Differential Effects of High-Fat and High-Carbohydrate Isoenergetic Meals on Cardiac Autonomic Nervous System Activity in Lean and Obese Women

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Food ingestion can influence autonomic nervous system activity. This study compares the effects of 2 different isoenergetic meals on sympathetic nervous system (SNS) activity, assessed by heart rate variability (HRV) and plasma norepinephrine (NE) levels, in lean and obese women. Fifteen lean and 15 obese healthy women were examined on 2 occasions: after a carbohydrate (CHO)-rich and after a fat-rich test meal. Measurements of blood pressure, heart rate, resting energy expenditure, plasma glucose, lipids, insulin, leptin, and NE, as well as spectral analysis of the HRV, were performed at baseline and every 1 hour for 3 hours after meals. At baseline, obese women had higher SNS activity than lean controls (higher values of low-to-high frequency ratio [LF/HF], 1.52 ± 0.31 *v* 0.78 ± 0.13, *P* = .04; and plasma NE levels, 405.6 ± 197.9 *v* 240.5 ± 95.8 pg/mL, *P* < .0001). After the CHO-rich meal a greater increase in LF/HF and in plasma NE levels was observed in lean, compared to obese women (1.21 ± 0.6 *v* 0.32 ± 0.06, *P* = .04; and 102.9 ± 35.4 *v* 38.7 ± 12.3 pg/mL, *P* = .01, respectively), while no differences were observed after the fat-rich meal. Meal-induced thermogenesis was higher after the CHO-rich as compared to the fat-rich meal and was comparable between lean and obese women. Changes in HRV were not associated with the thermogenic response to the test meals. In conclusion, consumption of a CHO-rich meal causes greater cardiac SNS activation in lean than in obese women, while fat ingestion does not result in any appreciable change in either group. SNS activation does not appear to influence the thermic effect of the food in either lean or obese women.

AUTONOMIC nervous system activity is influenced by food ingestion.[1] Among dietary substrates, carbohydrate (CHO) ingestion, but not fat or protein ingestion, is accompanied by increased sympathetic nervous system (SNS) activity in animals and humans,[2,3] whereas fasting has an inhibitory effect.[4] The putative sympathoexcitatory effect of feeding has been attributed mainly to hyperinsulinemia caused by the CHO content of the meals.[5] The relationship between SNS activity and obesity has long been studied.[6-14] Human studies examining adrenergic activity in obesity by whole-body methods (urinary excretion or plasma turnover of catecholamines) have given conflicting results, with reports of normal, decreased, or increased SNS activity.[6-12] The results of regional studies in obesity (assessment of muscle SNS activity, renal and cardiac NE spillover) have also been inconsistent.[12-18] Some studies have shown a positive association between obesity and SNS activity,[12-17] while others a negative one,[18,19] the latter suggesting that decreased SNS activity may have a role in the aetiopathogenesis of obesity.[20]

Simple catecholamine assays and kinetic studies provide a measure of pre-synaptic SNS activity, and not of post-synaptic end-organ responsiveness, thus reflecting only partly an individual's sympathetic drive.[5] On the other hand, spectral analysis of the heart rate variability (HRV) is a simple and noninvasive tool evaluating the cardiac autonomic nervous system activity, which integrates both pre-synaptic and post-synaptic cardiac responsiveness and, thus, it provides a more comprehensive evaluation of the autonomic nervous system activity at the heart level.[21,22] Vagal activity is the major contributor to the high-frequency (HF) component, while the low-frequency component (LF) reflects the activity of both parasympathetic and SNS activity, the latter being its main component.[21,22] The low-to-high frequency ratio (LF/HF) is therefore an index of sympathovagal balance at the heart level.[21] Interventions increasing or lowering LF/HF may indicate a shift of the cardiac sympathovagal balance towards a sympathetic or parasympathetic predominance, respectively.[21,22] Recent studies have shown that in healthy subjects glucose ingestion or insulin infusion results in an increase in LF/HF, suggesting a predominance of SNS activity.[23,24] The effect of consumption of different meals on HRV in lean and obese subjects has not been studied so far. Furthermore, animal studies have shown that leptin may stimulate the SNS.[25,26] However, no literature data exist concerning the potential relationship between plasma leptin levels and SNS activity in the postprandial state. The main aim, therefore, of this crossover study was to compare the changes of HRV in lean and obese subjects after consumption of isoenergetic meals of different composition. The potential association of LF/HF with metabolic parameters, such as plasma norepinephrine (NE), insulin, and leptin levels before and after food ingestion was also studied.

MATERIALS AND METHODS

We studied 15 lean and 15 obese healthy women, strictly matched for age, after getting informed consent. We studied only women because they represent the vast majority of the subjects attending the outpatient obesity clinic of our Department. All subjects were 20 to 60 years of age, nonsmokers, and on free diet. Inclusion criteria required that there had been no change in their body weight greater than 2 kg in the previous 6 months, and that they were not on hormone-replacement therapy, contraceptive tablets, hypolipidemic drugs, or on any other medication with known effects on the cardiac autonomic nervous

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system activity. They were all examined at the supine position, in a quiet room with stable temperature (22 to 24°C). After application and adjustment of the measured devices, a period of 30 minutes was allowed for acclimatization. As plasma estrogen levels are known to influence HRV,[27] all women of reproductive age were examined during the first half of their cycle. Premenopausal and postmenopausal women were included in the study groups in equal numbers.

In the morning, after a 12- to 14-hour fast, each subject attended the metabolic unit of our Department. Anthropometric measurements were recorded after voiding at around 8 AM. Weight and height were measured using standard techniques. Percentage of body fat (% body fat) was measured using a bioimpendance analyzer (Tanita TBF-215 body composition analyzer, Brooklyn, NY). Body mass index (BMI) and waist-to-hip ratio (WHR) were measured and calculated as previously described.[28] Afterwards, an intravenous catheter was inserted in a superficial forearm vein and kept patent by a slow infusion of saline solution 0.9% for blood sampling.

We designed a crossover study. Each subject received 2 standard test meals: (1) a meal rich in CHO, with a total energy content of 546 kcal, consisting of 130 g CHO, 0.26 g fat, and 6.1 g protein in the form of white bread and honey; and (2) a meal rich in fat, with a total energy content of 532 kcal, consisting of 52 g fat, 5 g CHO, and 11 g protein in the form of 100 g of walnuts. The meals were given in a random order with an interval of 7 days in between. Patients were permitted to consume only water during the study.

Respiratory gas exchange measurements were performed by an open-circuit ventilated hood system (Deltatrack monitor, Datex, Helsinki, Finland) for 30 minutes in the fasting condition and then every 1 hour for 3 hours after the meals. Resting energy expenditure was measured and respiratory quotient (RQ) was calculated from the oxygen consumption and the carbon dioxide production.[29] Blood pressure was measured at rest in the supine position on 3 occasions, separated by intervals of 1 minute using a Dinamap XL vital signs monitor (Johnson-Johnson, Arlington, VA). The average of the last 2 of the 3 measurements was taken as the final blood pressure value.

Short-term analysis of the HRV was performed in all subjects using a computer-aided examination and evaluation system VariaCardio TF4 (Sima Media, Olomouc, Czech Republic).[30] Three consecutive examination time intervals of 5 minutes duration each (total 15 minutes) and calculations were performed at each interval on a 256 beat-window basis. Spectral plots at the examined time intervals were derived from the average of the three 5-minute segments data. Computational method was based on fast Fourier transform modified by algorithm of coarse-graining spectral analysis.[30] Each dataset was filtered automatically by excluding recorded artifacts using a recognition algorithm. Parameters of the frequency-domain were observed within the HF band (0.15 to 0.50 Hz) and within the LF band (0.05 to 0.15 Hz). The values of the power of the LF and HF are expressed as either their natural logarithm or in normalized units; expression in normalized units represents the relative value of each power component in proportion to the total power minus the very-low-frequency component.[19] Subsequently, the LF/HF ratio was calculated.

All measurements were performed in the fasting state and at 1, 2, and 3 hours after meals. The thermic effect of the test meals (meal-induced thermogenesis) was calculated as the difference of the resting postprandial energy expenditure minus the fasting resting energy expenditure.[31] Venous blood samples where drawn just before and at 1, 2, and 3 hours after meal consumption.

Analytical Methods

Plasma lipids (total cholesterol, high-density lipoprotein [HDL]-cholesterol, triglycerides) were measured enzymatically on a Technicon analyzer RA-XT (Technicon Ltd, Dublin, Ireland). Low-density lipoprotein (LDL) levels were estimated using the equation of Friedewald et al.[32] Serum glucose was measured by the glucose oxidase-peroxidase method (Zafiropoulos, Hellas, Greece). Plasma insulin (Biosure, Brussels, Belgium; coefficient of variation [CV] = 3.3% ± 1.2%) and leptin (Linco Research, St Louis, MO; CV = 4.2% ± 0.5%) were determined by radioimmunoassay. Plasma NE concentrations were determined by high-performance liquid chromatography (Chromsystems, Munich, Germany; CV = 4.6% ± 1.0%). Insulin resistance was calculated by the homeostasis model assessment equation (HOMA).[33]

Statistical Analysis

Statistical analysis was performed using the SPSS program (SPSS, Chicago, IL). Analysis of variance (ANOVA) for repeated measurements was performed to test the timing effect of the studied parameters in the 2 phases of the study. Because the plasma values of insulin, triglycerides, and leptin were skewed, they were log-transformed to improve normality for statistical testing and back-transformed for presentation in figures. A paired Student's *t* test was used to compare the differences of the measured parameters between the 2 meals in each group, while a 2-sample *t* test was used to compare the measured differences between lean and obese women. Partial correlations were used to adjust for various parameters of the study. Multivariate regression analysis was performed using standard methods. P values $< .05$ were considered as statistically significant.

RESULTS

Baseline Data

At baseline, BMI, WHR, % body fat, postabsorptive energy expenditure ($P = .005$), plasma levels of glucose ($P < .0001$), insulin ($P = .003$), leptin ($P < .0001$), NE ($P < .0001$), and LF/HF ($P = .04$) were all significantly higher in the obese compared to the lean women. There was a trend for the mean values of systolic blood pressure to be higher in the obese women, but the differences were not statistically significant. In contrast, RQ, an indicator of substrate oxidation, was significantly higher in the lean compared to the obese subjects ($P = .008$) (Tables 1 through 3). Plasma levels of HDL-cholesterol were lower in the obese women ($P = .03$).

When all subjects were analyzed together, fasting energy expenditure was correlated significantly with BMI ($r = 0.69$, $P < .0001$), WHR ($r = 0.51$, $P < .001$), % body fat ($r = 0.63$, $P < .0001$), LF/HF ratio ($r = 0.42$, $P = .03$), plasma NE ($r = 0.53$, $P = 0.003$), plasma leptin ($r = 0.66$, $P < .0001$), and plasma insulin levels ($r = 0.59$, $P = .002$). No significant correlation was found between fasting energy expenditure and age. After adjustment for % body fat, none of these associations remained significant.

LF/HF correlated significantly with plasma insulin levels ($r = 0.43$, $P = .01$) and remained so after adjustment for % fat content (partial correlation coefficient $r = 0.32$, $P = .04$). LF/HF also correlated significantly with plasma leptin and NE levels ($r = 0.41$, $P = .01$ and $r = 0.35$, $P = .03$, respectively), but this significance was lost after controlling for % body fat (partial correlation coefficients $r = 0.21$, $P = .54$ and $r = 0.19$, $P = .67$, respectively).

Postprandial Comparisons Between the Test Meals

Resting energy expenditure increased after meals in both lean and obese women ($P < .0001$) (Tables 2 and 3). The magnitude of the thermogenic response was higher after the CHO-rich meal than the fat-rich meal in both lean (mean

Table 1. Clinical and Demographic Characteristics of the Study Groups

	Lean	Obese	*P*
n	15	15	
Age (yr)	35 ± 11	37 ± 16	.66
BMI (kg/m^2)	22.37 ± 2.42	35.86 ± 4.62	<.0001
WHR	0.75 ± 0.05	0.85 ± 0.06	.001
Body fat (%)	31.38 ± 6.23	53.35 ± 8.81	<.0001
Systolic blood pressure (mm Hg)	110 ± 12	125 ± 27	.08
Heart rate (beats/min)	69 ± 9	71 ± 8	.73
Diastolic blood pressure (mm Hg)	74 ± 8	79 ± 16	.33
Total cholesterol (mg/dL)	200 ± 37	208 ± 42	.53
HDL-cholesterol (mg/dL)	49 ± 4	42 ± 8	.03
LDL-cholesterol (mg/dL)	134 ± 30	143 ± 42	.47
Triglycerides (mg/dL)	83 ± 60	103 ± 46	.26
HOMA-IR*	1.1 (0.8-1.6)	2.7 (1.8-3.7)	<.0001

NOTE. Data are mean ± SD, unless otherwise is indicated.

*Median value (interquartile range).

Abbreviations: BMI, body mass index; WHR, waist-to-hip ratio; HDL, high-density lipoprotein; LDL, low-density lipoprotein; HOMA-IR, homeostasis model assessment insulin resistance.

difference ± SE, 7.4 ± 2.3 kcal · h, $P = .01$) and obese women (mean difference ± SE, 5.3 ± 1.6 kcal · h, $P = .004$) (Fig 1A). RQ increased significantly after the CHO-rich meal and declined after the fat-rich meal in both study groups ($P < .0001$) (Tables 2 and 3).

Plasma glucose increased in response to the CHO-rich meal in both lean and obese women ($P = .001$ and $P < .0001$, respectively). A smaller, but significant increase in plasma glucose was also observed after the fat meal in the lean ($P = .02$) but not in obese women ($P = .27$) (Tables 2 and 3). Plasma insulin levels also increased significantly in both lean and obese subjects after the CHO-rich meal ($P < .0001$), but not after the

Table 2. Fasting and Postprandial Profiles of the Measured Parameters in Lean Women

	Fasting	1st Hour	2nd Hour	3rd Hour	*P**
Glucose (mg/dL)					
CM	82.1 ± 12.8	111.9 ± 31.6	102.6 ± 27.4	103.2 ± 25.1	.001
FM	81.0 ± 11.2	79.3 ± 13.9	91.3 ± 13.6	90.0 ± 10.9	.02
Insulin (μU/mL)					
CM	5.9 ± 2.6	57.6 ± 61.5	43.6 ± 41.7	35.6 ± 34.6	<.0001
FM	7.0 ± 3.4	10.9 ± 7.7	10.5 ± 10.9	8.8 ± 6.9	.25
Leptin (ng/mL)					
CM	13.9 ± 6.2	12.6 ± 6.5	13.7 ± 7.1	13.7 ± 6.5	.19
FM	12.3 ± 5.2	12.2 ± 5.5	11.8 ± 5.1	11.7 ± 4.9	.63
PLF (ln ms^2)					
CM	5.86 ± 0.89	6.23 ± 0.66	7.12 ± 0.68	6.94 ± 0.93	.03
FM	5.43 ± 1.05	5.68 ± 0.84	5.35 ± 0.90	5.62 ± 0.85	.31
PHF (ln ms^2)					
CM	6.34 ± 0.87	5.39 ± 1.41	3.92 ± 1.12	4.92 ± 1.36	.02
FM	6.19 ± 0.86	5.95 ± 0.69	6.06 ± 0.60	5.86 ± 0.84	.44
LF/HF					
CM	0.78 ± 0.13	1.20 ± 0.28	1.36 ± 0.32	1.62 ± 0.68	.04
FM	0.95 ± 0.15	0.84 ± 0.19	0.92 ± 0.18	1.01 ± 0.27	.80
NE (pg/mL)					
CM	240.5 ± 95.8	277.2 ± 174.1	292.5 ± 141.9	295.0 ± 104.3	.03
FM	276.4 ± 165.8	239.1 ± 116.0	289.6 ± 173.6	234.7 ± 90.9	.65
RQ					
CM	0.88 ± 0.06	0.98 ± 0.08	0.98 ± 0.06	0.99 ± 0.06	<.0001
FM	0.90 ± 0.07	0.87 ± 0.06	0.85 ± 0.04	0.86 ± 0.07	<.0001
REE (kcal/24 h)					
CM	1,182.8 ± 187.7	1,380.6 ± 224.3	1,390.0 ± 212.2	1,372.7 ± 202.1	<.0001
FM	1,115.0 ± 161.5	1,228.7 ± 162.9	1,227.6 ± 157.7	1,244.0 ± 160.5	<.0001

NOTE. Data are mean ± SD.

*Time-dependent differences *v* baseline values (ANOVA for repeated measurements).

Abbreviations: CM, carbohydrate-rich meal; FM, fat-rich meal; PLF, power of low frequency; PHF, power of high frequency; ln, natural logarithm; LF/HF, low-to-high frequency ratio; NE, plasma norepinephrine; RQ, respiratory quotient; REE, resting energy expenditure.

Table 3. Fasting and Postprandial Profiles of the Measured Parameters in Obese Women

	Fasting	1st Hour	2nd Hour	3rd Hour	P*
Glucose (mg/dL)					
CM	101.0 ± 13.3	142.9 ± 32.6	123.0 ± 21.5	114.1 ± 17.9	<.0001
FM	98.8 ± 13.5	99.1 ± 13.9	97.7 ± 10.3	95.4 ± 7.0	.27
Insulin (μU/mL)					
CM	13.7 ± 10.1	87.6 ± 49.5	76.7 ± 58.0	60.5 ± 40.1	<.0001
FM	13.2 ± 9.9	13.5 ± 8.2	11.8 ± 5.5	11.0 ± 4.9	.31
Leptin (ng/mL)					
CM	34.7 ± 16.7	32.6 ± 17.1	32.7 ± 17.0	35.7 ± 20.7	.63
FM	31.7 ± 13.9	30.6 ± 16.1	29.9 ± 13.6	28.1 ± 10.9	.10
PLF (ln ms^2)					
CM	5.69 ± 0.98	5.97 ± 0.75	6.04 ± 0.88	5.94 ± 0.76	.48
FM	5.43 ± 0.05	5.68 ± 0.84	5.35 ± 0.90	5.62 ± 0.85	.31
PHF (ln ms^2)					
CM	5.69 ± 0.98	5.47 ± 0.75	5.45 ± 0.88	5.52 ± 0.76	.75
FM	5.76 ± 1.65	5.88 ± 1.39	5.71 ± 1.47	5.68 ± 1.49	.69
LF/HF					
CM	1.52 ± 0.31	1.79 ± 0.55	1.76 ± 0.48	1.41 ± 0.27	.33
FM	1.50 ± 0.39	1.79 ± 2.38	1.30 ± 0.33	1.93 ± 0.66	.46
NE (pg/mL)					
CM	405.6 ± 197.9	380.3 ± 129.1	420.2 ± 162.2	470.3 ± 156.4	.25
FM	426.3 ± 201.2	450.8 ± 230.9	365.6 ± 199.3	420.1 ± 245.2	.34
RQ					
CM	0.84 ± 0.05	0.93 ± 0.06	0.91 ± 0.04	0.90 ± 0.07	<.0001
FM	0.84 ± 0.05	0.80 ± 0.05	0.80 ± 0.02	0.81 ± 0.04	<.0001
REE (kcal/24 h)					
CM	1,410.5 ± 282.4	1,628.1 ± 270.5	1,602.9 ± 269.9	1,560.0 ± 246.4	<.0001
FM	1,385.0 ± 266.9	1,492.7 ± 292.4	1,519.1 ± 280.6	1,523.2 ± 297.9	<.0001

NOTE. Data are mean ± SD.

*Time-dependent differences vs baseline values (ANOVA for repeated measurements).

fat-rich meal (Tables 2 and 3). The overall increment in plasma insulin levels was higher after the CHO-rich meal than after the fat-rich meal in both lean and obese women (mean difference ± SE, 71.9 ± 10.2 μU · h/mL, $P < .0001$ and 161.3 ± 24.6 μU · h/mL, $P < .0001$, respectively) (Fig 1B).

LF/HF ratio increased progressively after the CHO-rich meal in lean ($P = .04$) but not in obese subjects ($P = .33$). No significant changes from baseline values were observed after the fat-rich meal in either study group ($P = .80$ and $P = .46$, respectively) (Tables 2 and 3). The magnitude of the increment in LF/HF was greater after the CHO-rich meal than the fat-rich meal in the lean, but not in the obese women (mean difference in area under the curve [AUC] ± SE, 1.75 ± 0.8 U · h, $P = .03$ and 1.01 ± 0.9 U · h, $P = .34$, respectively) (Fig 2A). Further analysis showed that the increase in LF/HF after the CHO-rich meal in the lean women was due to the combination of a significant increase in the power of LF and a decrease in the power of HF component of the HRV ($P = .03$ and $P = .02$, respectively) (Tables 2 and 3).

Plasma NE levels increased significantly in the lean group ($P = .03$) but not in the obese after the CHO-rich meal, while no change was found after the fat-rich meal in either study group (Tables 2 and 3). The overall increment in plasma NE was higher after the CHO-rich meal compared to the fat-rich meal in both the lean and the obese subjects (mean difference ± SE, 128.5 ± 42.9 pg · h/mL, $P = .01$ and 93.4 ± 39.2 pg · h/mL, $P = .03$, respectively) (Fig 2B).

Postprandial Comparisons Between Lean and Obese Women

The magnitude of the meal-induced thermogenesis was not different between lean and obese women after either the CHO- or the fat-rich meal ($P = .89$ and $P = .32$, respectively) (Fig 1A), nor was the incremental AUC of plasma glucose (CHO-rich meal, 45.8 ± 14.2 *v* 44.5 ±10.6 mg · h/mL, $P = .93$; fat-rich meal, 13.9 ± 7.9 *v* 11.4 ± 6.3 mg · h/mL, $P = .62$).

The magnitude of the increment in plasma insulin after the CHO-rich meal was higher in the obese than in the lean women ($P = .02$), while the increase after the fat-rich meal was not different between them ($P = .71$) (Fig 1B).

The AUCs of LF/HF and plasma NE levels were higher in the lean than the obese women after the CHO-rich meal ($P = .04$ and $P = .01$, respectively). The corresponding values after the fat-rich meal were not different between the study groups ($P = .70$ and $P = .85$, respectively) (Fig 2).

Other Relationships

Blood pressure (systolic and diastolic), heart rate, plasma total cholesterol, HDL-cholesterol, LDL-cholesterol, and leptin (Tables 1 and 2) concentrations did not change significantly in either lean or obese women, after either the CHO-rich or the fat-rich meal (time-dependent differences *v* baseline, $P > .05$). Plasma triglyceride levels, however, increased significantly after the fat-rich meal in both lean and obese subjects (time-

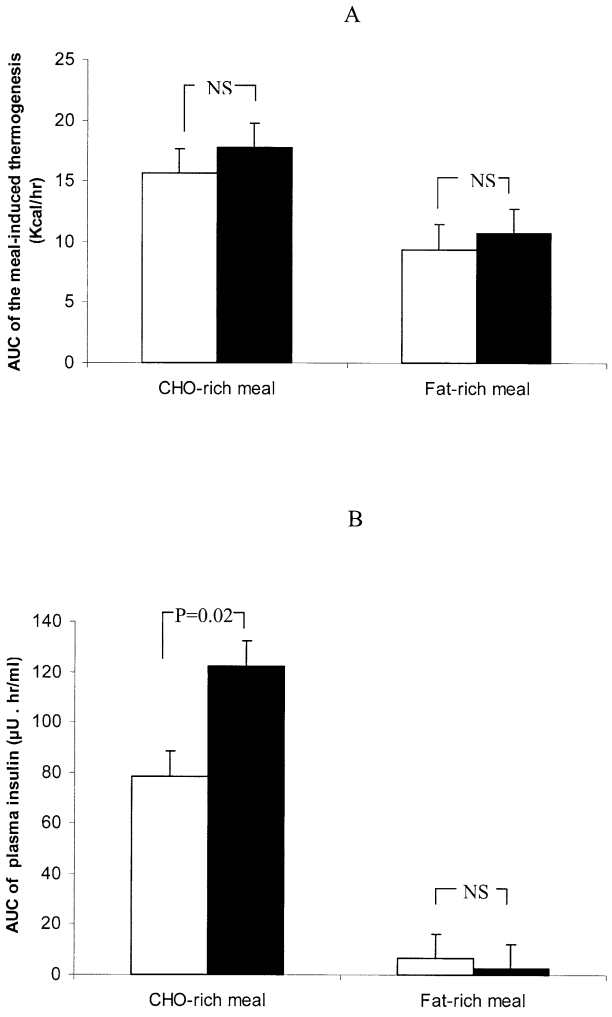

Fig 1. The incremental area under the curve (AUC) of the meal-induced thermogenesis (A) and plasma insulin concentrations (B) in the lean (□) and obese women (■) after consumption of the CHO-rich and the fat-rich meal; NS, no significant difference; CHO, carbohydrate.

dependent differences *v* baseline, $P < .0001$), but not after the CHO-rich meal.

Linear regression analysis did not reveal any significant relationship between meal-induced thermogenesis after either the CHO-rich or the fat-rich meal in the studied individuals and age, BMI, WHR, BMR, % body fat, increment in plasma insulin, NE, or LF/HF. Because the plasma levels of insulin peaked at the first hour after the CHO-rich meal, we also calculated the incremental areas (AUC) of the plasma glucose, insulin, and NE levels, as well as of the LF/HF and the meal-induced thermogenesis, until the first hour postprandially. Significant relationships were found in the lean, but not in the obese, subjects between the AUC of plasma insulin and the AUC of LF/HF ($r = 0.55$, $P = .02$) and plasma NE levels ($r = 0.48$, $P = .04$). However, no significant correlation was demonstrated between the incremental areas of plasma glucose and LF/HF or plasma NE levels. None of these variables correlated either with the incremental area of the meal-induced thermogenesis ($P > .05$). In addition, no significant relationship was found between the HOMA insulin resistance index and the magnitude of the LF/HF, power of LF and power of HF responses to either the CHO-rich or the fat-rich meal in both lean and obese women ($P > .05$).

DISCUSSION

The present study has shown that: (1) CHO, but not fat ingestion, resulted in a predominant increase of the SNS activity, assessed by measurement of plasma NE levels and LF/HF, in both lean and obese subjects; (2) however, the magnitude of the activation of the SNS activity after a CHO load was significantly blunted in the obese; (3) the energy expenditure response after either a CHO- or a fat-rich meal was similar in lean and obese women and did not correlate with the autonomic nervous system activity; and (4) consumption of a fat-rich meal did not influence cardiac SNS activity.

It is notoriously difficult to assess clinically the activity of the SNS. Plasma NE turnover and muscle sympathetic activity are the most commonly used methods to study its function.[5] However, both techniques have several limitations, because they are expensive, time-consuming, and technically demand-

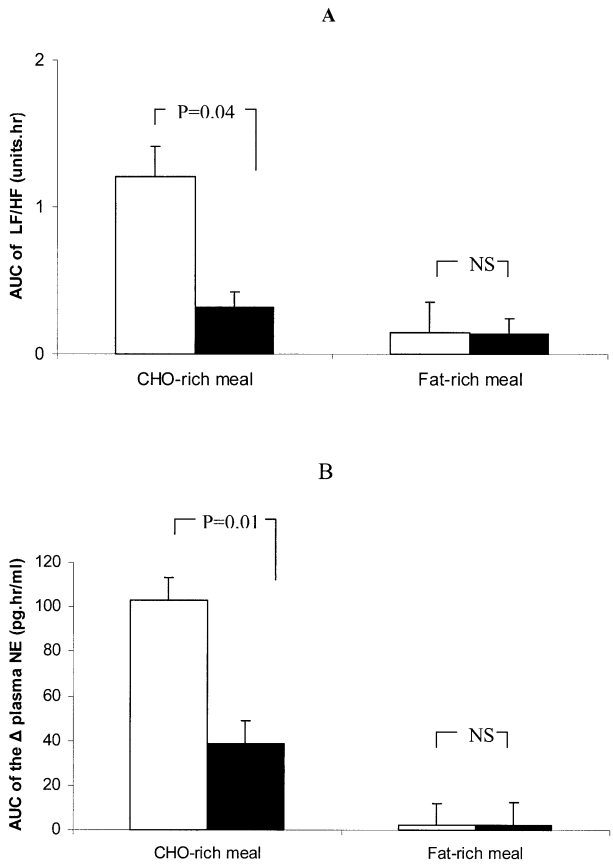

Fig 2. The incremental area under the curve (AUC) of low-to-high frequency ratio (LF/HF) (A) and plasma norepinephrine (NE) concentrations (B) after the test meals in lean (□) and obese women (■); NS, no significant difference; CHO, carbohydrate.

ing. Power spectral analysis of RR variability (HRV) is a safe and reliable tool to evaluate cardiac autonomic nervous system activity, and the ratio LF/HF is an indirect index of cardiac sympathovagal balance, reflecting autonomic input to the heart.[21,22]

Given the limitations described above concerning the evaluation of SNS activity, our findings agree with other reports that have shown increase of the sympathetic activity after a CHO load.[23,34-36] Using euglycemic hyperinsulinemic clamp techniques and measurements of HRV or microelectrode recordings of sympathetic nerve discharge to muscle, it has actually been demonstrated that the activation of the SNS after a pure glucose load is induced by the resulting hyperinsulinemia.[14,17,24,34,35] Adding onto that, our study has shown that a CHO-rich meal results in a greater activation of the SNS at the heart level (higher LH/HF), when compared with an isoenergetic fat meal. In addition, Emdin et al[37] described that fasting insulin levels predicted the LF/HF values, independent of age, sex, and BMI. The significant association between plasma insulin levels and the LF/HF in our study, which was independent of the body fatness, further supports the concept that hyperinsulinemia per se, and not the glucose content, shifts the sympathovagal balance towards a sympathetic predominance. Further, we have shown for the first time that consumption of fat, which does not induce hyperinsulinemia, does not affect cardiac autonomic nervous system activity in either obese or lean individuals.

It is of note that obese—in comparison with the lean—women showed a blunted SNS activation (lower plasma NE levels and LF/HF values) after the CHO-rich meal; this has happened despite a higher (by ~45%) increase in plasma insulin concentrations in the obese as compared with the lean women. In agreement with our findings, Spraul et al,[13] measuring directly the sympathetic neural outflow to skeletal muscle during an oral glucose tolerance test, found that obese subjects had a more than 2-fold higher muscle SNS activity than lean subjects in the fasting state. In the same study, insulin infusion resulted in a doubling SNS activity in lean subjects compared to a merely detectable response in obese subjects.

Leptin might also have effects on the SNS activity.[25,26] In our study plasma leptin levels were indeed higher (almost double) in obese compared with lean women, but they did not change during the study in response to the meals. In addition, we found no significant correlation between plasma leptin levels and LF/HF. It is also of note that the association between plasma leptin and NE levels did not remain significant after controlling for % body fat, suggesting that this relationship was mainly driven by the amount of body fatness.

In agreement with previous reports, we have shown that obese subjects had lower RQ values in both the postabsorptive and the postprandial states, which can be attributed to higher fat oxidation in these individuals.[31] Increased fat oxidation is considered to be a compensatory, although slow process; an increase in fat mass may increase fat oxidation, reestablishing fat balance and opposing further weight gain.[31]

This study has shown that although obese showed a much smaller SNS activation after the CHO-rich meal compared to the lean individuals, the thermic effect of the food was similar after the test meals between the 2 groups. Furthermore, we found no significant correlation between indices of SNS activity and the thermic effect of the food. This is in agreement with Welle et al,[3,38] who reported that pretreatment with propranolol did not reduce the thermic effect of fat or carbohydrates in humans. In addition, Ravussin and Swinburn[31] in their review of all studies comparing the thermic effect of the food in obese and lean subjects could not find any evidence for a reduced thermic effect of food in obese subjects.

One limitation of our study is that the heart consumes only a low percentage of the total oxygen consumption and cardiac sympathetic nerves are probably not involved in the regulation of thermogenesis. For this reason plasma NE was measured, which reflects—with the limitations discussed above—the total SNS activation. It has recently been shown that baroreflex sensitivity may provide a better index of the sympathetic modulation of the vascular tone than the HRV.[39] However, at the time the present study started, these literature data were not available and this parameter was not included into the study.

In conclusion, this study has shown that in the postabsorptive state, obesity is associated with cardiac sympathovagal imbalance, which may signify an adverse cardiovascular risk. We have also shown that consumption of a CHO-rich, but not of a fat-rich, meal activates the cardiac SNS in both lean and obese women; however, this response is significantly blunted in obese subjects. In addition, postprandial SNS activation has no apparent effect on the thermic effect of the food in either lean or obese women.

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