in the control group. However, plasma NPY level in BN was significantly higher as compared with AN and with the control group (CG). The observed increase of NPY in BN was independent of BMI because BMI in bulimia nervosa was normal.
CONCLUSIONS: The data may suggest that other factors than body weight changes may be involved in the modulation of leptin and NPY release in BN. The pathological behaviour of patients with bulimia nervosa may result from disturbed NPY release which is the strongest orexigenic factor.

Introduction

The pathogenesis of anorexia nervosa and bulimia nervosa remains poorly understood. Our previous studies showed that the neuropeptides and neurotransmitters modulating eating behaviour play an important role in the neuroendocrine control of hormonal secretion in anorexia nervosa [1, 2, 3, 4].

Neuropeptide Y (NPY) and galanin are orexigenic peptides in the hypothalamic control of feeding behaviour [5, 6, 7, 8, 9]. NPY and galanin may regulate appetite via both central and peripheral mechanisms. The interaction between central and peripheral signals is due to leptin.

Leptin – a peptide secreted by adipocytes may modulate the activity of NPY and other peptides which are known to affect feeding behaviour [10, 11, 12].

The aim of this study is to evaluate the relationship between leptin and NPY, and galanin in bulimia nervosa and in anorexia nervosa.

Subjects and Methods

The study subjects were 13 women with bulimia nervosa aged 17–25 yrs (mean 20 yrs), 19 women with anorexia nervosa aged 16–24 yrs (mean 19 yrs) and 19 healthy women of control group aged 17–26 yrs (mean 20 yrs). A diagnosis of bulimia nervosa and anorexia nervosa was made according to the criteria of DSM-IV [13]. Women with anorexia nervosa (AN) were investigated during the weight loss phase of the disease and the duration of clinical symptoms of anorexia nervosa was 20–24 months. All women with AN were amenorrhoeic. All women with bulimia nervosa (BN) except one normally menstruated. The duration of clinical symtoms of BN was 21–26 months. All healthy women and women with BN were investigated in the follicular phase of the menstrual cycle. No pharmacological or dietetic treatment was introduced before investigations. All gave their informed consent for the study. Blood samples for NPY, galanin, and leptin assays were taken at 8 am from fasting subjects. Plasma NPY, galanin, and leptin concentrations were measured by radioimmunoassay with commercial kits (Peninsula Laboratories, Belmont, CA). Sensitivity of the NPY assay was 2 pg/tube, and the interassay and intraassay coefficients of variation were 8.5% and 7.3%, respectively. Sensitivity of the galanin assay was 13 pg/tube, and the interassay and intraasay coefficients of variation were 7.3% and 6.1%, respectively. Sensitivity of the leptin assay was 0.5 ng/ml, and the interassay and intraassay coefficients of variation were 8.3% and 6.2%, respectively.

The data are presented as means ± SEM. Statistical analyses were performed with nonparametric tests using the program Statistics and Distribution Fitting (Statistica for Windows). The Kruskal-Wallis test and Anova test were also used.

Results and Discussion

It has been known that some neurotransmitters and neuropeptides play an important role in the control of appetite and hormone secretion [3, 4, 6, 9].

Multiple endocrine dysfunctions were observed not only in anorexic but also in bulimic eating disorders [14]. The existence of central neurotransmitter disturbances in bulimia nervosa was suggested by some authors [15, 16, 17, 18]. Leibowitz [16] accumulated some evidence that noradrenaline plays a role in the regulation of hunger and satiety as well as in the regulation of many neuroendocrine systems controlling hypothalamo-hypophyseal system. Kay et al [17] found that noradrenaline concentrations in the plasma and in cerebro-spinal fluid (CSF) were significantly lower in patients with bulimia nervosa. It was not a proof of diminution in the noradrenaline turnover because noradrenaline in the CSF is derived not only from the brain but the catecholamines can also come from the blood stream. However, Kay et al [17] observed increases in plasma noradrenaline concentrations during "binge eating". They concluded that sympathetic nervous system activity decreases due to the periods of intermittent undernutrition. Jimmerson et al [18] suggested that decreased activity of the central serotonin system may be involved in the mechanism of bulimia.

In our paper we presented plasma leptin, NPY and galanin concentrations in women with bulimia nervosa (BN), anorexia nervosa (AN), as compared with the control group (CG) (table I).

Table 1. Plasma leptin, NPY, galanin concentrations in women with bulimia nervosa, anorexia nervosa as compared with the control group.

Plasma Concentrations ($\bar{X} \pm$ SEM)	Bulimia Nervosa n = 13	Anorexia Nervosa n = 19	Control Group n = 19
LEPTIN (ng/ml)	19,6 ± 3,7 *	8,6 ± 1,4 ** *	31,7 ± 4,0
NPY pg/ml	6,7 ± 0,9 ** *	2,6 ± 0,2	3,1 ± 0,3
Galanin pg/ml	14,1 ± 0,7	16,7 ± 1,3	21,6 ± 7,0
BMI kg/m^2	22,0 ± 1,4	15,6 ± 0,3	20,2 ± 1,0

* p<0,01 ** p<0,001

We found that the arithmetical mean of plasma leptin concentration in BN was significantly higher than that in AN ($p<0.01$).

The higher plasma leptin in BN as compared with AN may be explained by higher BMI (body mass index) in BN than that in AN.

However plasma leptin level in BN was lower as compared with the control group, despite the same BMI in both the groups.

Other authors also observed lower leptin concentrations in the normal weight untreated bulimic patients as compared with the controls [19]. They demonstrated that after acute refeeding plasma leptin increased in both the bulimic patients and the controls, however, in the bulimic patients it did not reach the values observed in the normal controls.

The observations may suggest that other factors than body weight changes may be involved in the modulation of leptin production in BN. Plasma galanin concentrations in AN and BN did not differ significantly from the control group. Our previous studies demonstrated the significant positive correlations between leptin, NPY and BMI [2]. We observed a marked increase of both NPY and leptin in the obese patients. However, in the anorectic patients we found low leptin levels and low NPY concentrations. The results indicated that in patients with anorexia nervosa low production of leptin did not cause any increase of NPY. Our previous data may suggest the existence of disturbances in the feedback mechanism of leptin-NPY in both the obese and anorectic patients [2].

Our present results confirm previous studies. The plasma leptin level in AN was significantly lower ($p<0,001$) as compared with the controls. The plasma leptin in AN also was significantly lower than that in BN ($p<0.01$). The plasma NPY concentration in AN was lower than that in the control group. However, the plasma NPY level in BN was significantly higher as compared with AN ($p<0,001$) and with the control group (CG) ($p<0,01$). The observed increase of NPY in BN was independent of BMI because BMI in bulimia nervosa was normal.

It may be speculated that other factors than changes in body weight may be involved in the increased production of NPY in bulimia nervosa. The pathological eating behaviour of patients with bulimia nervosa may result from disturbed NPY release which is the strongest orexigenic factor.

REFERENCES

1 Baranowska B, Radzikowska M, Wasilewska-Dziubinska M, Roguski K, Borowiec M, Disturbed release of gastrointestinal peptides in anorexia nervosa and in obesity. Diabetes, Obesity and Metabolism 2000, **2**:99–103.

2 Baranowska B, Wasilewska-Dziubinska E, Radzikowska M, Płonowski A, Roguski K, Neuropeptide Y, galanin and leptin release in obese women and in women with anorexia nervosa. Metabolism, 1997, **46**:1384–1389.

3 Baranowska B, Rozbicka G, Jeske W, Abdel-Fattah H. The role of endogenous opiates in the mechanism of inhibited luteinizing hormone (IH) secretion in women with anorexia nervosa :the effect of naloxone on LH, follicle stimulating hormone, prolactin and β-endorphin secretion. J Clin Endocrinol Metab 1984,**59**:412–416.

4 Baranowska B, Are disturbances in opioid and adrenergic systems involved in the hormonal dysfunction of anorexia nervosa. Psychoendocrinology 1990, **5**:371–379.

5 Kalra SP, Kalra PS. Neuropeptide Y a novel peptidergic signal for the control of feeding behavior. Curr Top Neuroendocrinol, 1990, **10**:192–217.

6 Leibowitz SF. Central physiological determinants of eating behavior and weight. In: Brownell D, Fairburn CG, editors. Eating Disorders and Obesity, New York, NY, Guilford John Willey, Sons pp 1995, 3–5.

7 Rokaeus A. Galanin, a newly isolated biologically active neuropeptide. Trends Neurosci 1987, **10**:158–164.

8 Koenig JI, Gabriel SM, Kaplan LM. Galanin. A potentially significant neuroendocrine modulator in: Barnes CD, John Stonca, editors. Brain – Gut Peptides and Reproductive Function Boca Raton, FI CRC, 1991, 194–208.

9 Sahu A, Kalra SP. Neuropeptidergic regulation of feeding behaviour: Neuropeptide Y. Trends Endocrinol Metab 1993, **4**:217–224.

10 Zhang Y, Proenca R, Maffei M et al. Positional cloning of the mouse obese gene and its human homologue. Nature,1994, **3**:425–443.

11 Schwartz MW, Baskin DG, Bukowski TR et al. Specificity of leptin action on elevated blood glucose levels and hypothalamic neuropeptide Y gene expression in ob/ob mice. Diabetes, 1996, **45**:531–535.

12 Rohner-Jeanrenaud F, Jeanrenaud B. CNS and body weight regulation. Annales D'Endocrinologie,1997, **58**:137–142.

13 American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders 4th ed. Washington, DC: American Psychitric Press; 1994.

14 Fichter MM, Pirke KM, Endocrine dysfunctionsin bulimia nervosa. In: Bulimia Nervosa, Basic Research. Diagnosis and Therapy. Ed M. M, Fichter, J. Willey and Sons. N York, Brisbane, Toronto, Singapore: Chichester; 1990, 235–257.

15 Pirke KM. Central neurotransmitter disturbances in bulimia nervosa. In Bulimia Nervosa. Basic Research Diagnosis and Therapy. Ed MM Fichter, J Willey and Sons, N York, Brisbane, Toronto Singapore: Chichester; 1990 223–234.

16 Leibowitz SF. Noradrenergic function in the medial hypothalamus: potential relation to anorexia nervosa and bulimia. The Psycholology of Anorexia Nervosa. Ed by KM Pirke and D Ploog Springer Berlin, 1984, 35–45.

17 Kaye WH, Ebert NH, Raleigh M Lake R. Abnormalities in CNS monoamine metabolism in anorexia nervosa. Arch Gen Psych 1984, **41**:350

18 Jimmerson DC, Brant H A, Brewerton TD. Evidence for altered serotonin function in bulimia and anorexia nervosa: behavioral implications. In Psychobiology of Bulimia Nervosa. D Ploog, editor. Berlin, Heidelberg, New York: Springer. pp 1998, 83–89.

19 Manteleone P, Bartolotti E, Fabrazzo M, La Rocca A, Fuschino A, Maj M. Plasma leptin to acute fasting and refeeding in untreated women with bulimia nervosa. J Clin Endocrinol Metab, 2000, **85**:2499–2503.