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ORIGINAL ARTICLE

Plasma orexin A, orexin B, leptin, neuropeptide Y (NPY) and insulin in obese women

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Abstract

OBJECTIVE: It has been reported that the peptides such as orexins, neuropeptide Y (NPY) and leptin may play an important role in the regulation of appetite and energy metabolism. The interaction between leptin, orexins and NPY, as well as between peptides and insulin and cortisol in the different nutritional states have been investigated in animals. However, at present this relationship is poorly understood in humans.
RESEARCH METHODS: Material consisted of 36 obese women and 16 lean women. Plasma orexin A, orexin B, neuropeptide Y (NPY), leptin, insulin concentrations were measured with RIA methods.
RESULTS: Plasma orexin A concentrations were significantly lower in obese women as compared with control group. Plasma orexin A was significantly lower in severe obesity (BMI > 40 kg/m^2) than that in moderate obesity (BMI < 40 kg/m^2) Plasma orexin B concentrations did not change. However, plasma NPY, leptin and insulin levels were markedly higher in obese women, especially in severe obesity.
CONCLUSIONS: Our results confirmed the thesis that orexin A, NPY, leptin play an important role in the regulation of energy metabolism in humans. In obesity the activity of these peptides is disturbed.

Introduction

It has been reported that the peptides such as orexins, neuropeptide Y (NPY) and leptin play an important role in the regulation of appetite and energy metabolism [1, 2, 3].

Orexin A and orexin B stimulate appetite and food intake in rats. Orexines and orexin receptors were discovered in the central nervous system especially in hypothalamus as well as in the enteric nervous system, the pancreas and the gut [3, 4].

Orexin A, a 33-amino acid peptide has a more potent and prolonged effect on appetite as compared with orexin B, a 28 amino acid peptide [3].

Dalal et al. [5] and Arihara et al. [6] showed for the first time that orexin A can be detected in human plasma. Animal experiments showed that orexin A crosses the blood-brain barrier [7].

Since orexin A rapidly crosses the blood-brain barrier and reaches brain tissue, a peripheral in-

crease in orexin A might, at least in part, also contribute to appetite control and to energy expenditure in humans [7]. The interaction between the peptides leptin, orexins and NPY as well as between peptides and insulin and cortisol in the different nutritional states have been investigated in animals [1, 8, 9, 10, 11].

However, at present this relationship is poorly understood in humans.

The aim of this study was to evaluate plasma orexin A and B concentrations and their relationships with leptin, NPY and insulin in obese patients.

Material and methods

Material consisted of 36 obese women: 28 women, aged 21–57 years mean – 35 years. Their BMI ranged 30–40 kg/m^2, mean 34,8 kg/m^2, WHR < 0,8, 8 obese women aged 21–44 years, mean 34 years with BMI over 40 kg/m^2, mean – 44,3 kg/m^2, WHR < 0,8. The control group consisted of 16 lean women aged 25–60 years, mean 38 years, with BMI 21–25 kg/m^2, mean 23 kg/m^2.

The diagnosis of simple obesity was established after exclusion of other hormonal diseases. Plasma orexin A, B were measured with RIA methods using commercial kits from Peninsula. Plasma leptin, NPY and insulin were measured using commercial kits (Linco, Peninsula, Świerk, respectively).

Results

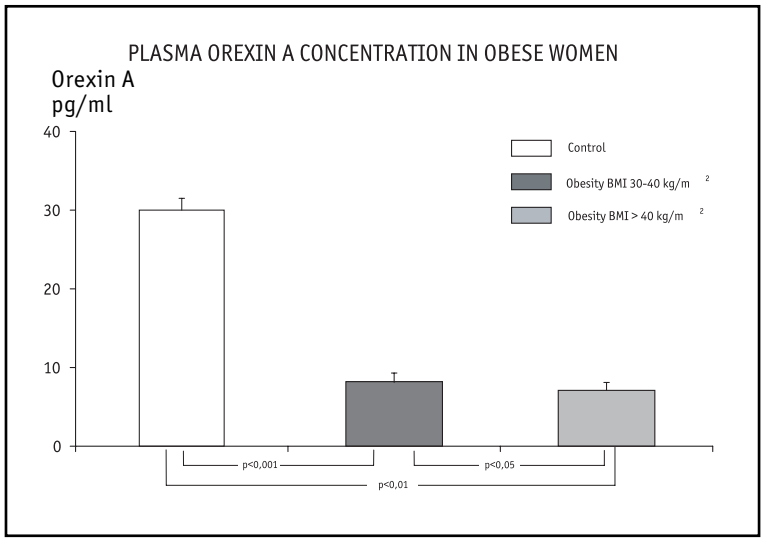
Plasma orexin A concentrations in the obese women as compared with the lean women were presented in *Figure 1*. Plasma NPY, leptin concentrations and insulin were demonstrated in *Figures 2, 3* and *4*.

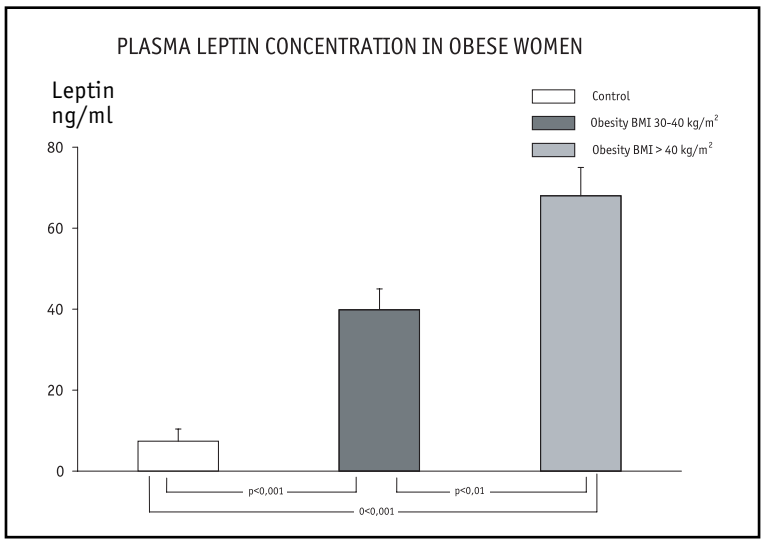
Mean plasma orexin A concentration was significantly lower in the obese women with BMI 30–40 kg/m^2 and BMI > 40 kg/m^2 as compared with the control group (p < 0,001, p < 0,001), respectively). Plasma orexin A level was significantly lower in severe obesity (BMI > 40 kg/m^2 than that in moderate obesity (BMI 30–40 kg/m^2) (p <0.05).

We did not observe any changes in plasma orexin B (data not shown).

Plasma leptin concentrations were significantly higher in moderate and severe obesity as compared with the control group (p <0.001), p <0.001, respectively). Plasma leptin level in the obese women with BMI over 40 kg/m^2 was significantly higher as compared with the group of the obese women with BMI 30–40 kg/m^2 (p <0.01).

Plasma NPY concentrations were markedly increased in the obese women both with BMI 30–40 kg/m^2 and BMI > 40 kg/m^2 comparing





them with the control group (p <0.001, p <0.001), respectively. In the obese women with BMI > 40 kg/m^2 plasma NPY was significantly higher than that in the obese women with BMI 30–40 kg/m^2. Similarly, plasma insulin concentrations were enhanced in two groups of obese women (p <0.001, p <0.001) and the highest level of insulin was observed in severe obesity.

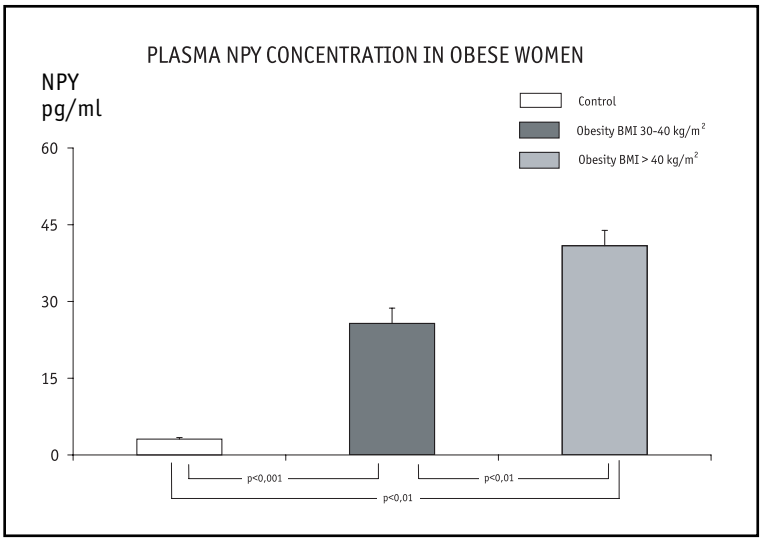
Discussion

Our results are in agreement with the studies of Adam et al. [4]. The authors showed that orexin A levels correlated negatively with plasma leptin concentrations. They observed that in obese patients orexin A levels were significantly lower and leptin levels were significantly higher than that in the control group.

Adam et al. [4] have suggested that orexin A acted also in the peripheral manner and it might be involved in the regulation of human energy metabolism.

Komaki et al. [12] investigated plasma leptin, NPY and orexin concentrations in association with nutritional and metabolic parameters in humans.

They have demonstrated that plasma orexin-A concentration was significantly increased during fasting as compared with the prefasting value and returned to the basal value after refeeding.



However, plasma leptin was significantly decreased during fasting and negatively correlated with orexin-A.

The observed changes in plasma orexin A in obese patients and during fasting [4, 12] may indicate that orexin is a strong regulator of food intake [3].

Komaki et al. [12] found only a slight decrease of NPY levels but they were not significantly different to prefasting values, although animal studies during fasting found an increase in the hypothalamic NPY mRNA. Matsumura et al. [13] demonstrated that orexin-A concentrations significantly correlated with BMI and fat mass values in normal subjects. They observed the higher levels of orexin A in the group of patients aged more than 60 years and they suggested that orexin A could be involved in aging in healthy population [14].

We have published previously that plasma leptin and plasma NPY concentrations were significantly higher in the obese patients and strongly correlated with BMI [15]. We demonstrated that the neuroendocrine disturbances in obesity and in anorexia nervosa are opposite [16]. We have suggested that an abnormal activity of neuropeptides may lead to disturbed control of appetite and hormonal dysregulation in eating disorders [16].

Our present results demonstrate a decrease in plasma orexin A in the obese patients and the negative correlation with BMI. However, plasma NPY, leptin and insulin markedly increased in the obese women.

Our results and results of other authors may suggest that there is direct effect of circulating orexin A on the peripheral gut tissue [17].

On the other hand, since orexin-A rapidly crosses the blood-brain barrier [7], it might, at least in part, also contribute to appetite control and to energy expenditure in humans.

Conclusion

The decrease of plasma orexin A in association with the increase of plasma leptin and NPY, and insulin in the obese subjects confirmed the thesis that these peptides play an important role in the regulation of energy metabolism in humans and the activity of these peptides is disturbed in obesity.

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