Diabetes & Metabolism 45 (2019) 160–166

Available online at ScienceDirect www.sciencedirect.com

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Original article

Ghrelin concentration as an indicator of eating-disorder risk in obese women

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ARTICLE INFO

Article history:
Received 18 August 2017
Received in revised form 21 December 2017
Accepted 8 January 2018
Available online 30 January 2018

Keywords:
Drive for thinness
Eating disorders
Ghrelin
Impulsive behaviour
Obesity
Vulnerability

ABSTRACT

Aim. – Eating disorders (EDs), disordered eating (DE) and obesity are thought to have overlapping aetiological processes. DE in obesity can jeopardize weight-loss results, and acyl ghrelin (AG) is a hormone that stimulates food intake and reward processes. The main study objective was to determine whether higher-than-expected concentrations of AG in common obesity are associated with DE symptoms.

Methods. – The study population included 84 women, aged 20–55 years, free of established EDs: 55 were severely obese (OB) and 29 were of normal weight (NW). OB participants were stratified into two groups according to their median concentration of fasting AG distribution. The OB women with a high fasting plasma ghrelin concentration (HGC) were compared with both OB women with a low fasting plasma ghrelin concentration (LGC) and NW women. Participants were assessed by the Eating Disorder Inventory (EDI-2), Three-Factor Eating Questionnaire (TFEQ) and Hospital Anxiety and Depression Scale (HADS). Fasting glucose, insulin, leptin and ghrelin plasma concentrations were also quantified.

Results. – Between the two AG groups of OB women, there was no statistical difference in either anthropometric or metabolic parameters, HADS, TFEQ or fasting hunger scores. However, the HGC group scored significantly higher than the LGC group on the drive-for-thinness subscale of EDI-2 (9.30 ± 0.99 vs. 6.46 ± 0.83, respectively; $P = 0.033$).

Conclusion. – Results support the hypothesis of a potential relationship between fasting plasma AG concentrations and ED risk, regardless of mood and anxiety. AG may be considered a potential biomarker of vulnerability for developing EDs.

Introduction

Obesity remains a major concern in patients with diabetes, and the management of obese patients is also still difficult, especially when associated with eating disorders (EDs) or disordered eating (DE). EDs have primarily been considered a psychiatric condition, whereas obesity has been regarded predominantly as a medical concern. However, there is now a widespread movement to consider EDs, DE and obesity as part of the same continuum of weight-related disorders. The basic components necessary for an integrated theory of DE and obesity include sociological and psychological parameters leading to the perception that "I am too fat" is a problem, maladaptive limitation of food intake (dietary restraint) to correct the problem, hunger (from eating less food) and the physiological reaction to hunger (hormonal control of food intake). To enhance preventative and interventional efforts, there is a strong need for early detection of psychological factors contributing to the development and maintenance of EDs and obesity.

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https://doi.org/10.1016/j.diabet.2018.01.006
1262-3636/

Food intake is tightly controlled in humans by homoeostatic and non-homoeostatic mechanisms that maintain stable body weight and neutral energy balance [1]. Ghrelin, a 28 amino-acid peptide synthesized by the stomach, is a leading player in this physiological regulation [2]. The acylated form of ghrelin (AG) stimulates appetite and food intake [2] by activating neuropeptide Y neurons in the arcuate nucleus of the hypothalamus and inhibiting the melanocortin pathway [3]. However, the action of ghrelin in the brain is not restricted to homoeostatic control of energy balance within the hypothalamus. Indeed, AG also induces reward-seeking behaviours for food, alcohol and other substance abuse [4–7]. Moreover, AG modulates the dopaminergic and serotoninergic pathways involved in the regulation of impulsivity [8,9] and, when injected into the lateral hypothalamus of rodents, it increases both motor and choice impulsivity [10].

As ghrelin impacts food intake, food reward and impulsivity, its plasma concentrations may reflect certain behavioural traits. Overeating, increased food reward sensitivity and impulsivity are characteristics shared by many patients with obesity and/or EDs [11] and, contrary to expectations, obese participants usually exhibit lower plasma ghrelin concentrations than their normal-weight counterparts [12–14]. These low plasma ghrelin concentrations have been considered a physiological adaptation to the positive energy balance associated with obesity [14], and the same adaptive phenomenon has been described in some EDs, including binge-eating [15]. However, in clinical practice, a wide range of plasma ghrelin concentrations is observed in obese individuals, with some exhibiting unexpectedly high concentrations approaching those observed in normal-weight individuals.

Based on this clinical observation, our hypothesis is that patients with obesity and high concentrations of ghrelin might display greater feelings of hunger, a higher prevalence of DE-related psychopathology/behaviours and, especially, food impulsivity. Thus, the aim of the present study was to determine whether obese patients with unexpectedly high concentrations of ghrelin differ from those with low ghrelin concentrations in terms of hunger and behavioural traits leading to a DE risk.

Materials and Methods

Participants

Women aged between 20 and 55 years and with either normal weight [body mass index (BMI) 20–25 kg/m^2] or severe obesity (BMI $\geq$ 35 kg/m^2) were recruited prospectively between July 2013 and June 2015 through printed advertisements on notice boards at various sites of Lyon 1 university, including the cafeteria of the University Hospital and department of endocrinology and nutrition (groupement hospitalier Sud, hospices civils de Lyon, Lyon). Exclusion criteria included being male, a smoker, psychotropic medication use and substance abuse according to the *Diagnostic and statistical manual of mental disorders, 4th edition* (DSM-IV), anxiety and depression [Hospital Anxiety and Depression Scale (HADS), subscale anxiety and/or depression scores > 11], medical illness, previous bariatric surgery, diabetes and ongoing pregnancy. Patients with previous or current obvious EDs (defined by DSM-5) as assessed by TFEQ and/or medical interview were also excluded. To avoid metabolic and hormonal disturbances linked to physical activity and diet, participants had to report stable weight and no change in physical activity over the past 3 months.

Initially, 108 women were included in the study. Five normal-weight participants were excluded for uncontrolled eating scores > 8 (n = 4) or contraindicated medication use (n = 1), while 13 obese participants were excluded for anxiety scores > 11 (n = 7), unstable body weight (n = 4), unknown diabetes (n = 1) or recent cessation of tobacco use (n = 1). A flow chart detailing participant recruitment is presented in Fig. 1.

Study design

Following their inclusion, participants had to arrive at the study nutrition research centre (Centre de Recherche en Nutrition Humaine Rhône-Alpes, CRNH-RA) at 07 00 h after an overnight fast. Anthropometric parameters were assessed, and fasting blood samples drawn for acyl ghrelin (AG) and des-acyl ghrelin (DAG), leptin, glucose and insulin quantification. Participants were then asked to complete three self-administered psychometric questionnaires: the validated French translation of the Eating Disorder Inventory (EDI(EDI-2), the Three-Factor Eating Questionnaire (TFEQ) and the Hospital Anxiety and Depression Scale (HADS). Fasting hunger was evaluated at 09 00 h using a 10-cm visual analogue scale (VAS), which rated hunger strength from 0 (not hungry) to 10 (extremely hungry). More precisely, participants had to answer the question "How hungry do you feel at this moment?" by placing a mark along the VAS.

Self-administered questionnaires

The Eating Disorder Inventory (EDI-2) is a 91-item multidimensional self-reported questionnaire that assesses attitudes, feelings and behaviours typically associated with EDs. Although 11 subscales were used in this study, there was a particular interest in the five subscales that could be affected by appetite, feelings of satiety and food intakes: drive for thinness; bulimia; body dissatisfaction; interoceptive awareness; and impulse regulation.

The Three-Factor Eating Questionnaire (TFEQ) is a food-intake-behaviour questionnaire [16] comprising 51 items that measure three dimensions of human eating behaviour: cognitive restraint (21 items); uncontrolled eating (16 items); and emotional eating (14 items). Each item has a binary score (0 or 1) that is summed with the others, and each subscore corresponds to the three dimensions of eating behaviour: the higher the score, the more problematic the related behaviour. Uncontrolled eating scores > 8 were an exclusion criterion for the normal-weight participants in this study.

The Hospital Anxiety and Depression Scale (HADS) is a questionnaire [17] of 14 items commonly used to determine the probability of anxiety (seven items) and depression (seven items). Each item has a score between 0 and 3: the higher the score, the higher the probability of exhibiting anxiety or depression. The threshold of each subscore to detect the presence of anxiety or depressive symptoms is 8/21.

Blood samples

Venous blood was collected in EDTA tubes and centrifuged immediately for 10 min at 4°C at 4500 rpm. Plasma glucose was determined by the hexokinase method using an Architect ci8200 clinical chemistry analyzer (Abbott Laboratories, Abbott Park, IL, US). Insulin concentrations were determined by immunoradiometric assay using Bi-Ins-IRMA kits (IBA Molecular–Cis Biointernational, Gif-sur-Yvette, France). For AG determinations, 1 mM p-hydroxymercuribenzoic acid in HCl was added to blood samples to prevent protease degradation of AG (as recommended by Cayman Chemical, Ann Arbor, MI, USA). Plasma samples were then immediately stored at < −20°C until needed for analysis. Plasma AG and DAG concentrations were measured by enzyme-linked immunosorbent assay (ELISA) using SPI-Bio kits (Bertin Pharma, Montigny-le-Bretonneux, France), and leptin was also measured by ELISA (Clinical Range, BioVendor, Brno, Czech Republic). Homoeostasis model assessment of insulin resistance

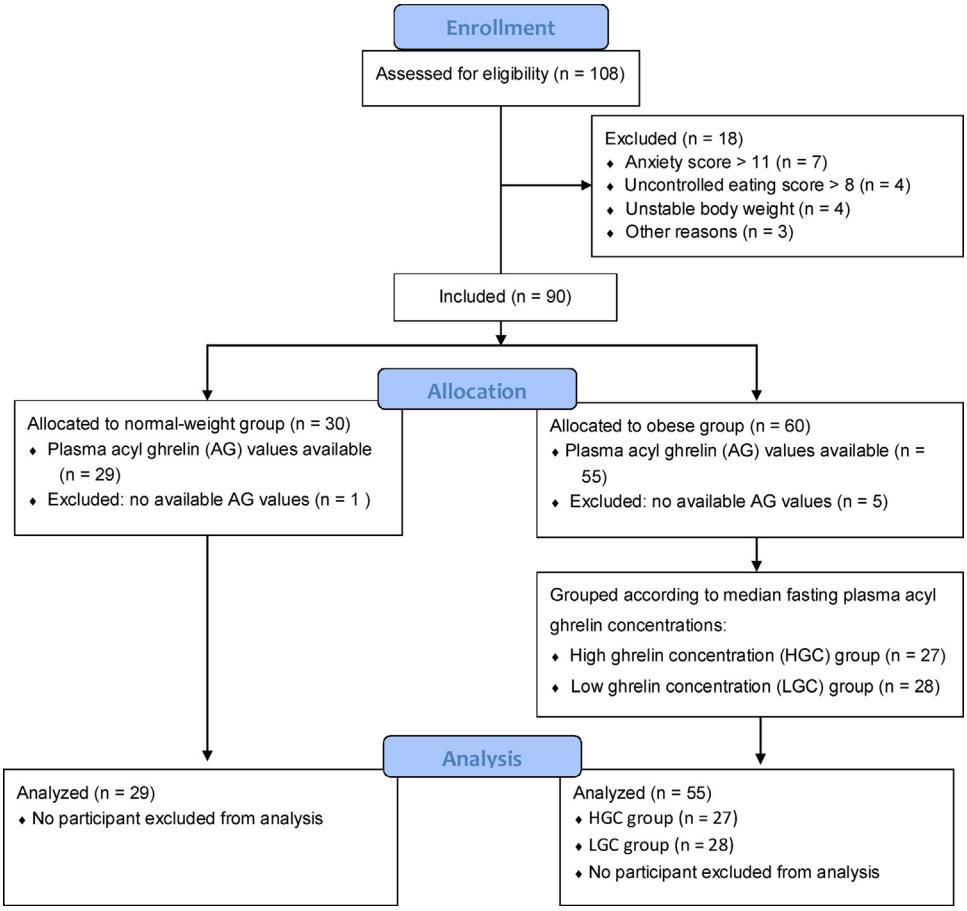

Fig. 1. Flow chart of participant recruitment into the study.

(HOMA-IR) was used as a surrogate marker of insulin resistance and calculated as glucose (mmol/L) × insulin (mIU/L)/22.5.

Stratification of obese participants according to fasting plasma AG concentrations

Plasma AG values were available for 84/90 participants, and the six participants lacking AG values were excluded from the analysis. The severely obese participants were stratified into two groups according to the median AG value obtained in this sample.

Ethics

All participants gave their written informed consent to participate. The study promoter was the hospices civils de Lyon (University Hospital), and the study was performed after a favourable opinion from the Committee for the protection of persons concerned (CPP) in accordance with French law (Data Protection and Civil Liberties) and the ethical standards laid down by the 1964 Declaration of Helsinki. The ClinicalTrials.gov identifier is NCT01948414.

Statistical analysis

Data were analyzed using SPSS version 19.0 software (IBM Corp., Armonk, NY, USA) and expressed as the mean ± SEM (standard error of mean). Normality of each variable was checked using the Shapiro–Wilk test. Differences between normal-weight (NW) and obese (OB) participants were assessed by a parametric (t) test or a non-parametric test (Mann–Whitney U test, for non-normal distributions). Anthropometric, biological and psychometric differences among the three groups (NW and two OB groups) were assessed using one-way analysis of variance (Anova) or by Kruskal–Wallis test. Multiple comparisons were performed using Tukey's post-hoc test, while effect sizes were assessed by Cohen's d. Linear correlations between AG and drive-for-thinness (DT) scores were assessed by the Pearson correlation coefficient. For all statistical analyses, the level of significance was the conventional two-sided 5% alpha error.

Results

Participants' characteristics

These are presented in Table 1. The population included 29 NW and 55 severely OB (BMI $\geq$ 35 kg/m^2) women. The severely OB women were stratified into two groups according to the median AG value observed in this sample (19.0 pg/mL; 95% CI: 12.0–44.0; Fig. 1): 28 participants were allocated to the low ghrelin concentration (LGC) group (mean AG value: 7.51 ± 1.11 pg/mL); and 27 were allocated to the high ghrelin concentration (HGC) group (mean AG value: 65.77 ± 8.67 pg/mL).

The three groups did not differ in either age or height, although OB participants exhibited higher systolic and diastolic blood pressures than did NW participants. Stratification of the OB group according to fasting plasma AG concentration revealed no anthropometric differences between the LGC and HGC groups.

Biological profiles

These profiles are presented in Table 1 and, compared with those in the NW group, women in the OB groups had higher fasting

Table 1
Clinical and biological characteristics and fasting hunger scores in the study population.

	Normal-weight (NW) women	Obese (OB) women		OB women grouped by fasting plasma acyl ghrelin concentration		
	(n = 29)	(n = 55)	OB vs. NW	(n = 28)	(n = 27)	LGC vs. HGC
	Mean ± SEM	Mean ± SEM	P	Mean ± SEM	Mean ± SEM	P
Clinical characteristics						
Age (years)	37 ± 2.0	38 ± 1.5	NS	37 ± 2.2	38 ± 2.1	NS
Height (cm)	163.9 ± 1.0	163.8 ± 0.8	NS	162.9 ± 1.2	164.7 ± 1.1	NS
Weight (kg)	57.8 ± 1.1	111.5 ± 2.5	< 0.001	113.4 ± 4.0*	109.5 ± 3.1*	NS
Body mass index (kg/m^2)	21.5 ± 0.4	41.5 ± 0.8	< 0.001	42.6 ± 1.3*	40.3 ± 0.9*	NS
Waist circumference (cm)	78 ± 1.2	119 ± 2.1	< 0.001	122 ± 2.5*	116 ± 3.5*	NS
Hip circumference (cm)	94 ± 0.8	129 ± 1.9	< 0.001	129 ± 2.8*	128 ± 2.5*	NS
Waist-to-hip ratio	0.83 ± 0.01	0.91 ± 0.01	< 0.001	0.94 ± 0.02*	0.89 ± 0.02*	NS
SBP (mmHg)	110 ± 1.7	124 ± 1.5	< 0.001	126 ± 2.2*	123 ± 2.1*	NS
DBP (mmHg)	71 ± 1.2	75 ± 1.2	0.042	76 ± 1.9	74 ± 1.6	NS
Heart rate (bpm)	65 ± 1.9	70 ± 1.6	0.046	74 ± 2.0*	66 ± 2.4	NS
Biological characteristics						
Glucose (mmol/L)	4.8 ± 0.1	5.1 ± 0.1	0.002	5.1 ± 0.1*	5.1 ± 0.1*	NS
Insulin (mIU/L)	4.5 ± 0.4	9.7 ± 0.7	< 0.001	10.8 ± 1.0*	8.6 ± 0.8*	NS
HOMA-IR	0.95 ± 0.1	2.21 ± 0.2	< 0.001	2.45 ± 0.25*	1.96 ± 0.18*	NS
Leptin (ng/mL)	12.5 ± 1.3	57.7 ± 2.9	< 0.001	61.2 ± 4.3*	54 ± 3.8*	NS
Acyl ghrelin (pg/mL)	107 ± 12	36 ± 6	< 0.001	8 ± 1*	66 ± 9*	< 0.05
Des-acyl ghrelin (pg/mL)	365 ± 32	145 ± 15	< 0.001	101 ± 8*	190 ± 27*	< 0.05
Total ghrelin (pg/mL)	471 ± 40	181 ± 20	< 0.001	109 ± 8*	256 ± 33*	< 0.05
Acyl ghrelin/total ghrelin	0.23 ± 1.7	0.18 ± 1.8	0.049	0.083 ± 1.5*	0.27 ± 2.0	< 0.05
Visual analogue scale						
Hunger scale	3.86 ± 0.45	3.93 ± 0.32	NS	3.38 ± 0.43	4.51 ± 0.46	NS

* P < 0.05 vs. NW group. NS: not significant; LGC/HGC: low/high ghrelin concentration; SBP/DBP: systolic/diastolic blood pressure; HOMA-IR: homoeostasis model assessment of insulin resistance.

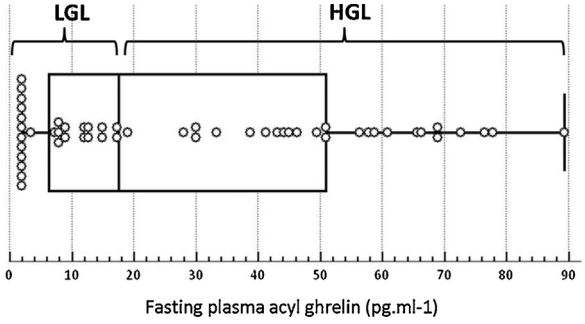

Fig. 2. Fasting plasma ghrelin distribution in obese women stratified into two groups according to the median acyl ghrelin value (19.0 pg/mL, indicated by the vertical line in the boxplot).
LGL/HGL: low/high ghrelin levels.

glucose and insulin values, and higher levels of insulin resistance, whereas there were no significant differences in metabolic parameters between the HGC and LGC subgroups. Leptin was higher, whereas fasting AG, DAG and total ghrelin levels were lower in the OB vs. NW groups, although leptin did not differ between the LGC and HGC groups. In the OB groups, mean fasting plasma AG was 36.11 ± 5.8 pg/mL and the median was 19.0 pg/mL. AG values in these OB groups were not normally distributed and, as shown in Fig. 2, a bimodal distribution of ghrelin in this sample corresponded to the HGC and LGC subgroups. Also in keeping with the study design, significant differences in plasma ghrelin concentrations were observed between LGC, HGC and NW groups (Anova-1; P < 0.001). The HGC subgroup had a fasting plasma AG concentration approaching that of the NW group, but nevertheless remained significantly lower than that of the NW group (Table 1).

Hunger scores

Fasting hunger scores were similar between OB and NW groups, although a trend was observed towards higher hunger scores in the HGC vs. LGC groups (4.51 ± 0.46 vs. 3.38 ± 0.43, respectively; P = 0.08) with a medium effect size (d = 0.49).

Self-administered questionnaire scores

The EDI-2, TFEQ and HADS scores are presented in Table 2. Psychological states assessed by HADS showed similar anxiety scores in both the NW and OB groups, but a significantly greater depression score in the OB groups (P = 0.008). However, no difference in anxiety and depression scores was found between the HGC and LGC subgroups.

As for the TFEQ, both OB groups scored significantly higher in uncontrolled and emotional eating (P < 0.001; Fig. 3A, Table 2) than did the NW group, although there was no significant difference in cognitive restraint. Also, no significant difference was found in the three subscales of the TFEQ between the LGC and HGC subgroups (Fig. 3B), although a small effect size was observed for cognitive restraint (d = 0.19; Table 2). Behavioural profiles frequently associated with EDs were assessed by EDI-2 (Table 2), and almost all subscales, especially the five of particular interest (Fig. 3C), differed between the OB and NW groups, except for the "maturity fears" subscale, albeit not significantly (P > 0.05; Table 2). The LGC and HGC subroups differed significantly only for the DT subscale (Table 2, Fig. 3D): OB participants in the HGC group had a higher DT score than the LGC group (9.30 ± 0.99 vs. 6.46 ± 0.83, respectively; P < 0.05). A medium effect size was observed between groups for DT (d = 0.63), whereas there were small effect sizes for body dissatisfaction (d = 0.39) and interpersonal distrust (d = 0.36), although both were higher in the HGC group. In addition, a positive and significant linear correlation was observed between AG values and DT scores in the entire OB population (rho = 0.297, P = 0.03).

Discussion

The present study confirms our assumption, based on clinical experience, that fasting AG values are wide-ranging in OB participants, with some of them having unexpectedly high

Table 2
Eating Disorder Inventory (EDI)-2, Three-Factor Eating Questionnaire (TFEQ) and Hospital Anxiety and Depression Scale (HADS) scores on psychometric evaluation of the study population.

	Normal-weight (NW) women	Obese (OB) women		OB women grouped by fasting plasma acyl ghrelin concentration			
	(n = 29)	(n = 55)	OB vs. CT	LGC (n = 28)	HGC (n = 27)	LGC vs. HGC	LGC vs. HGC
	Mean ± SEM	Mean ± SEM	P	Mean ± SEM	Mean ± SEM	Cohen's d	P
EDI-2							
Drive for thinness	2.14 ± 0.46	7.85 ± 0.67	< 0.001	6.46 ± 0.83*	9.30 ± 0.99*	0.63	0.032
Bulimia	0.10 ± 0.08	2.07 ± 0.40	< 0.001	1.93 ± 0.61*	2.22 ± 0.53*	0.09	0.72
Body dissatisfaction	4.21 ± 0.83	21.67 ± 0.86	< 0.001	20.32 ± 1.32*	23.07 ± 1.06*	0.39	0.11
Ineffectiveness	1.83 ± 0.69	3.13 ± 0.52	0.011	3.39 ± 0.78*	2.85 ± 0.69*	0.13	0.61
Perfectionism	1.31 ± 0.38	5.29 ± 0.57	< 0.001	5.71 ± 0.91*	4.85 ± 0.70*	0.18	0.45
Interpersonal distrust	1.76 ± 0.42	3.51 ± 0.46	0.019	3.00 ± 0.54	4.04 ± 0.75*	0.36	0.26
Interoceptive awareness	0.76 ± 0.24	3.49 ± 0.58	0.001	3.32 ± 0.88*	3.67 ± 0.76*	0.07	0.77
Maturity fears	4.93 ± 0.38	5.20 ± 0.31	0.59	5.25 ± 0.45	5.15 ± 0.44	0.04	0.87
Asceticism	2.83 ± 0.39	5.22 ± 0.45	< 0.001	5.46 ± 0.64*	4.96 ± 0.64*	0.15	0.58
Impulse regulation	1.24 ± 0.54	2.40 ± 0.49	0.031	2.43 ± 0.61	2.37 ± 0.79	0.02	0.95
Social insecurity	1.79 ± 0.53	3.49 ± 0.44	0.002	3.64 ± 0.60*	3.33 ± 0.65*	0.10	0.72
TFEQ							
Cognitive restraint	6.45 ± 0.75	8.02 ± 0.43	0.055	7.68 ± 0.67	8.37 ± 0.55	0.19	0.43
Uncontrolled eating	3.41 ± 0.39	8.84 ± 0.44	< 0.001	8.89 ± 0.65*	8.78 ± 0.62*	0.03	0.90
Emotional eating	2.07 ± 0.32	5.31 ± 0.47	< 0.001	5.25 ± 0.68*	5.37 ± 0.66*	0.03	0.89
HADS							
Anxiety score	5.72 ± 0.38	6.65 ± 0.37	0.11	6.75 ± 0.47	6.56 ± 0.57	0.08	0.79
Depression score	2.52 ± 0.30	4.07 ± 0.38	0.008	4.61 ± 0.55*	3.52 ± 0.50	0.37	0.15

* $P < 0.05$ vs. NW group. LGC/HGC: low/high ghrelin concentration; SEM: standard error of mean.

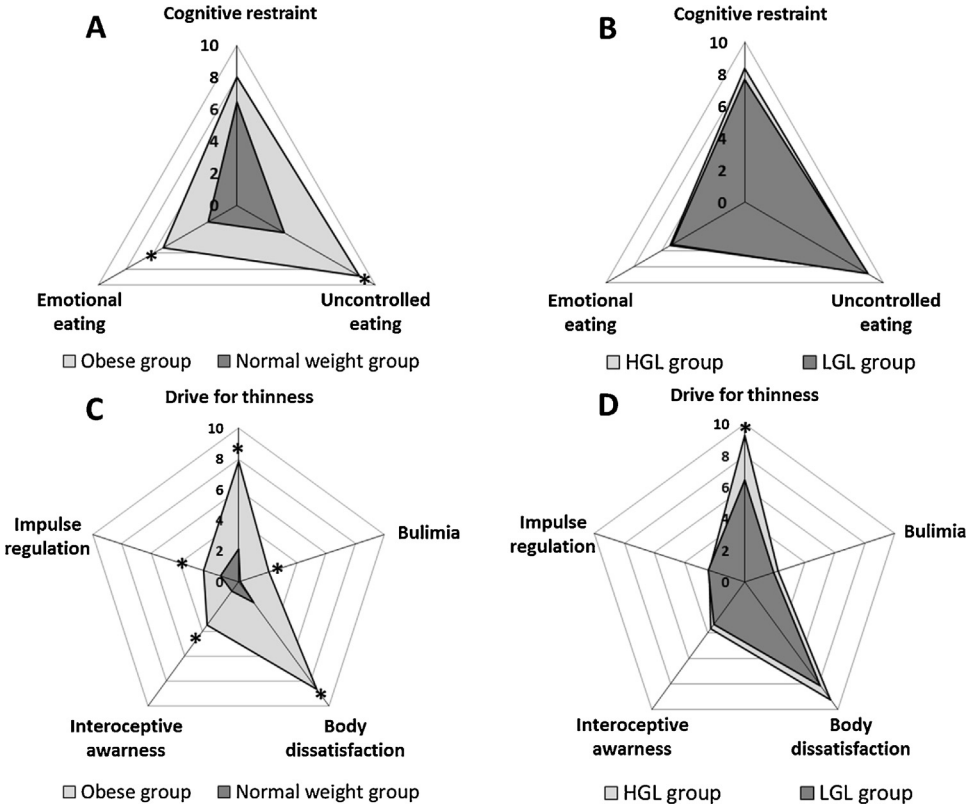

Fig. 3. Kiviat diagrams of the results of self-administered questionnaires. A, B. Results of the Three-Factor Eating Questionnaire (TFEQ). C, D. Results for the five subscales of interest in the Eating Disorder Inventory (EDI-2) in obese and normal-weight (control) groups and in obese groups with low (LGL) and high (HGL) ghrelin levels.
* $P < 0.05$.

concentrations of ghrelin approaching those observed in their NW counterparts. This observation might be a reflection of the variability in central ghrelin resistance associated with obesity, a feature that has also been demonstrated in animal models of obesity [18,19]. However, high fasting concentrations of AG in OB participants were indicative of higher DT subscale scores in the EDI-2 and a trend towards higher hunger scores.

The concept of DT includes aspiring to a thin body ideal, thereby placing excessive importance on thinness while experiencing extreme fear of becoming fat. It is considered a key motivational

variable underlying dieting/weight-loss efforts [20,21]. While DT may reflect a healthy motivation to lose weight in obesity, other studies of OB binge-eaters, using the EDI-2, have found that DT is also a strong predictor of ED severity [22,23].

In the present study, all EDI-2 scores remained under the cutoff values usually considered indicative of the presence of an ED (DT > 14, body dissatisfaction > 16, bulimia > 8) [24–26]. However, it has been shown that DT scores are more relevant to binge-eating disorder (BED) than to obesity [27]. Yet, little data are available in the scientific literature on the links between DT and obesity other than BED. Nevertheless, it has been reported in previous research that a higher DT is associated with bigger body-size [28,29] and with more intentional weight-loss behaviours [30]. Obesity is associated with body dissatisfaction, leading some patients to have a high desire for thinness which can, in turn, trigger intentional weight-loss behaviours with repetitive food restrictions that can induce EDs such as BED [31]. Given this possibility, it is not surprising to find an association between DT and BED. Indeed, in a 2016 study by Mustelin et al. [32], it was proposed that the DT and other EDI-2 subscales could be useful in combination for the diagnosis of BED, in particular, the drive for thinness, bulimia and body dissatisfaction subscales. The fact that our study focused on patients without EDs and our final sample size might explain why those dimensions did not differ significantly between our HGC and LGC subgroups.

In the available literature thus far, only a few studies have focused on ghrelin concentrations and the DT subscale. In women who exercise and in women with anorexia, high DT scores have been associated with significantly higher ghrelin concentrations in comparison to normal DT groups, independently of BMI [21,22]. Those authors considered that high ghrelin concentrations were adaptations for chronic energy deficiencies.

Although ghrelin has been a topic of DE research for > 10 years, its causal involvement has still not been resolved. It remains unclear whether ghrelin plays a functionally important role in the aetiology of DE and EDs. Common polymorphisms in human ghrelin and ghrelin receptor genes are unlikely to represent major contributors to the pathogenesis of obesity [33]. In one large case-control study, three common single nucleotide polymorphisms (SNPs) in the human ghrelin gene were studied in 692 Caucasian cases with EDs (366 with anorexia nervosa and 326 with bulimia nervosa) and found no specific associations [34]. Concerning binge-eating, a positive correlation between fasting concentrations of plasma ghrelin and frequency of binge/vomiting episodes in bulimic women was reported, but not confirmed in later studies [35–37]. In addition, the majority of studies reported lower plasma ghrelin concentrations in OB participants with BED, which was contrary to the expected higher concentrations [38].

Ghrelin is also involved in the regulation of impulsivity [8–10]. Injecting ghrelin into the lateral ventricle of rodents increased both motor and choice impulsivity [10]. However, in the present study, impulsivity in the HGC subgroup, as assessed by the impulse regulation subscale of EDI-2 and the uncontrolled and emotional eating subscales of TFEQ, did not differ from that in the LGC group. An obesity-induced central ghrelin resistance, a phenomenon that has yet to be demonstrated in humans, might partly explain the absence of a strong association between plasma ghrelin concentrations and eating behaviours, especially food impulsivity, in the present study [19].

One limitation of our study is that the findings refer to a single morning measurement of plasma AG. As circulating concentrations of this orexigenic peptide fluctuate throughout the day [39], the pathophysiological relevance of a single fasting measurement could be questioned. In addition, it is possible that circulating ghrelin does not reflect ghrelin's intracerebral concentration or activity. Moreover, the use of self-administered questionnaires may have introduced a disorder underestimation bias through either the participants' underreporting or lack of sensitivity. The use of neurocognitive tests may have been more efficient in detecting subthreshold impairments in eating or impulsivity, but such tests are difficult to access in routine care. Finally, the unknown menstrual status of our participants is a potential limitation when interpreting our data.

Conclusion

The present results support the hypothesis of a potentially positive relationship between fasting plasma AG concentrations and the risk of developing EDs, regardless of mood and anxiety, in OB women. While no inferences can be made as regards the direction of causality, it can be concluded that OB woman with high fasting plasma AG may be prone to display the problematic traits commonly associated with EDs. Thus, it is possible to postulate that fasting plasma ghrelin might be a biomarker of vulnerability for developing DE and, potentially, EDs in obesity. This vulnerability should be assessed and managed to prevent the weight cycling wherein the excessive importance of eating, body shape and weight leads to strict dieting that, in turn, results in binge-eating and weight regain.

Authors' contributions

ED, SLP and PC designed the research; BJ, BS, EB and SLP conducted the research; BJ, ED and KS analyzed the data or performed the statistical analyses; SI, BJ and ED wrote the paper; BS, SLP and ML performed a critical revision of the manuscript for important intellectual content. ED is primarily responsible for its final content; all authors read and approved the final version of the manuscript.

Funding

This work was supported by the Young Investigator Award of the Hospices Civils de Lyon, France.

Disclosure of interest

The authors declare that they have no competing interest.

Acknowledgments

We thank the staff of the Centre de Recherche en Nutrition Humaine Rhône-Alpes for their helpful assistance. We also thank Philip Robinson for his writing assistance, language editing and proofreading.

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