Leptin/adiponectin ratio in obese women with and without binge eating disorder

Paula Paraguassu Brandao [1], Erica Patricia Garcia-Souza [1], Fabiana Alves Neves [1], Mario Jose dos Santos Pereira [1], Rosely Sichieri [2], Egberto Gaspar de Moura [1], Patricia Cristina Lisboa da Silva [1], Anibal Sanchez Moura [1]

1 Department of Physiology, Department of Physiological Sciences, Institute of Biology, State University of Rio de Janeiro, Rio de Janeiro, Brasil.
2 Institute of Social Medicine, Epidemiology, State University of Rio de Janeiro, Rio de Janeiro, Brasil.

Correspondence to: Anibal Sanchez Moura, PhD.
Physiology Department, Institute of Biology
State University of Rio de Janeiro (UERJ)
Avenida 28 de setembro 87 fundos, Vila Isabel,
Rio de Janeiro, RJ, 20551-030, Brasil.
TEL: +55 (21) 2587-6434; FAX: +55 (21) 2587-6129; E-MAIL: asmoura@nebin.org

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Abstract

BACKGROUND: Adipose tissue-derived hormones are involved in the pathophysiology of eating disorders and other mental disorders. Studies have suggested that the serum leptin/adiponectin ratio is highly correlated with BMI. Furthermore, it is associated with a number of metabolic processes and inflammatory markers that are involved in obesity and mental disorders, such as the physiopathology of binge eating disorder (BED). We investigated whether variations in leptin and adiponectin serum concentrations differed between adult women with and without BED before and after a meal.
METHODS: The study group was composed of 8 normal weight women (20–25 kg/m^2) without BED, 8 obese women (≥30 kg/m^2) with BED, and 7 obese women without BED (non-BED). Blood samples were collected before and after the consumption of a meal composed of 55% carbohydrates, 15% protein, and 30% lipids.
RESULTS: Body mass index (p<0.0001), leptin (p<0.0001) and the leptin/adiponectin ratio (p<0.0001) were higher in obese non-BED women than in obese BED and normal weight groups. Adiponectin (p=0.01) concentrations were lower in the obese BED group than in the other groups before and after the meal.
CONCLUSIONS: The hypoadiponectinemia followed by the altered levels of leptin in obese BED woman may predispose these subjects to an inadequate energy balance, which could promote weight gain and an increased food intake in woman that may contribute to obesity and binge eating in these subjects.

Abbreviations:

BES - Binge Eating Scale
BED - Binge Eating Disorder
BMI - Body Mass Index

ORIGINAL ARTICLE

INTRODUCTION

Binge eating refers to a pathological form of overeating that is characterized by the consumption of large amounts of food and a lack of compensatory methods or an inappropriate application of these methods (Devlin *et al.* 1997) over discrete periods of time (less than two hours, two times per week in six months). The overeating is mainly associated with a sense of loss of control, as described by Appendix B of the Diagnostic and Statistical Manual of Mental Disorders (American Psychiatry Association 1994). The disease is considered to be an important risk factor for obesity as well as discontinuation of treatment for obesity (Marchesini *et al.* 2004).

Obesity is associated with changes in adipocytokines such as leptin and adiponectin, which participate in the regulation of inflammation and insulin resistance (Hotta *et al.* 2000; Matsubara *et al.* 2002; Kern *et al.* 2003; Walker *et al.* 2007; Hyun *et al.* 2008). These adipose tissue-derived hormones are also involved in the pathophysiology of eating disorders and other mental disorders (Zeman *et al.* 2009; Monteleone *et al.* 2000; Adami *et al.* 2002; Housova *et al.* 2005; Tagami *et al.* 2004).

Adiponectin is a peptide hormone that is secreted from the adipose tissue (Yang *et al.* 2002) and plays a preventative role in the pathogenesis of obesity, atherosclerosis, coronary heart disease and breast cancer (Miyoshi *et al.* 2003; Mantzoros *et al.* 2004). It has been hypothesized that low serum adiponectin levels may be associated with insulin resistance in obese woman (Hotta *et al.* 2000). Leptin is a protein produced by white adipose tissue (Bouloumie *et al.* 1998), and it displays a positive correlation with obesity, insulin resistance and breast cancer risk (Markowska *et al.* 2004; Tessitore *et al.* 2000). In addition, leptin acts on receptors expressed in the hypothalamus to promote satiety and regulate energy balance (Yamauchi *et al.* 2009).

Fat mass is positively associated with circulating leptin (Carnier *et al.* 2008) and negatively associated with adiponectin (Nazal *et al.* 2010). Consequently, the serum leptin/adiponectin ratio has been found to be highly correlated with BMI (Kumagai *et al.* 2005; Kotani *et al.* 2006; Oda *et al.* 2008). We tested the hypothesis that the leptin/adiponectin ratio would be associated with binge eating disorder (BED). The aim of this study was to observe the serum concentrations of leptin and adiponectin to determine the leptin/adiponectin ratio in obese binge eaters and compare these values to obese women without BED as well as normal weight women without BED.

MATERIAL AND METHODS

Participants and procedures

Thirty to fifty-year-old women who attended the Piquet Carneiro Policlinic at the State University of Rio de Janeiro, were not taking any medications and had no evidence of disease other than obesity and BED were invited to participate in the study. All participants answered a questionnaire about binge-eating episodes (Binge Eating Scale, BES) (Gormally *et al.* 1982), which allowed us to select participants according to their binge eating scores. Participants were classified as binge eaters if they scored higher than or equal to 18 points on the BES.

After screening for body mass index (BMI) and BES, 60 women (20 for each group) were invited to participate in the study. The women were divided into the following three groups: normal weight without BED (20–25 kg/m^2); obese with BED (≥30 kg/m^2); and obese non-BED. Out of the 60 women invited to participate in the study, only 23 women returned to the study, and each group consisted of 8, 8 and 7 participants, respectively. Women with a diagnosis of hypothyroidism, hyperthyroidism, diabetes, hypertension, and polycystic ovary syndrome were excluded. Women who were pregnant, breastfeeding or menopausal were also excluded. Participants had given written informed consent, and the study was approved by the State University of Rio de Janeiro (UERJ) Ethics Committee.

All participants received nutritional counseling in their first visit to the clinic and a diet containing six meals per day with 55% carbohydrates, 15% protein and 30% lipids to be eaten during the month prior to the experimental day. On the experimental day, the women ate a meal similar to their diet of the previous month. All participants received identical portions of the same foods on the day of the experiment. At breakfast, all patients ate a 200 g meal consisting of bread, white cheese, and milk with coffee sweetened with sucralose.

Procedures

After 12 hours of fasting, each group participated in a laboratory section that started at 8:00 am. Blood samples were collected during fasting, 1 hour before breakfast (time 0), and 15 and 60 minutes after meal consumption. Vacuum tubes containing the anticoagulant EDTA were used during the blood collection to obtain plasma samples. Upon arrival in the laboratory, the samples were immediately centrifuged at 3,000 rpm for 10 minutes at 4 °C. The samples were stored in a –70 °C freezer for later evaluation of hormone concentrations. Bioimpedance analysis (BIA) was done on the procedure day during the fasting period. The standard tetrapolar technique employing a single current apparatus (50 kHz) was used (Biodynamics model 310, Biodynamics, Seattle, Washington, USA).

Serum concentrations of leptin and adiponectin hormones were measured by radioimmunoassay (RIA) using a commercial kit for humans (Linco Research, St Charles, MO). Total cholesterol, triglyceride and HDL-C concentrations were determined by a specific commercial kit (GoldAnalisa), and the results of LDL-C and VLDL-C were obtained indirectly from the results of triglycerides and HDL-C. Plasma TSH was determined by immunoradiometric assay (IRMA) using specific reagents for human TSH (ICN Pharmaceuticals

Inc., CA, USA), and plasma concentrations of triiodothyronine (T3) and free thyroxine (T4) were quantified by RIA using commercial reagents (MP Biomedicals Inc., NY, USA).

Statistical analysis

Statistical analyses were carried out using the Statistical Analysis System (SAS) version 9.1. An analysis of repeated measurements was conducted using mixed effects (procedure proc mixed in SAS) to test the differences among the three groups over time. This model included an estimation of effects common to individuals of the same group. Baseline differences were assessed using the analysis of variance (ANOVA) followed by Tukey post-hoc test. Pearson correlation coefficients (r) between leptin, adiponectin and the ratio of leptin/adiponectin were also calculated.

RESULTS

Regarding the socioeconomic variables, the age of the women ranged from 32 to 50 years old, 72% of the women had high school degree and 76% of the women were married. The obese non-BED women had a significantly higher BMI when compared to obese BED women, but measures of fat percentage were not different between the obese BED and obese non-BED women (Table 1). In addition, there were no statistically significant differences between serum lipid and thyroid hormone levels in any of the groups (Table 1).

Leptin

Over time, the leptin concentration (ng/dl) in the obese non-BED women was significantly higher than the normal weight group (p<0.0001). Figure 1 shows that women in the obese BED group had a significantly higher leptin concentration compared to the normal weight group (p=0.04) but a lower concentration than women in the obese non-BED group (p=0.002).

Adiponectin

Over time, the adiponectin concentration (ng/ml) was significantly lower in the obese BED women than the normal weight group (p=0.01). Although we observed a lower concentration of adiponectin during fasting in obese BED women compared to the normal weight group (p=0.04) and the obese non-BED group (p=0.06), after breakfast intake, differences only existed between the obese BED group and the normal weight group (Figure 1, p=0.006).

Tab. 1. Study groups socioeconomic and body composition variables.

	Normal Weight (n=8)		Obese without BED (n=7)		Obese with BED (n=8)		
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	***p*-value**
Age (years)	44.9	6.6	38.3	5.5	42.1	6.3	0.12
BES scores	5.8	3.3	9.2	3.4	25.6	8.1	<0.0001*
Weight (kg)	57.7 [a]	5.0	88.6 [b]	7.5	84.9 [b]	4.7	<0.0001*
Height (m)	156.1 [a]	4.6	159.4 [b]	4.8	162.3 [b]	4.5	0.04*
BMI (kg/m^2)	23.6 [a]	1.0	34.9 [b]	3.9	32.3 [c]	2.1	<0.0001*
Muscle Weight (kg)	40.11 [a]	3.12	52.90 [b]	3.81	51.70 [b]	2.69	<0.0001*
Fat Weight (kg)	18.94 [a]	2.52	34.98 [b]	3.92	33.15 [b]	2.96	<0.0001*
Fat percentage (%)	32.00[a]	2.55	39.74 [b]	1.71	39.03 [b]	1.98	<0.0001*
Resistance (ohms)	601.4 [a]	81.8	503.7 [b]	52.7	489.6 [b]	55.7	<0.0001*
Reactance (ohms)	67.0 [a]	8.3	52.7 [b]	14.1	55.7 [b]	12.00	0.0006*
Cholesterol (mg/dl)	168.17	46.45	158.33	25.20	153.91	21.70	0.66
Triglycerides (mg/dl)	73.10	42.66	98.23	39.00	81.31	41.88	0.48
HDL-c (mg/dl)	63.00	11.00	54.08	10.80	58.21	12.41	0.31
LDL-c (mg/dl)	90.55	26.91	84.59	6.60	79.44	0.90	0.75
VLDL-c (mg/dl)	14.62	8.53	19.65	7.80	16.26	8.38	0.48
T3 (pg/mL)	2.84	0.44	2.85	0.47	2.89	1.47	0.99
T4 (ng/dL)	1.66	0.23	1.60	0.10	1.45	0.35	0.25
TSH (IU/L)	1.91	1.36	2.30	2.37	2.14	1.70	0.91

A BES score of ≥ 17 was the cut-off to be considered BED. The results are expressed as mean and standard deviation (SD) after ANOVA. Different letters (a, b, c) mean statistical difference after Tukey *post-hoc* test between groups; p<0.05.

Tab. 2. Hormone correlations.

Normal Weight (n=8)	Leptin		Adiponectin	
	r	*p*-value	r	*p*-value
Leptin				
Adiponectin	0.09	0.65		
Leptin/Adiponectin Ratio	0.73	<0.0001*	–0.54	0.006*
Obese without BED (n=7)	Leptin		Adiponectin	
	r	*p*-value	r	*p*-value
Leptin				
Adiponectin	–0.29	0.19		
Leptin/Adiponectin Ratio	0.77	<0.0001*	–0.76	<0.0001*
Obese with BED (n=8)	Leptin		Adiponectin	
	r	*p*-value	r	*p*-value
Leptin				
Adiponectin	–0.08	0.67		
Leptin/Adiponectin Ratio	0.89	<0.0001*	–0.47	0.01*

Comparisons were made by simple linear regression analyses.
* Statistically significant at $p<0.05$.

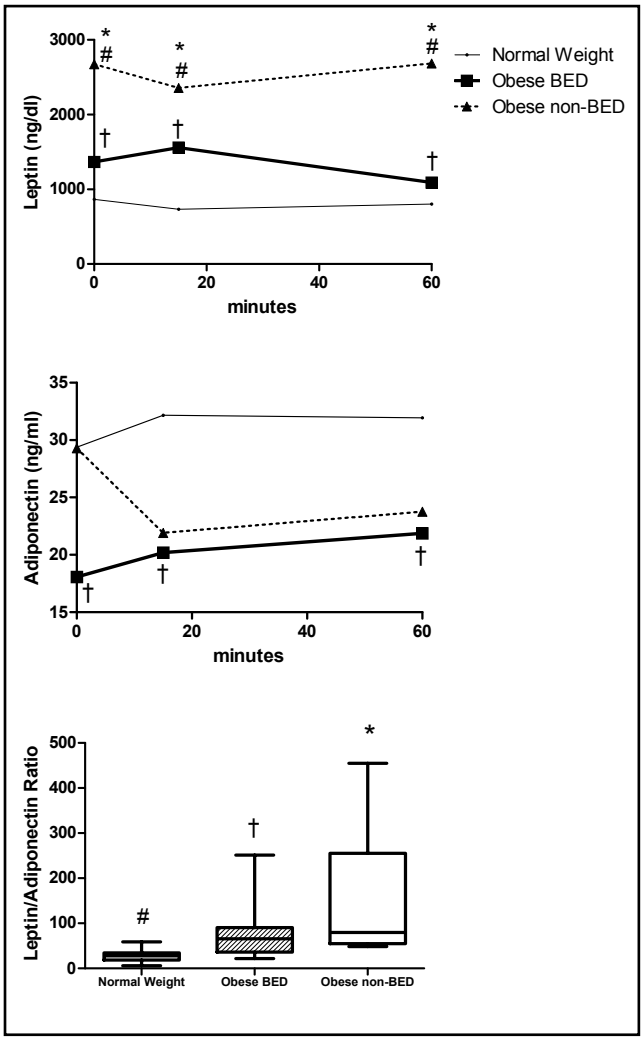

Fig. 1. This figure shows the mean hormone values over time as well as the leptin/adiponectin ratio. Serum leptin concentrations (ng/dl) were significantly different between the obese non-BED women compared to the obese BED group (p=0.002*) and the normal weight group (p<0.0001#). In addition, the leptin concentrations of the obese BED women were different from the normal weight group (p= 0.04†). The serum adiponectin concentrations (ng/ml) were significantly different between the obese BED group and the normal weight group (p=0.01†). The leptin/adiponectin ratio was significantly different in the obese non-BED group compared to the obese BED group (p<0.05*) and the normal weight group (p<0.0001#). In addition, the leptin/adiponectin ratio was also different between the obese BED group and the normal weight group (p< 0.05†).

Leptin/adiponectin ratio

The leptin/adiponectin ratio was significantly higher in obese non-BED women compared to the normal weight group (p<0.0001). In addition, we observed a higher leptin/adiponectin ratio in the obese BED group compared to the normal weight group (p<0.05) and the obese non-BED group (Figure 1, p<0.05).

Hormone correlations

Pearson correlation coefficients (r) showed that the adiponectin serum concentration correlated negatively with the leptin/adiponectin ratio in normal weight (p=0.006), obese BED (p= 0.01) and non-BED (p<0.0001) women. However, no significant correlations were found between leptin and adiponectin concentrations in obese BED (p=0.67), obese non-BED (p=0.19) and normal weight (p=0.65) groups (Table 2).

DISCUSSION

A comparison of the biochemical parameters between groups demonstrated that the concentration of total cholesterol, triglycerides, VLDL-C, LDL-C and HDL-C were not statistically different. In addition, thyroid hormones (T3, T4 and TSH) were all in the range of the recommended limits in all groups of study. The similarity between these biochemical parameters may allow us to avoid confounding factors. For instance, higher concentrations of thyroid hormones could represent the main cause of an energy balance perturbation that subsequently affects weight gain and causes increased food intake in these women (Sari *et al.* 2003; Kozlowska & Rosolowska-Huszcz 2004). Furthermore, it could make it difficult to interpret the roles of leptin and adiponectin.

In our study, we found a higher leptin/adiponectin ratio in the obese non-BED group compared to the other groups. Furthermore, we observed a negative correlation between the leptin/adiponectin ratio and the adiponectin concentration in all groups irrespective of BED. Despite the fact that our study did not find any statistically significant correlations between leptin and adiponectin concentrations, these hormones displayed inverse concentrations. Our data of hormonal values were in accordance with other authors who have obtained similar results (Kumagai *et al.* 2005; Kotani *et al.* 2006; Oda *et al.* 2008). For instance, recent studies have shown a strong positive correlation between the leptin/adiponectin ratio and obesity-related hormones, such as leptin, and BMI (Kumagai *et al.* 2005; Kotani *et al.* 2006; Oda *et al.* 2008). Beyond these similarities, our results also showed a positive correlation between leptin and the leptin/adiponectin ratio in all groups of the study.

Studies have shown that a higher leptin/adiponectin ratio is related to obesity (Matsubara *et al.* 2002) as well as a number of metabolic processes, including energy regulation, body composition control (Hotta *et al.* 2000), coronary heart disease (Hyun *et al.* 2008) and the increase of inflammatory markers that are involved in the physiopathology of obesity (Chu *et al.* 2001; Maachi *et al.* 2004; Guzik *et al.* 2006; Hyun *et al.* 2008).

In this context, it has been suggested that obesity and BED are important factors for the secretion of leptin and adiponectin (Fusco *et al.* 2007; Kempa *et al.* 2007). Another study with normal-weight women 22 to 47 years old found a negative correlation between leptin and adiponectin hormones. The same study also found that adiponectin was negatively correlated to body composition and BMI parameters (Kempa *et al.* 2007).

Fasting adiponectin concentrations were significantly lower in the obese BED women compared to the other groups. Although there are only a few studies that consider findings of adiponectin in women, a study by Monteleone *et al.* showed that obese BED women have a reduced plasma concentration of adiponectin (Matsubara *et al.* 2003). Findings from other studies have also shown a low concentration of serum adiponectin in obese people (Yang *et al.* 2002; Matsubara *et al.* 2002; 2003; Maahs *et al.* 2009) as well as in BED participants (Geliebter *et al.* 2005; Monteleone *et al.* 2003). However, there is not a study in the literature that considers the findings of the leptin/adiponectin ratio in obese women with binge eating disorder.

Adiponectin has been reported to modulate insulin sensitivity; therefore, it has a role in energy balance mechanisms. In addition, the serum concentration of adiponectin is inversely associated with BMI regardless of age. Moreover, this hormone has an anti-atherogenic action, and the presence of hypoadiponectinemia may predispose individuals to atherosclerosis and atherogenesis in the presence of obesity (Matsubara *et al.* 2002; 2003; Yamamoto *et al.* 2002). However, it is unclear whether adiponectin exerts its positive effects on insulin sensitivity in the presence of obesity. The inverse relationship between the concentrations of adiponectin and leptin may suggest that these hormones are involved in the regulation of adiposity and insulin sensitivity in middle-aged women (Maahs *et al.* 2009).

Leptin promotes satiety and controls body composition and energy balance (Weigle *et al.* 2005). If the energy balance is negative, the leptin concentration decreases and signals block the activity of peptides expressed in the arcuate nucleus (POMC / CART) that decrease the energy expenditure. In this study, the serum leptin concentration was significantly higher in the obese non-BED group than the other groups over time. Another study showed that leptin concentrations in the circulation are high in obese patients, but leptin fails to perform its action with its receptor because of resistance to this hormone action, which ultimately prevents the effect of satiety (Jequier 2002).

In conclusion, the decreased production of adiponectin in BED may be a risk factor for the development of energy unbalance. Moreover, our data show that adiponectin has a negative correlation to the leptin/adiponectin ratio that is independent of BMI and could be the factor connecting the energy unbalance. Additionally, despite the fact that leptin has satiety properties, the hypoadiponectinemia followed by the hyperleptinemia in obese BED woman may predispose these subjects to an inadequate energy balance that promotes weight gain and increases food intake. Together, these factors may lead to the progression of obesity and binge eating in these women.

Competing interests

The authors declare that they have no competing interests.

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