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ORIGINAL ARTICLE

Leptin level as a biomarker of uncontrolled eating in obesity and overweight

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Abstract

Background Uncontrolled eating (UE) showed important relationships with the development of obesity. Homeostatic regulations of feeding and energy balance, as well as hedonic eating, are regulated by leptin.

Aims The aims of this study were (1) to assess eating behaviors of Algerian adults as measured by the 51-item eating inventory; we also evaluate changes in the Three-Factor Eating Questionnaire (TFEQ) scores according to the body mass index (BMI) category; (2) to examine the association between the scores of the three TFEQ factors and the BMI values of the participants; and (3) to examine whether leptin concentrations are associated with eating behavior. Our hypothesis is that participants with obesity and high concentrations of leptin might display uncontrolled eating behavior.

Methods The subjects were 190 participants (60 obese, 60 overweight, and 70 lean subjects). The eating behavior was measured by using the 51-item eating inventory. Serum insulin concentrations were assessed by radioimmunoassay and were used to calculate homeostasis model assessment (HOMA). Serum leptin was quantified by the enzyme-linked immunosorbent assay (ELISA).

Results Obese and overweight subjects showed hyperphagic behavior, i.e., uncontrolled eating. The logistic regression analysis showed an effect of leptin, HOMA, uncontrolled eating, and emotional eating on BMI. Leptin levels were associated with the uncontrolled eating and influenced by insulin sensitivity.

Conclusions The uncontrolled eating reflects hyperphagic eating behavior in obese and overweight subjects. Coexistence of uncontrolled eating and high level of leptin demonstrates a state of leptin resistance resulting in an inability to detect satiety. High circulating leptin can be considered a potential biomarker of uncontrolled eating.

Keywords Insulin resistance · Leptin · Obesity · Overweight · Uncontrolled eating

Introduction

Obesity and overweight are associated with the risk of developing type 2 diabetes and cardiovascular and metabolic diseases [1–3]. The number of overweight and obese people has reached epidemic proportions [4]. Obesity is associated with dysregulated secretion of adipokines and a chronic low-grade inflammation [5], overexpression of leptin and hyposecretion of adiponectin [6], and excessive recruitment and infiltration of immune cells specifically macrophages [7].

Leptin is mainly produced by adipocytes in proportion to the amount of body fat [8]. It has a critical role in body weight homeostasis [9]; it improves insulin sensitivity [10], increases energy expenditure [11], and reduces appetite [12]. Homeostatic regulations of feeding and energy balance, as well as hedonic eating, are regulated by leptin signaling along the lateral hypothalamus to ventral tegmental area axis [13].

Leptin exerts its homeostatic action mainly in the hypothalamus, where it stimulates anorexigenic neurons expressing proopiomelanocortin [14], and inhibits orexigenic pathways expressing neuropeptide Y and the melanocortin antagonist Agouti-related peptide [15]. It regulates body energy state

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via suppression of excitatory synaptic drive upon orexin and melanin-concentrating hormone neurons projecting from the lateral hypothalamus to ventral tegmental area neural pathway [16]. Moreover, leptin reduces the activity of dopaminergic neurons involved in the rewarding properties of food [13].

The interaction of multiple genetic, environmental, metabolic factors and eating behaviors lead to the development of overweight and obesity [17]. Eating behaviors showed important relationships with weight gain and obesity [18]. In fact, palatable foods lead to an increasing proportion of human food consumption [19]. The homeostatic and brain reward system interactions expose individuals to obesogenicity of the environment [20]. The activation of food reward centers can override controls from homeostatic systems [21].

The hedonic proprieties of palatable food can influence feeding independent to energy status; even if individuals are satiated, palatable food can be consumed just for pleasure [22, 23].

The aims of this study were (1) to assess eating behaviors of Algerian adults as measured by the 51-item eating inventory; we also evaluate changes in three-factor eating questionnaire (TFEQ) scores according to the body mass index (BMI) category; (2) to examine the association between the scores of the three TFEQ factors and the BMI values of the participants; and (3) to examine whether leptin concentrations are associated with eating behavior. Our hypothesis is that participants with obesity and high concentrations of leptin might display uncontrolled eating behavior.

Participants and methods

The present study included 190 Algerian participants aged from 36 to 43 years, divided into three groups, i.e., 60 obese (age, 40.11 ± 3.09 years), 60 overweight (age, 39.62 ± 3.02 years), and 70 lean participants (age, 37 ± 1.13 years).

Procedures

The study was followed in the Diabetology Department, Mohamed Seghir Nekkache Hospital, Algiers, Algeria. The exclusion criteria were cardiovascular disease, diabetes, smoking habits, or any other treatment. The clinical protocol was approved by the Ethical committee of the Algerian Ministry of Public Health according to the Declaration of Helsinki. All participants provided written informed consent.

The study was conducted between January and August 2019; during their first visit, the participants were familiarized with the procedures of the study; before assessment, they received explanations about the eating inventory and they were interrogated for any family history of obesity and diabetes. Personal (gender, age, weight, height) and clinical data were also recorded for all participants. During the second visit, venous blood samples were collected for tests.

Eating behavior assessment

Eating behavior was measured by using the 51-item eating inventory also called the Three-Factor Eating Questionnaire (TFEQ) [24]. The eating inventory consists three distinct constructs: cognitive restraint, uncontrolled eating or disinhibition, and "susceptibility" to hunger or emotional eating. Cognitive restraint describes the intention to restrict food intake in order to control body weight (contrary to physiological control, such as hunger and satiety); uncontrolled eating originally defined as "disinhibition of cognitive control of eating," describes a tendency to overeating accompanied by subjective loss of control in response to environmental triggers, such as the sight and smell of palatable food, social or emotional eating; and emotional eating indicates a tendency to overeat in response to dysphoric emotions, which reflects a person's stable underlying sensitivity to hunger feelings and predisposition to eat [24–26]. The results are presented as a mean and standard deviations.

Anthropometry

Body weight was measured with an electronic scale (Lanaform) to the nearest 0.1 kg, while height was measured using a stadiometer to the nearest 0.1 cm. Waist circumference was measured at the midpoint between the iliac crest and the rib cage on the mid-axillary line at the end of a gentle exhalation. BMI was calculated as weight (kg)/height (m^2).

Serum biochemistry

Venous blood samples were collected after an overnight fast (12 h). Serum glucose, TG, total cholesterol, HDL, and LDL levels were quantified by enzymatic spectrophotometric methods using an automatic biochemical analyzer (COBAS, Roche Diagnostics). Insulin was measured and quantified by radioimmunoassay (Cis bio, Biomérieux). The state of insulin resistance was determined by homeostasis model assessment (HOMA), determined by the following formula: insulin (mU/l) × glucose (mmol/l) / 22.5 [27].

Serum leptin was quantified using commercially available enzyme-linked immunosorbent assay (ELISA) kits (DRG) according to the manufacturer's instructions. All samples were analyzed in duplicate.

Statistical analyses

The Statistica 10·0 software was used for statistical calculations. The analysis of variance (ANOVA) test was used for comparisons between all groups. The results are presented as means and standard deviations, with a significance level, $P < 0.05$. For the study of eating behavior, the data were processed by the multivariate analysis to assess the contribution of the three factors of the eating inventory. A logistic regression analysis was performed to analyze the link between BMI and the three TFEQ scores, leptin, and HOMA.

A one-way ANOVA was performed to evaluate whether uncontrolled eating, cognitive restraint, and emotional eating scores were different between the groups of patients classified as having low, normal, or high serum leptin concentrations (Table 4). To determine if the association between leptin levels and eating inventory is influenced by insulin sensitivity, the analysis of covariance (ANCOVA) was used; the HOMA was added to the model as a covariate (Table 4).

Results

Our cohort has an average BMI of 27.66 ± 4.72 kg/m^2 with a mean age of 38.5 ± 2.7 years. Concerning eating inventory assessment, the average scores were 4.55 ± 1.64 for cognitive restraint scores, 3.43 ± 1.39 for emotional eating, and 7.26 ± 3.46 for uncontrolled eating (Table 1). As illustrated in Fig. 1, obese and overweight subjects show a higher uncontrolled eating and a slight no significant increase in cognitive restraint and emotional eating score compared with lean participants.

The evolution of uncontrolled eating scores according to the BMI category shows a significant BMI effect ($p < 0.001$). Uncontrolled eating scores were significantly higher for obese and overweight subjects than for lean (Table 1).

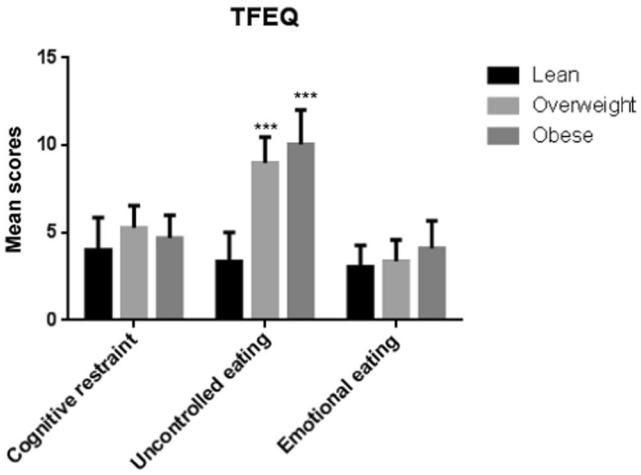

Fig. 1 Scores of eating behaviors. The Three-Factor Eating Questionnaire was used to measure the three domains of eating behaviors

An increase was observed in BMI (Fig. 2a), waist circumference, total cholesterol, and triglycerides across the two groups compared with the lean group; however, HDL was decreased (Table 2). Waist circumference shows an abdominal adiposity and state of insulin resistance in obese and overweight participants. The HOMA values confirm this state (Fig. 2b). Hyperinsulinemia was observed in overweight and obese participants (Table 2).

As illustrated in Fig. 2c, leptin concentration was higher in obese and overweight subjects as compared with the healthy participants. Individuals with obesity express the highest values of serum leptin. The overweight participants show an important increase versus the lean group (Table 1). Women show higher levels than men in all groups.

Table 3 represents the results of the logistic regression analysis including subscales, leptin, and HOMA, with BMI. Considering the overall cohort, the logistic regression analysis showed an effect of leptin, HOMA, uncontrolled eating, and

Table 1 Variations in TFEQ, leptin and HOMA by BMI and BMI category

	Overall participants	Lean (*n* = 70) (a)	Overweight (*n* = 60) (b)	Obese(*n* = 60) (c)
BMI (kg/m^2)	27.66 ± 4.72	22.8 ± 0.29	27.95 ± 0.31***	32.65 ± 0.51$^{£££}$
Eating inventory				
Cognitive restraint	4.55 ± 1.64	4 ± 0.43	5.05 ± 0.89^{ns}	4.71 ± 0.64 ^{ns}
Emotional eating	3.43 ± 1.39	3.1 ± 0.21	3.5 ± 0.22^{ns}	4.11 ± 0.21^{ns}
Uncontrolled eating	7.26 ± 3.46	3.36 ± 0.57	9 ± 0.43***	10.2 ± 0.39$^{£££}$
Leptin (ng/mL)				
Women	14.98 ± 10.53	4.95 ± 0.31	12.31 ± 1.09***	29.18 ± 1.22$^{£££}$
Men	6.99 ± 4.65	3.01 ± 0.58	6.12 ± 0.88*	12.55 ± 3.21$^{£££}$
HOMA	4.75 ± 2.65	2 ± 0.15	5.52 ± 0.58***	7.36 ± 0.80$^{£££}$

* b vs a, $^{***}p < 0.001$, $^{*}P < 0.05$; $^{£}$ c vs a, $^{£££}p < 0.001$; *ns* not significant. All results are compared with lean participants

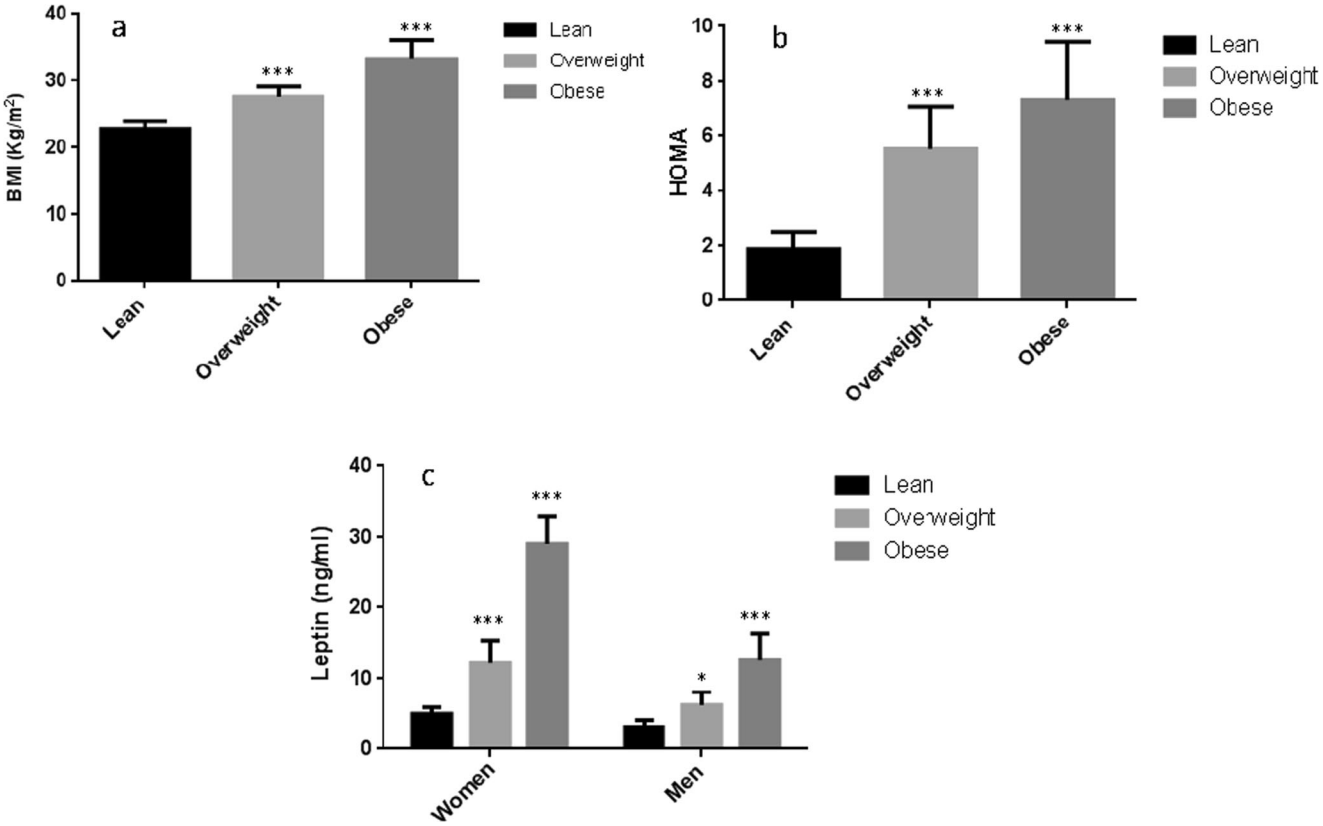

Fig. 2 The body mass index (a) homeostasis model assessment (b) and serum leptin (c) variations in lean, overweight, and obese participants

emotional eating on BMI. Cognitive restraint was not significantly correlated with BMI.

A one-way ANOVA was performed to evaluate whether uncontrolled eating, cognitive restraint, and emotional eating scores were different between the groups of participants classified as having low, normal, or high serum leptin concentrations. Regardless of gender, uncontrolled eating scores were higher in low leptin and high leptin participants compared with normal leptin participants (Table 4). This group effect was statistically significant when comparing low leptin and high leptin with normal leptin participants. Using the ANCOVA, this group effect remained when the HOMA was added to the model as covariate (Table 4). In women, the cognitive restraint score did not differ significantly between

Table 2 General and clinical variables in the study groups

Parameters	Lean ($n = 70$) (a)	Overweight ($n = 60$) (b)	Obese ($n = 60$) (c)
Age (years)	37 ± 1.13	39.62 ± 3.02^{ns}	40.11 ± 3.09^{ns}
WC (cm)			
Women	77.3 ± 1.22	$99.05 \pm 1.56^{***}$	$107.65 \pm 1.94^{£££}$
Men	86.3 ± 1.52	$101.1 \pm 1.02^{***}$	$109.4 \pm 1.24^{£££}$
Glycemia (mg/dL)	86 ± 2	91 ± 1^{ns}	94 ± 2^{ns}
Insulinemia (μUI/L)	8.95 ± 0.64	$24.28 \pm 2.29^{***}$	$31.43 \pm 3.13^{£££}$
Triglycerides (mg/dL)	56 ± 4	$166 \pm 23^{***}$	$176 \pm 2^{£££}$
Total cholesterol (mg/dL)	164 ± 6	$183 \pm 7^{*}$	$196 \pm 6^{£}$
HDL cholesterol (mg/dL)			
Women	61 ± 3	$43 \pm 3^{*}$	$41 \pm 0.02^{££}$
Men	48 ± 2	$36 \pm 0.02^{*}$	$37 \pm 0.02^{££}$
LDL cholesterol (mg/dL)	112 ± 0.06	1.19 ± 0.07^{ns}	1.31 ± 0.05^{ns}

* b vs a, $^{***}p < 0.001$, $^{*}P < 0.05$; $^{£}$ c vs a, $^{£££}p < 0.001$, $^{££}p < 0.01$, $^{£}p < 0.05$; *ns* not significant. All results are compared with lean participants

Table 3 Regression analysis for the association between variables including TFEQ and BMI

Tested variable: BMI in overall cohort	Odds ratio	95% Confidence interval	*p* Value
Leptin	1.595	[1.204–1.987]	0.000
HOMA	0.577	[0.455–0.699]	0.000
Uncontrolled eating	0.481	[0.391–0.572]	0.000
Emotional eating	0.143	[0.074–0.212]	0.000
Cognitive restraint	- 0.058	[− 0.167– − 0.05]	NS

ns not significant

low leptin, normal leptin, and high leptin participants, but reached significance when the HOMA was added to the model as covariate (Table 4).

Discussion

This study aimed first to assess eating behaviors of Algerian adults as measured by the 51-item eating inventory and evaluated changes in TFEQ scores according to the BMI category. Algerian adults have low levels of cognitive restraint, uncontrolled eating, and hunger scores.

We compare our results to other studies, on a population of 233 working adults (BMI = 29.8 ± 6.4 kg/m^2 and age = 42.6 ± 11.2 years). The average TFEQ scores were 6 ± 3.5 for cognitive restraint, 8.2 ± 4.4 for uncontrolled eating, and 4.6 ± 3.3 for emotional eating [25]. In another study, on French young people aged between 20 and 39 yrs with a mean BMI of 23.7 kg/m^2. The average TFEQ scores were 6.3 ± 0.1 for dietary restraint, 6.0 ± 0.1 for uncontrolled eating, and 5.0 ± 0.1 for emotional eating [28]. Both studies found higher restraint and emotional eating scores than our population. The first one found a higher level of uncontrolled eating and the second one lower level. This might be due to the differences in age and BMI in the characteristics of the population.

Uncontrolled eating scores were significantly higher in obese and overweight subjects versus lean. We examined the association between the scores in the three TFEQ factors and the BMI values of the participants. The results of the logistic regression analysis showed that higher scores on uncontrolled eating and emotional eating are significantly associated with higher BMI values. The strongest positive association was found for uncontrolled eating and BMI. The present study corroborates the results of several reports [25, 29–32]. Disinhibited eating is a robust predictor of long-term weight gain [33].

Cognitive restraint was not associated with BMI, in accordance with other studies [29, 30, 34]. Two types of cognitive restraint have been differentiated: a rigid and a flexible one; they are oppositely associated with obesity (high BMI and low BMI respectively) and together they may show no association with BMI [29, 34].

The leptin profile in obese and overweight subjects shows an inflammatory state, with high concentration of leptin. Similar findings have been reported in other studies [35, 36]. Women shows higher serum leptin levels than men in all groups, which can be due to fat metabolism and distribution. Sex differences in fat size and distribution, testosterone, and estrogens play a role in the sex differences of circulating leptin [37].

Coexistence of a high level of leptin with an uncontrolled eating in obese and overweight subjects reflects a state of

Table 4 Results of one-way ANCOVA of eating inventory scores in participants classified as having low, normal, or high plasma leptin concentrations

Variables	*One-way ANOVA followed by Bonferroni's test*				*One-way ANCOVA*	
	P	*P* LL vs. NL	*P* LL vs. HL	*P* NL vs. HL	Covariate	*P* Covariate
Men						
Uncontrolled eating	0.0001	0.0001	1	0.0001	HOMA	0.0001
Cognitive restraint	0.135	0.149	0.267	1		0.140
Emotional eating	0.06	1	0.162	0.137		0.454
Women						
Uncontrolled eating	0.0001	0.486	0.475	0.0001	HOMA	0.0001
Cognitive restraint	0.059	0.295	1	0.119		0.028
Emotional eating	0.142	1	0.997	0.175		0.736

LL low leptin, *NL* normal leptin, *HL* high leptin

leptin resistance, resulting in an inability to detect satiety. In obesity, leptin resistance is reflected by hyperleptinemia due to impaired leptin signaling or action [38].

In obese and overweight individuals, elevated insulinemia is noticed in spite of the increasing leptin; a value of HOMA expresses an insulin resistance state. Study shows positive associations between high level of leptin and insulin resistance [39].

Our third objective was to examine whether leptin concentrations are associated with eating behavior. The results of one-way ANCOVA of eating inventory scores showed that leptin levels were associated with the uncontrolled eating and influenced by insulin sensitivity. The plasma soluble leptin receptor is positively correlated with insulin sensitivity [40] and inversely correlated with insulin resistance measured by the HOMA [41].

Leptin inhibits insulin secretion in pancreatic β cells [42]; however, leptin resistance induces pancreatic β cells to secrete insulin continuously, thus promoting hyperinsulinemia which leads to insulin resistance [43].

Conclusion

Our study shows that the TFEQ scores of Algerian adults are in the low range. Uncontrolled eating is the major factor influencing weight gain; this factor reflects hyperphagic eating behavior in obese and overweight subjects. The coexistence of an uncontrolled eating and high level of leptin demonstrates a state of leptin resistance, resulting in an inability to detect satiety. Leptin resistance may play a pivotal role in the pathophysiology of uncontrolled eating by providing a possible link between motivated behaviors, reward processes, cognitive functions, and energy balance. Fasting on serum leptin might be a biomarker of eating behavior pattern, and the cognitive control of eating behavior should be considered key tools in controlling obesity.

Author contributions HB wrote the MS and collected and analyzed the data. AB analyzed the data. EAK designed research (development of overall research plan and study oversight). All authors have read and approved the final content of the article.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Research involving human participants The work was conducted in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans and was approved by the Ethical Committee of the Algerian Ministry of Public Health.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

1. Must A, Spadano J, Coakley EH, Field AE, Colditz G, Dietz WH (1999) The disease burden associated with overweight and obesity. Jama 282(16):1523–1529. https://doi.org/10.1001/jama.282.16.1523
2. Mehta NK, Patel SA, Ali MK, Narayan KMV (2017) Preventing disability: the influence of modifiable risk factors on state and national disability prevalence. Health Aff (Project Hope) 36(4):626–635. https://doi.org/10.1377/hlthaff.2016.1281
3. Meigs JB, Wilson PW, Fox CS, Vasan RS, Nathan DM, Sullivan LM, D'Agostino RB (2006) Body mass index, metabolic syndrome, and risk of type 2 diabetes or cardiovascular disease. J Clin Endocrinol Metab 91(8):2906–2912. https://doi.org/10.1210/jc.2006-0594
4. James WP (2008) WHO recognition of the global obesity epidemic. Int J Obes (2005) 32(Suppl 7):S120–S126. https://doi.org/10.1038/ijo.2008.247
5. Jung UJ, Choi MS (2014) Obesity and its metabolic complications: the role of adipokines and the relationship between obesity, inflammation, insulin resistance, dyslipidemia and nonalcoholic fatty liver disease. Int J Mol Sci 15(4):6184–6223. https://doi.org/10.3390/ijms15046184
6. Skurk T, Alberti-Huber C, Herder C, Hauner H (2007) Relationship between adipocyte size and adipokine expression and secretion. J Clin Endocrinol Metab 92(3):1023–1033. https://doi.org/10.1210/jc.2006-1055
7. Cancello R, Henegar C, Viguerie N, Taleb S, Poitou C, Rouault C, Coupaye M, Pelloux V, Hugol D, Bouillot JL, Bouloumié A, Barbatelli G, Cinti S, Svensson PA, Barsh GS, Zucker JD, Basdevant A, Langin D, Clément K (2005) Reduction of macrophage infiltration and chemoattractant gene expression changes in white adipose tissue of morbidly obese subjects after surgery-induced weight loss. Diabetes 54(8):2277–2286. https://doi.org/10.2337/diabetes.54.8.2277
8. Considine RV, Sinha MK, Heiman ML, Kriauciunas A, Stephens TW, Nyce MR, Ohannesian JP, Marco CC, McKee LJ, Bauer TL et al (1996) Serum immunoreactive-leptin concentrations in normal-weight and obese humans. N Engl J Med 334(5):292–295. https://doi.org/10.1056/nejm199602013340503
9. Halaas JL, Gajiwala KS, Maffei M, Cohen SL, Chait BT, Rabinowitz D, Lallone RL, Burley SK, Friedman JM (1995) Weight-reducing effects of the plasma protein encoded by the obese gene. Science (New York, NY) 269(5223):543–546. https://doi.org/10.1126/science.7624777
10. Lam NT, Lewis JT, Cheung AT, Luk CT, Tse J, Wang J, Bryer-Ash M, Kolls JK, Kieffer TJ (2004) Leptin increases hepatic insulin sensitivity and protein tyrosine phosphatase 1B expression. Mol Endocrinol (Baltimore, Md) 18(6):1333–1345. https://doi.org/10.1210/me.2002-0193
11. Commins SP, Watson PM, Padgett MA, Dudley A, Argyropoulos G, Gettys TW (1999) Induction of uncoupling protein expression in brown and white adipose tissue by leptin. Endocrinology 140(1):292–300. https://doi.org/10.1210/endo.140.1.6399
12. Pelleymounter MA, Cullen MJ, Baker MB, Hecht R, Winters D, Boone T, Collins F (1995) Effects of the obese gene product on body weight regulation in ob/ob mice. Science (New York, NY) 269(5223):540–543. https://doi.org/10.1126/science.7624776
13. Davis JF, Choi DL, Schurdak JD, Fitzgerald MF, Clegg DJ, Lipton JW, Figlewicz DP, Benoit SC (2011) Leptin regulates energy balance and motivation through action at distinct neural circuits. Biol Psychiatry 69(7):668–674. https://doi.org/10.1016/j.biopsych.2010.08.028
14. Münzberg H, Huo L, Nillni EA, Hollenberg AN, Bjørbaek C (2003) Role of signal transducer and activator of transcription 3

in regulation of hypothalamic proopiomelanocortin gene expression by leptin. Endocrinology 144(5):2121–2131. https://doi.org/10.1210/en.2002-221037
15. Morrison CD, Morton GJ, Niswender KD, Gelling RW, Schwartz MW (2005) Leptin inhibits hypothalamic Npy and Agrp gene expression via a mechanism that requires phosphatidylinositol 3-OH-kinase signaling. Am J Phys Endocrinol Metab 289(6):E1051–E1057. https://doi.org/10.1152/ajpendo.00094.2005
16. Liu JJ, Bello NT, Pang ZP (2017) Presynaptic regulation of Leptin in a defined lateral hypothalamus-ventral tegmental area. Neurocircuitry depends on energy state. J Neurosci 37(49):11854–11866. https://doi.org/10.1523/jneurosci.1942-17.2017
17. Renner B, Sproesser G, Strohbach S, Schupp HT (2012) Why we eat what we eat. The eating motivation survey (TEMS). Appetite 59(1):117–128. https://doi.org/10.1016/j.appet.2012.04.004
18. Thomas EA, Bechtell JL, Vestal BE, Johnson SL, Bessesen DH, Tregellas JR, Cornier MA (2013) Eating-related behaviors and appetite during energy imbalance in obese-prone and obese-resistant individuals. Appetite 65:96–102. https://doi.org/10.1016/j.appet.2013.01.015
19. Sterling P (2012) Allostasis: a model of predictive regulation. Physiol Behav 106(1):5–15. https://doi.org/10.1016/j.physbeh.2011.06.004
20. Levitsky DA, Pacanowski CR (2012) Free will and the obesity epidemic. Public Health Nutr 15(1):126–141. https://doi.org/10.1017/s1368980011002187
21. Grill HJ, Skibicka KP, Hayes MR (2007) Imaging obesity: fMRI, food reward, and feeding. Cell Metab 6(6):423–425. https://doi.org/10.1016/j.cmet.2007.11.007
22. Shomaker LB, Tanofsky-Kraff M, Zocca JM, Courville A, Kozlosky M, Columbo KM, Wolkoff LE, Brady SM, Crocker MK, Ali AH, Yanovski SZ, Yanovski JA (2010) Eating in the absence of hunger in adolescents: intake after a large-array meal compared with that after a standardized meal. Am J Clin Nutr 92(4):697–703. https://doi.org/10.3945/ajcn.2010.29812
23. Wang GJ, Volkow ND, Telang F, Jayne M, Ma J, Rao M, Zhu W, Wong CT, Pappas NR, Geliebter A, Fowler JS (2004) Exposure to appetitive food stimuli markedly activates the human brain. NeuroImage 21(4):1790–1797. https://doi.org/10.1016/j.neuroimage.2003.11.026
24. Stunkard AJ, Messick S (1985) The three-factor eating questionnaire to measure dietary restraint, disinhibition and hunger. J Psychosom Res 29(1):71–83. https://doi.org/10.1016/0022-3999(85)90010-8
25. French SA, Mitchell NR, Wolfson J, Finlayson G, Blundell JE, Jeffery RW (2014) Questionnaire and laboratory measures of eating behavior. Associations with energy intake and BMI in a community sample of working adults. Appetite 72:50–58. https://doi.org/10.1016/j.appet.2013.09.020
26. Akabas SR, Lederman SA, Moore BJ (2012) Textbook of obesity: biological, psychological and cultural influences. Wiley
27. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC (1985) Homeostasis model assessment: insulin resistance and β-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia 28(7):412–419. https://doi.org/10.1007/BF00280883
28. Lesdéma A, Fromentin G, Daudin JJ, Arlotti A, Vinoy S, Tome D, Marsset-Baglieri A (2012) Characterization of the three-factor eating questionnaire scores of a young French cohort. Appetite 59(2):385–390. https://doi.org/10.1016/j.appet.2012.05.027
29. Provencher V, Drapeau V, Tremblay A, Després JP, Lemieux S (2003) Eating behaviors and indexes of body composition in men and women from the Québec family study. Obes Res 11(6):783–792. https://doi.org/10.1038/oby.2003.109
30. Kruger R, De Bray JG, Beck KL, Conlon CA, Stonehouse W (2016) Exploring the relationship between body composition and eating behavior using the three factor eating questionnaire (TFEQ) in young New Zealand women. Nutrients 8(7). https://doi.org/10.3390/nu8070386
31. Barkeling B, King NA, Näslund E, Blundell JE (2007) Characterization of obese individuals who claim to detect no relationship between their eating pattern and sensations of hunger or fullness. Int J Obes (2005) 31(3):435–439. https://doi.org/10.1038/sj.ijo.0803449
32. Bellisle F, Clément K, Le Barzic M, Le Gall A, Guy-Grand B, Basdevant A (2004) The eating inventory and body adiposity from leanness to massive obesity: a study of 2509 adults. Obes Res 12(12):2023–2030. https://doi.org/10.1038/oby.2004.253
33. Seage CH, Lee M (2017) Do disinhibited eaters pay increased attention to food cues? Appetite 108:151–155. https://doi.org/10.1016/j.appet.2016.09.031
34. Westenhoefer J, Stunkard AJ, Pudel V (1999) Validation of the flexible and rigid control dimensions of dietary restraint. Int J Eat Dis 26(1):53–64. https://doi.org/10.1002/(sici)1098-108x(199907)26:1<53::aid-eat7>3.0.co;2-n
35. Lopes LR, Ribeiro S, Figueiredo VP, Leite ALJ, Nicolato RLC, Gomes JAE, de Oliveira FLP, Talvani A (2018) The overweight increases circulating inflammatory mediators commonly associated with obesity in young individuals. Cytokine 110:169–173. https://doi.org/10.1016/j.cyto.2018.04.024
36. Graßmann S, Wirsching J, Eichelmann F, Aleksandrova K (2017) Association Between Peripheral Adipokines and Inflammation Markers: A Systematic Review and Meta-Analysis. 25(10):1776–1785. https://doi.org/10.1002/oby.21945
37. Lanas F, Serón P, Saavedra N, Ruedlinger J, Salazar L (2015) Genetic and non-genetic determinants of circulating levels of adiponectin in a cohort of Chilean subjects. Mol Diagn Ther 19(4):197–204. https://doi.org/10.1007/s40291-015-0146-3
38. Sáinz N, Barrenetxe J, Moreno-Aliaga MJ, Martínez JA (2015) Leptin resistance and diet-induced obesity: central and peripheral actions of leptin. Metab Clin Exp 64(1):35–46. https://doi.org/10.1016/j.metabol.2014.10.015
39. Kang YE, Kim JM, Joung KH, Lee JH, You BR, Choi MJ, Ryu MJ, Ko YB, Lee MA, Lee J, Ku BJ, Shong M, Lee KH, Kim HJ (2016) The roles of adipokines, proinflammatory cytokines, and adipose tissue macrophages in obesity-associated insulin resistance in modest obesity and early metabolic dysfunction. PLoS One 11(4):e0154003. https://doi.org/10.1371/journal.pone.0154003
40. Sommer C, Lee S, Gulseth HL, Jensen J, Drevon CA, Birkeland KI (2018) Soluble leptin receptor predicts insulin sensitivity and correlates with upregulation of metabolic pathways in men. J Clin Endocrinol Metab 103(3):1024–1032. https://doi.org/10.1210/jc.2017-02126
41. Misra M, Miller KK, Almazan C, Ramaswamy K, Aggarwal A, Herzog DB, Neubauer G, Breu J, Klibanski A (2004) Hormonal and body composition predictors of soluble leptin receptor, leptin, and free leptin index in adolescent girls with anorexia nervosa and controls and relation to insulin sensitivity. J Clin Endocrinol Metab 89(7):3486–3495. https://doi.org/10.1210/jc.2003-032251
42. Borer KT (2014) Counterregulation of insulin by leptin as key component of autonomic regulation of body weight. World J Diabetes 5(5):606–629. https://doi.org/10.4239/wjd.v5.i5.606
43. Mohammadzadeh G, Zarghami N (2013) Serum leptin level is reduced in non-obese subjects with type 2 diabetes. Int J Endocrinol Metab 11(1):3–10. https://doi.org/10.5812/ijem.6535