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Serum leptin and total dietary energy intake: the INTERLIPID Study

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Abstract

Purpose—It has been hypothesized that leptin-induced appetite suppression is impaired in obese individuals, but little human evidence is available documenting this. We investigated relations between serum leptin and total energy intake using INTERLIPID/INTERMAP data on Japanese-Americans in Hawaii and Japanese in Japan.

Methods—Serum leptin and nutrient intakes were examined by standardized methods in men and women aged 40–59 years from two population samples, one Japanese-American in Hawaii (88 men, 94 women), the other Japanese in central Japan (123 men, 111 women). Multiple linear regression analyses stratified by BMI category (<25 kg/m², 25–29.9 kg/m², and ≥ 30 kg/m²) with adjustment for possible confounders were used to examine the relation between log-leptin and total dietary energy intake.

Results—In multivariate regression analyses, in those with BMI < 25 kg/m² and in those with BMI between 25 and 29.9 kg/m², log-leptin was not significantly related to total dietary energy intake; in those with BMI ≥ 30 kg/m², it was significantly inversely related to total dietary energy intake ($P = 0.029$), independent of body weight and physical activity. Physical activity score was significantly positively related to total dietary energy intake only in participants with BMI < 25 kg/m² ($P < 0.001$).

Conclusion—Leptin was significantly inversely associated with dietary energy intake in obese persons, but not in overweight and normal-weight persons.

Keywords

Leptin; Japanese in Japan and Hawaii; Obesity; Body mass; Total energy intake; Population study

Introduction

Leptin, named after the Greek leptos meaning thin, was identified by positional cloning of the mouse obese (ob) gene; it is regarded as a key molecule in the physiological regulation of energy balance and body weight [1]. Leptin is produced and secreted mainly by adipocytes. It acts on the hypothalamus, reducing energy intake by decreasing appetite and increasing energy expenditure via sympathetic stimulation of several tissues [2, 3]. Obese individuals, however, are reported to be hyperphagic despite high serum leptin concentrations—a finding interpreted as indicating hypothalamic insensitivity (resistance) to leptin [4]. Caro et al. reported that mean serum leptin was 318 % higher in eight obese than in 23 lean individuals. However, the cerebrospinal fluid leptin concentration in obese individuals was only 30 % higher than in lean people. Consequently, the ratio of cerebrospinal fluid to serum leptin concentrations in lean individuals was 4.3-fold higher than in obese individuals [5]. These data suggest that the capacity of leptin transport into brain was lower in obese individuals, and this was indicated as a possible mechanism for leptin resistance.

The leptin sympathoexcitatory effect, on the other hand, is apparently preserved [6], hence the concept of selective leptin resistance [7]. The concept of selective leptin resistance was based on the findings indicating that obese individuals remained hyperphagic despite their high circulating leptin concentrations [4] and the sympathoexcitatory effect of leptin was preserved after either systemic or central neural administration of leptin [6].

As used recently, “leptin resistance” appears to have diverse meanings in varied contexts and to different investigators, for example, as applied to the coexistence of hyper-leptinemia in obesity and the failure of pharmacologic leptin to suppress food intake [8]. Human research data examining these phenomena are limited. Here we use INTERLIPID/INTERMAP data [9, 10] to assess the relationship of serum leptin concentration with total energy intake of middle-aged male and female Hawaiian Japanese-Americans and Japanese residing in Japan. We assess whether there is an inverse relation between serum leptin and energy intake for all participants from the two population samples, and for normal-weight, overweight, and obese substrata. The effects of leptin were statistically isolated from those of a number of covariates.

Methods

Detailed methods of the INTERMAP Study have been described [11, 12]; they are summarized here. Two standardized BP measurements were made on each of four different days; medical and lifestyle information, including four in-depth 24-h dietary recalls and two timed 24-h urine collections, was obtained for each participant. In addition, non-fasting blood was drawn from INTERLIPID participants [9, 10]. We used data on analytes measured in the INTERLIPID samples, as well as data from INTERMAP.

Participants

INTERLIPID participants aged 40–59 years were from five INTERMAP population samples: four in Japan and one in Hawaii [9, 10]. Serum leptin concentrations were measured on individuals from two of these samples, one from Japan and one from Hawaii. The two population samples were the following: (1) Japanese residents in Aito Town, a rural town in Shiga prefecture, central Japan (129 men and 129 women), and (2) third- and fourth-generation offspring of Japanese emigrants living in Honolulu, Hawaii (100 men and 106 women) [13]. Among those in the two samples, 48 persons (24 Japanese, 24 Japanese–Americans) were excluded because volume of their stored serum specimen was not enough to measure leptin, leaving 234 Japanese individuals (123 men and 111 women) and 182 Japanese-Americans (88 men and 94 women).

Ethics committees of the Shiga University of Medical Science, the Pacific Health Research Institute, and North-western University approved the study protocol. Written informed consent was obtained from all participants.

Anthropometric and lifestyle assessment

The participants visited clinics four times on two pairs of consecutive days approximately 3 weeks apart. At each visit, height and weight were measured without shoes and without heavy clothes (e.g., jackets or coats), four times, total. BMI was calculated as weight divided

by height squared (kg/m^2). To evaluate physical activity, questions were posed about the number of hours per day spent in heavy activity, moderate activity, light activity, watching TV, and other sedentary and no activity (sleeping); the interviewer ensured that the total time added up to 24 h. A physical activity index score was calculated by multiplying the time spent in different activities by corresponding weighting factors that parallel the increased rate of oxygen consumption associated with increasingly more intense physical activity; for this, the procedure in the Framingham Offspring Study [14] was followed. In the calculation, hours of watching television were designated sedentary activity. Participants were asked whether they were on a special diet, including a weight-loss diet. Menopausal status was also asked of women.

Dietary assessment

Four in-depth multi-pass 24-h dietary recalls per participant were conducted during the four visits by specially trained and certified dietary interviewers. Prior to data collection, a supervising nutritionist in each country trained all interviewers and certified that they had the appropriate skills to conduct dietary interviews and process dietary data using computers. Standardized ongoing quality control procedures were adopted to optimize quality of dietary data throughout data collection [11]. A low coding error rate identified by a random 10 % samples of three recalls, a good score on 12-item review of recall audiotapes, and good correlations between dietary and urinary measurement of total protein, sodium, and potassium have been reported previously [12]. All participants for the present study attended all four study visits; their energy intakes from all 24-h dietary recalls were between 500 and 5,000 kcal/day.

Biochemical measurements

For the INTERLIPID Study, non-fasting blood was drawn on the second day of the first two-day visit pair just after blood pressure measurement. Time of last meal and blood pressure measurement were recorded. Serum and plasma were obtained by centrifugation within 30 min of blood drawing and immediately refrigerated. Within 24^h, all specimens were frozen and stored locally at -70°C . Samples from the Hawaiian and Japanese centers were shipped to a central laboratory in Japan on dry ice. Individual samples from the two centers were randomly allocated for analysis to avoid systematic measurement bias. Serum leptin concentrations were measured by immune-assay from Linco Research [Millipore (Billerica, MA)] (inter-CV: 4.44%; intra-CV: 4.11 %; SD: 0.20; linear range: 0.5–100 ng/ml). It has been shown that leptin concentrations did not change acutely with food intake in normal and obese persons, as well as in patients with type II diabetes mellitus [15, 16]. Serum adiponectin concentrations were measured by an enzyme-linked immunosorbent assay using the ELISA kit (Otsuka Pharmaceutical Co., Ltd., Tokyo, Japan) [13].

Data analyses

SAS version 9.2 for Windows (SAS Institute, Cary, NC) was used. Because the distribution of serum leptin was positively skewed, a logarithmic transformation was used to normalize the distribution (log-leptin). For descriptive statistics, sex-specific participant characteristics by quartile of serum leptin concentration, as well as participant characteristics stratified by BMI category ($<25 \text{ kg/m}^2$, $25\text{--}29.9 \text{ kg/m}^2$, and $\geq 30 \text{ kg/m}^2$) using all sex-site-combined data

were analyzed. The Mantel-Haenszel chi-square statistical test for nominal variables and the “contrast” option for analysis of variance for continuous variables were performed to assess whether or not there were significant trends across quartiles of leptin concentration (controlled for age) as well as across three BMI categories. Partial correlation coefficients between log-leptin and total dietary energy intake stratified by BMI category adjusted for none; age and sex (Model 1); Model 1 + site, height, BW (Model 2); Model 2 + physical activity score (Model 3); Model 3 + menopausal state (Model 4) were obtained using all sex-site data combined. Multiple linear regression analyses (all sex-site combined) stratified by BMI category with adjustment for confounders were used to examine the relation between log-leptin and total dietary energy intake. Because resting metabolic rate is determined by body weight, height, age, and sex, these variables were included in the models [17]. In addition, physical activity index score and site were included.

To examine the effect of time between last meal and blood drawn on serum leptin concentration, multiple linear regression analysis was used, taking log-leptin as dependent variable and time difference between last meal and blood pressure measurement (blood was drawn just after blood pressure measurement) as independent variable, adjusted for age, sex, site, height, body weight, and physical activity index score. The analysis stratified by BMI category was performed as well. To examine the effect of time of day blood drawn on serum leptin concentration, the similar multiple linear regression analysis was used, replacing time difference between last meal and blood pressure measurement with time blood drawn. All *P* values were two-tailed; *P* < 0.05 was considered significant.

Results

Descriptive statistics

The range of BMI in this population was 17.2–39.0 kg/m². Characteristics of participants by quartile of serum leptin concentration for men and women separately are shown in Table 1. Percentage of participants from Hawaii, mean BMI, body weight, SBP, and protein and fat intakes (% kcal) were significantly greater in the higher leptin concentration groups in both genders (age-controlled *P*s 0.010 to <0.001). Mean carbohydrate intake (% kcal), physical activity index score, and mean adiponectin concentrations were significantly lower in the higher leptin concentration groups in both men and women (*P* < 0.001 and 0.005). Mean pulse rate was significantly greater in the higher leptin concentration groups of both sexes (*P* = 0.049 and 0.013). Percentage of participants on weight-loss diet was higher in the higher leptin concentration groups in men, but not in women. Mean age, total dietary energy intake, and height were not significantly different in either men or women. Percentage of now or past menopause was not significantly different in women.

For all participants combined, characteristics of participants by BMI category are shown in Table 2. Mean leptin concentration, body weight, height, SBP, pulse rate, and total dietary energy intake were significantly higher in the higher BMI groups. Percentage of participants from Hawaii and that of men were significantly higher in the higher BMI groups. Mean adiponectin concentration and physical activity score were significantly lower in the higher BMI groups. Mean age and percentage of participants on weight-loss diet were not different.

Relation between serum leptin and total energy intake

Partial correlation coefficients between log-leptin and total dietary energy intake stratified by BMI category are shown in Table 3. Without adjustment, correlation coefficients between log-leptin and total dietary energy intake were significant in all the three BMI categories. In model 2, where adjustment was made for age, sex, site, height, and body weight, the partial correlation coefficient in the middle BMI category lost statistical significance. By further addition of physical activity in the model, statistical significance of the partial correlation coefficient remained only in the highest BMI category (Model 3). Addition of menopausal state in Model 4 did not cause any difference.

The results of multivariate regression analyses stratified by BMI are shown in Table 4. In participants with BMI < 25 kg/m² and those with BMI between 25 and 29.9 kg/m², log-leptin was not significantly related to total dietary energy intake ($P = 0.268$ and 0.236); in those with BMI ≥ 30 kg/m², it was significantly inversely related to total dietary energy intake ($P = 0.029$). Physical activity score was significantly positively related to total dietary energy intake only in participants with BMI < 25 kg/m² ($P < 0.001$).

Relationship of post-meal time and of time of day blood drawn with serum leptin

Mean time difference between last meal and blood pressure measurement (blood was drawn just after blood pressure measurement) was 3.5 ± 3.1 h (range: 0.5–16.6 h). The results of multivariate regression analyses on relation between post-meal time and log-leptin revealed that post-meal time did not have effect on log-leptin ($P = 0.924$ in all participants combined, 0.649 – 0.915 in analyses stratified by BMI). Sex, body weight, and height contributed significantly to log-leptin in general. Site significantly contributed to log-leptin in total and in those with BMI < 25.0 kg/m². Physical activity index score significantly contributed to log-leptin in total, in those with BMI < 25.0 kg/m², and in those with BMI 25.0–29.9 kg/m². Likewise, blood drawn time did not have effect on log-leptin. Plots of leptin against post-meal time and against blood drawn time did not show any systematic trend (data not shown).

Discussion

Using two population samples of common genetic background and diverse lifestyles, Japanese-Americans in Hawaii and Japanese in Japan, with wide-ranging BMIs (range: 17.2 – 39.0 kg/m²), we demonstrated significant independent inverse relation between log-leptin and total dietary energy intake for those with BMI ≥ 30 kg/m² (obese) by multivariate regression analysis. This finding does not support the concept that in obese persons there is resistance to the appetite-suppressing effect of leptin even with elevated leptin concentrations and rather implies the obese persons are leptin sensitive. Lack of significant relations in those with BMI < 25 kg/m² and in those with BMI between 25 and 29.9 kg/m² may indicate that leptin had no clear effect on caloric intake in lean and overweight participants.

For the present study, non-fasting blood was drawn. It has been shown that leptin concentrations did not change acutely with food intake in normal and obese persons, as well

as in patients with type II diabetes mellitus [15, 16]. However, Licinio et al., who measured leptin levels every 7 min for 24 h, found that human leptin levels were pulsatile with 32.0 ± 1.5 pulses every 24 h (i.e., every 45 min) and a pulse duration of 32.8 ± 1.5 min [18]. Schoeller et al., who measured leptin levels hourly, reported that plasma leptin demonstrated a strong diurnal rhythm with an amplitude of 21 %, zenith at 2400 h, and nadir between 0900 and 1200 h. Day/night reversal caused a 12 ± 2 h shift in the timing of the zenith and nadir. Food intake did not cause any significant changes in leptin level, but when meals were shifted 6.5 h without changing the light or sleep cycles, the leptin shifted by 5–7 h [19]. In our present study, plots of leptin against post-meal time and against blood drawn time did not show any systematic trend. Multivariate regression analyses on relationship of post-meal time and of time of day blood drawn with log-leptin both showed no significant relations to log-leptin. Relatively small diurnal changes in leptin (up to 20 %) might have obscured among larger effects of sex, body weight, height, and others on leptin concentrations. Thus, we believe single daytime sample taken in our study represented the effective 24-hour leptin concentration in the participant.

Contrary to the generally held assumption that obese individuals are leptin resistant, our findings showed obese individuals are leptin sensitive. There have been several reports of studies that support our findings. Administration of leptin to severely obese leptin-deficient (ob/ob) mice corrected their obesity by reducing their food intake and increasing energy expenditure [20–22]. Leptin treatment of a severely obese child with congenital leptin deficiency brought about a significant decrease in hunger and food intake leading to a substantial loss of body weight [23]. Heymsfield et al. conducted a randomized, controlled, dose-escalation trial of subcutaneous recombinant leptin injections in 54 lean and 73 obese participants and observed a dose-response relationship between weight and fat loss in all participants at 4 weeks [24]. Westerterp-Plantega et al. [25] conducted a randomized, double-blind, placebo-controlled trial of weekly subcutaneous leptin administration in 30 obese men (mean BMI 34.2 ± 3.6 kg/m²) and found that appetite and hunger before breakfast decreased and remained lower in the leptin-treated groups, whereas they increased and remained higher in the placebo groups. Kissileff et al. [26] studied the effect of leptin repletion in obese humans after weight loss. They found significant increases in satiation by leptin repletion and suggested use of medications that stimulate the leptin-signaling pathway as weight-maintenance drugs. These findings on leptin administration effects in animals and human do not support the concept of leptin resistance in obese persons with elevated endogenous concentrations, but rather showed obese persons are leptin sensitive.

No previous studies examined the relation between leptin concentrations and dietary total energy intake in normal-weight, overweight, and obese substrata. Very few studies took physical activity factors into consideration. Larsson et al. [27] studied the relation between leptin and habitual food intake in 64 healthy postmenopausal women with BMI 25.0 ± 3.5 kg/m² and found that leptin concentrations were negatively correlated to total energy intake. However, they did not examine the relation stratified by BMI categories, nor was physical activity evaluated. Murakami et al. examined associations between nutrient and food intake and serum leptin concentrations in young Japanese women with mean BMI 21.4 kg/m [28]. They found that total energy intake was not related to leptin concentration, but intake of dietary fiber, vegetable, and pulses showed an independent inverse association with leptin

concentration. Thus, as our present findings, leptin may not have clear effect on caloric intake in lean and overweight participants. However, even if caloric intake in lean and overweight participants was well controlled by leptin, it is possible that we did not see a correlation with daily caloric intake within the relatively narrow leptin and BMI ranges represented in the sample, as is the case with the effect of insulin on blood glucose in insulin-sensitive individuals.

The lack of differences in mean total energy intakes across quartile of serum leptin concentrations in men and women was unexpected. However, the facts that physical activity scores were smaller in the higher leptin groups in men and women and the prevalence of weight-loss diet was higher in the higher leptin groups in men may explain this. Furthermore, the association of physical activity score with total energy intake was significant only among participants with normal weight. Thus, it may be that physical activity plays a role in determining energy intake in physically active participants with normal BMI and lower leptin concentrations. Similar findings were reported previously by Chu et al. [29].

In animal studies, leptin increases sympathetic nerve activity to the kidneys, hindlimbs, and adrenal glands [2]. Infusion of leptin for 7 days increases arterial pressure and heart rate in conscious rats [30]. In our previous study, we showed that BMI and log-leptin related significantly and independently to SBP and DBP and suggested that leptin was an independent mediator for obesity-related adverse BP levels [31]. In the present study, we found mean pulse rate was significantly greater in the higher leptin concentration groups in men, consistent with the inference that the sympathoexcitatory effect of leptin was preserved in obese persons.

The main strengths of the present study are the following: (1) its population-based samples; (2) standardized collection of high-quality nutrition, BP, and blood data; and (3) use of multiple procedures for quality control. The study was limited by its two-sample cross-sectional design. Findings may or may not be generalizable to other populations. Due to the cross-sectional nature of this study, its results must be interpreted cautiously in regard to cause-effect relationships. Regrettably, we do not have adiposity data other than BMI, such as fat mass. Because the number of participants with BMI ≥ 30 was relatively small, we could not further stratify them by sex. Previously, sex difference in the prediction of weight loss by leptin, sex differences in the response of leptin concentrations to weight loss, and the effect of menopause on leptin were reported [32–35]. We could not examine sex-related regulation of weight by leptin. Finally, although our dietary records system is best in the epidemiological sciences, the method itself is indirect in nature.

In conclusion, leptin was significantly inversely associated with dietary energy intake in obese persons, but not in normal-weight and overweight participants.

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Table 1

Participant characteristics by quartile of serum leptin in 416 participants (211 men and 205 women)—Japanese in Aito Town, Japan, and Japanese-Americans in Honolulu, HI, USA—1997–1999—INTERLIPID Study

Variable	Leptin (ng/ml)				Trend <i>P</i>
	1.4–2.7	2.8–3.8	3.9–5.5	5.6–57.4	
<i>Men</i>					
<i>N</i>	50	54	53	54	
Hawaii (%)	10.0	35.2	45.3	74.1	<0.001
Age (yr)	49.4 ± 6.2	49.6 ± 5.7	49.5 ± 6.2	51.5 ± 5.0	0.080
BMI (kg/m ²)	21.8 ± 2.2	24.2 ± 2.1	25.6 ± 3.0	29.9 ± 4.5	<0.001
BW (kg)	60.7 ± 7.8	66.9 ± 7.5	71.4 ± 9.8	83.0 ± 14.1	<0.001
Height (cm)	166.9 ± 6.5	166.3 ± 6.2	167.1 ± 5.7	168.4 ± 5.3	0.067
SBP (mmHg)	116.9 ± 10.9	121.2 ± 13.7	122.1 ± 14.0	123.5 ± 11.2	0.010
Pulse (/min)	70.1 ± 8.0	71.6 ± 10.8	71.9 ± 9.1	74.0 ± 9.6	0.049
Energy (kcal/24 h)	2,470 ± 576	2,393 ± 496	2,324 ± 610	2,399 ± 580	0.446
Protein (%kcal)	15.4 ± 2.3	16.0 ± 2.5	16.1 ± 3.1	16.8 ± 2.8	0.006
CarbH (%kcal)	55.5 ± 8.6	54.3 ± 8.4	53.5 ± 8.3	48.9 ± 7.5	<0.001
Fat (%kcal)	22.7 ± 5.4	24.0 ± 6.9	26.2 ± 7.5	29.9 ± 7.3	<0.001
Weight-loss diet (%)	10.0	7.4	18.9	25.9	0.074
Adiponectin (μ/ml)	9.3 ± 4.0	7.9 ± 3.5	7.6 ± 3.3	5.9 ± 2.9	<0.001
PA score	40.5 ± 13.6	35.0 ± 11.1	33.7 ± 8.3	31.0 ± 8.0	<0.001
<i>Women</i>					
<i>N</i>	50	53	51	51	
Hawaii (%)	20.0	34.0	60.8	68.6	<0.001
Age (yr)	50.0 ± 5.7	49.5 ± 6.2	49.7 ± 5.4	49.8 ± 5.2	0.953
Menopause (%)	68.0	43.4	54.9	56.9	0.506
BMI (kg/m ²)	21.1 ± 1.7	23.2 ± 2.0	24.6 ± 2.6	28.6 ± 5.2	<0.001
BW (kg)	50.2 ± 5.5	55.4 ± 5.8	57.9 ± 6.3	67.9 ± 11.7	<0.001
Height (cm)	154.0 ± 5.5	154.5 ± 4.9	153.6 ± 4.6	154.2 ± 5.5	0.918
SBP (mmHg)	111.8 ± 9.7	115.1 ± 11.5	116.0 ± 13.7	121.2 ± 14.6	<0.001
Pulse (/min)	69.5 ± 6.5	70.7 ± 6.9	71.1 ± 7.2	73.5 ± 9.9	0.013

Variable	Leptin (ng/ml)					Trend <i>P</i>
	1.4–2.7	2.8–3.8	3.9–5.5	5.6–57.4		
Energy (kcal/24 h)	1,859 ± 387	1,796 ± 400	1,813 ± 382	1,856 ± 357		0.983
Protein (%kcal)	16.1 ± 2.6	16.0 ± 2.4	16.5 ± 2.5	17.5 ± 3.0		0.004
CarbH (%kcal)	55.7 ± 7.1	57.3 ± 7.2	55.2 ± 6.7	49.9 ± 9.3		<0.001
Fat (%kcal)	27.2 ± 5.2	25.9 ± 6.6	27.9 ± 6.4	32.0 ± 8.2		<0.001
Weight-loss diet (%)	24.0	30.2	25.5	27.4		0.892
Adiponectin (μ/ml)	14.8 ± 5.7	12.5 ± 5.6	10.0 ± 4.9	7.8 ± 3.1		<0.001
PA score	37.4 ± 13.5	34.6 ± 9.4	32.7 ± 8.7	32.0 ± 8.0		0.005

Values are mean ± SD. Trend *P* values are for the age-controlled (except for variable: age) relationship between the variables listed on the left and quartile of leptin, obtained by the Mantel–Haenszel chi-square test and the “contrast” option for analysis of variance. *BM*/body mass index (range: 17.2–39.0 kg/m²), *SBP*/systolic blood pressure (mmHg), *Pulse*/pulse rate (/min), *Energy*/dietary energy intake (kcal/day), *CarbH*/carbohydrate intake, *PA score* the Framingham Study physical activity index score. Menopause = percentage of now or past menopause

Table 2

Participant characteristics by BMI category in 416 participants (211 men and 205 women)—Japanese in Aito Town, Japan, and Japanese–Americans in Honolulu, HI, USA—1997–1999—INTERLIPID Study

Variable	BMI range (kg/m ²)			Trend <i>P</i>
	<25	25–29.9	30	
<i>N</i>	255	116	45	
Leptin (ng/ml)	6.0 ± 3.9	8.8 ± 5.9	15.5 ± 1.1	<0.001
Hawaii (%)	28.6	58.6	91.1	<0.001
Men (%)	44.7	58.6	64.4	0.002
Age (yr)	49.4 ± 5.9	50.8 ± 5.5	50.0 ± 4.7	0.596
BW (kg)	57.4 ± 7.8	70.3 ± 8.2	91.0 ± 11.8	<0.001
Height (cm)	160.0 ± 8.4	161.2 ± 8.4	163.4 ± 9.5	0.016
SBP (mmHg)	116 ± 13	124 ± 13	122 ± 11	0.004
Pulse (/min)	70.6 ± 8.1	72.4 ± 8.7	75.0 ± 11.0	0.002
Energy (kcal/24 h)	2,066 ± 525	2,120 ± 570	2,396 ± 645	<0.001
Weight-loss diet (%)	10.2	12.9	15.6	0.253
Adiponectin (μ/ml)	10.7 ± 5.3	7.9 ± 4.0	6.0 ± 2.3	<0.001
PA score	35.7 ± 11.2	34.0 ± 10.2	30.7 ± 6.1	0.004

Values are mean ± SD. Trend *P* values are relationship between the variables listed on the left and BMI category, obtained by the Mantel–Haenszel chi-square test and the “contrast” option for analysis of variance. BMI = body mass index (range: 17.2–39.0 kg/m²), *BW* body weight (kg), *SBP* systolic blood pressure (mmHg), *Pulse* pulse rate (/min), *Energy* dietary energy intake (kcal/day), *PA score* the Framingham Study physical activity index score

Table 3

Partial correlation coefficient between log-leptin and energy intake stratified by BMI category adjusted for other variables — INTERLIPID Study

Variables adjusted for	<25		25–29.9		30	
	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>
None	–0.423	<0.001	–0.481	<0.001	–0.528	<0.001
Model 1: age, male	–0.138	0.029	–0.149	0.114	–0.301	0.050
Model 2: Model 1 + site, height, BW	–0.147	0.020	–0.130	0.176	–0.349	0.027
Model 3: Model 2 + PA score	–0.070	0.268	–0.114	0.236	–0.350	0.029
Model 4: Model 3 + menopause state (now or past)	–0.071	0.269	–0.119	0.216	–0.358	0.027

Partial correlation coefficients (*r*) and *P* values between log-leptin and energy intake adjusted for other adjusted for variables listed. *Log-leptin* log-transformed leptin concentration, *Energy* dietary energy intake (kcal/day), *BMI* body mass index (kg/m²), *BW* body weight (kg), *SBP* systolic blood pressure (mmHg), *Pulse* pulse rate (/min), *PA score* the Framingham Study physical activity index score

Table 4

Relation between variables and dietary energy intake (kcal/24 h): stratified analyses by BMI category among 416 participants (211 men and 205 women)—Japanese in Aito Town, Japan, and Japanese-Americans in Honolulu, HI, USA—INTERLIPID Study

N	<u>Body weight</u>		<u>PA score</u>		<u>Log-leptin</u>		<u>Other variables</u>	
	Coef	P	Coef	P	Coef	P	In models	
BMI < 25 kg/m ²	255	5.30	0.440	13.20	<0.001	−198	0.268	Age, male*, Hawaii, height
BMI 25–29.9 kg/m ²	116	8.98	0.528	2.34	0.638	−358	0.236	Age, male*, Hawaii, height
BMI ≥ 30 kg/m ²	45	12.8	0.299	−2.95	0.833	−1,077	0.029	Age, male, Hawaii, height

Results of multivariate regression analyses on relation between variables and dietary energy intake stratified analyses. Coefficients (Coef.) and *P*-values for body weight, the Framingham Study physical activity index score, and log-leptin in multiple linear regression models used to examine the relations between variables and dietary energy intake (kcal/24 h) in men (123 in Japan and 88 in Hawaii) and women (111 in Japan and 94 in Hawaii). Covariates in Model = age, sex, site, body weight, height, and the Framingham Study physical activity index score + log-transformed leptin concentration. *Log-leptin* log-transformed leptin concentration, *BMI* body mass index (kg/m²), *PA score* the Framingham Study physical activity index score.

P values for other variables are indicated by * *P* < 0.05