Impact of Diet-Induced Weight Loss on the Cardiac Autonomic Nervous System in Severe Obesity

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Abstract

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Objective: To determine the impact of diet-induced weight loss on cardiac autonomic nervous system modulation and arrhythmias in subjects with severe obesity and the influence of a high-fat or a high-carbohydrate diet regimen on heart rate variability in reduced-obese individuals.

Research Methods and Procedures: Eight severely obese subjects (BMI $\geq$ 40.0 kg/m^2) underwent a 3-month weight loss program followed by a 3-month reduced-weight maintenance regimen. Thereafter, each subject was admitted for an inpatient period of 17 days on two separate occasions. A high-carbohydrate (60%) or high-fat (55%) diet of appropriate energy content for weight maintenance was prescribed during each inpatient phase. Heart rate variability was derived from a 24-hour Holter monitoring system in all subjects during their inpatient stay. Cardiac Holter monitoring was performed at three occasions (baseline, diet phase I, and diet phase II), including the second night of a two overnight calorimetry chamber stay.

Results: After the diet regimen, there was a 10% decrease in weight. There were no significant changes in systolic and diastolic blood pressure, arrhythmias, glucose, insulin, total cholesterol, low-density lipoprotein-cholesterol, high-density lipoprotein-cholesterol, respiratory exchange ratio, and resting energy expenditure between experiments. Mean heart rate was lower after weight loss compared with baseline ($p < 0.001$). After weight loss, there was an increase in the parasympathetic indices of heart rate variability showing an increase in cardiac vagal modulation (all $p < 0.05$).

Discussion: Weight loss is associated with significant improvement in autonomic cardiac modulation through enhancement of parasympathetic modulation, which clinically translates into a decrease in heart rate.

Introduction

Severe obesity is associated with increased total mortality with a concomitant increased risk of sudden death (1). In the Framingham study, the risk of sudden cardiac death with increasing weight was encountered in both genders (2), and the annual sudden cardiac mortality rate in obese men and women was estimated at ~40 times higher than the rate of unexplained cardiac arrest in a matched nonobese population (3). Specifically, in severely obese men, a 6- to 12-fold excess mortality rate was demonstrated (4). The autonomic nervous system is an important contributor to the regulation of both the cardiovascular system and energy expenditure, and it is assumed to play a role in the pathophysiology of obesity and related complications (1,5).

Obesity and the cardiac autonomic nervous system are intrinsically related. A 10% increase in body weight is associated with a decline in parasympathetic tone, accompanied by a rise in mean heart rate, and conversely, heart rate declines during weight reduction (6). There is a paucity of data regarding the metabolic and autonomic nervous system effects of weight loss in severely obese subjects by methods other than gastric surgery (7). This is of importance because increment in heart rate has been shown as a marker associated with increased mortality (8,9). Also, liquid protein diets are frequently associated with potentially life-threatening arrhythmias, a relationship documented by 24-hour Holter recording (10). Reductions in vagal activity with increment in weight may be one mechanism for the arrhythmias and other cardiac abnormalities that accompany

obesity. Moreover, because elevated plasma free fatty acid (FFA)[1] concentrations, which are often encountered in obesity, may play a role in arrhythmogenesis (11–13) and there may be an association between FFA concentration and premature ventricular complexes (PVCs) (14), it is of clinical importance to evaluate the impact of a high-fat (HIF) diet on autonomic cardiac modulation and arrythmogenicity in severe obesity after weight loss.

Because a diet rich in carbohydrates is associated with decreased FFAs (15), the purpose of this study was to evaluate the influence of an HIF and high-carbohydrate (HC) diet regimen on both cardiac autonomic nervous system modulation and the presence of arrhythmias in reduced-obese individuals.

Research Methods and Procedures

Study Population

Originally, 14 severely obese subjects were recruited from the community or from the Endocrinology Clinic at the University of Colorado Health Sciences Center to participate in the study. Complete metabolic and cardiovascular data were available for eight patients (six women and two men) and are reported herein. The Colorado Multiple Institutional Review Board approved the protocol, and the participant and investigator each signed the consent form. Inclusion criteria were 1) age between 18 and 50 years (women must be premenopausal) and 2) BMI ≥ 40.0 kg/m^2. Exclusion criteria were 1) presence of diabetes, uncontrolled hypertension, or documented cardiovascular disease or significant abnormal electrocardiogram at screening, 2) narcolepsy, sleep apnea requiring chronic positive airway pressure therapy, chronic respiratory disease, smoking, or arterial blood gas indicative of obesity hypoventilation syndrome (Pa$CO_2 \geq 45$ mm Hg while awake), 3) body weight > 182 kg, thus meeting the weight restrictions of 182 kg for the calorimetry chamber, and 4) medications that alter carbohydrate (CHO) metabolism or drugs known to influence the autonomic nervous system (i.e., sex steroid hormones, antidepressants, appetite suppressants).

Study Design

Subjects began a 3-month weight-loss program on Slim-Fast product as the sole source of nutrition (4 to 6 servings/d, 1000 to 1500 kcal/d). The caloric prescription was determined by the dietitian and calculated according to each subject's initial body weight. Subjects were seen on a weekly basis in the Adult General Clinic Research Center (GCRC) outpatient clinic for dietary compliance. Each subject was asked to keep a dietary record including any missed servings of Slim-Fast and/or any additional foods ingested. After the 3-month weight-loss period, each subject participated in a 3-month reduced-weight maintenance regimen using two to three Slim-Fast servings plus two mixed-food meals per day (~1500 to 2500 kcal/d, as determined by the dietitian). During the weight maintenance period, each subject was seen in the GCRC outpatient clinic a minimum of every 2 weeks.

After 3 months of weight loss and 3 months of reduced-weight maintenance, each subject was admitted to the GCRC as an inpatient for a period of 17 days on two separate occasions. The subject was prescribed an experimental diet, i.e., either an HC or HIF diet of appropriate energy (kilocalories) content for weight maintenance and weight stability during each inpatient phase. Compositions of the diets were as follows: 1) HC diet composition = ~60% carbohydrate, 25% fat, 15% protein; and 2) HIF diet composition = ~30% carbohydrate, 55% fat, 15% protein.

Between each diet phase (HC or HIF), there was a washout phase under free-living conditions (4 to 6 weeks washout phase dependent on scheduling of next diet phase). During that period, each subject was seen once each week in the GCRC outpatient clinic to monitor weight stability. Subjects were assigned to the two diets in a random-order sequence and crossed over to the other diet at the end of the washout period.

Resting energy expenditure (REE) was determined by indirect calorimetry using the open circuit technique with the subject in the supine position after a 10- to 12-hour overnight fast. The criterion for a valid metabolic rate was a minimum of 15 minutes of steady state, which was defined as $<10\%$ fluctuation in minute ventilation and oxygen consumption and $<5\%$ fluctuation in respiratory quotient. Metabolic rate was calculated using the Weir equation (16). BMI was calculated as weight (kilograms)/height (meters squared).

Biochemistry

Serum glucose was measured by a glucose hexokinase assay, and insulin (17), FFAs (18), glycerol (19), and lipid profile (20,21) were measured as described elsewhere. Low-density lipoprotein-cholesterol (LDL-C) was calculated with the Friedewald formula (22).

Heart Rate Variability

Twenty-four-hour cardiac Holter monitoring was performed on three occasions (baseline, diet phase I, and diet phase II), including the second night of the two overnight calorimetry chamber stays. Heart rate variability (HRV) was derived from a 24-hour Holter monitoring system (Del Mar Medical Systems, Irvine, CA) in all subjects during their inpatient stay in the GCRC. HRV derived from 24-hour

Table 1. Subject characteristics at baseline, on the HC diet, and on the HIF diet regimen

	Weight-reduced state		
	Baseline	**Carbohydrate**	**Fat**
Weight (kg)	126.4 ± 12.2	113.3 ± 11.0*	112.2 ± 10.2*
BMI (kg/m^2)	45.4 ± 6.8	40.8 ± 6.6*	40.5 ± 6.3*
SBP (mm Hg)	133 ± 14	126 ± 19	126 ± 14
DBP (mm Hg)	74 ± 7	73 ± 10	69 ± 12
Glucose (mM)	5.4 ± 0.5	5.3 ± 0.7	5.3 ± 0.4
Insulin (pM)	140 ± 50	123 ± 49	89 ± 28
Cholesterol (mM)	5.2 ± 1.4	4.8 ± 1.0	4.7 ± 1.2
LDL-C (mM)	3.3 ± 1.2	3.0 ± 0.7	3.1 ± 1.0
HDL-C (mM)	1.1 ± 0.2	1.1 ± 0.2	1.0 ± 0.2
Triglycerides (mM)	1.9 ± 0.6	1.4 ± 0.6*	1.5 ± 0.7†
FFAs (g/L)	0.25 ± 0.07	0.12 ± 0.06†	0.22 ± 0.10‡
Glycerol (mM)	0.10 ± 0.05	0.05 ± 0.02§	0.08 ± 0.05
RER	0.768 ± 0.044	0.786 ± 0.109	0.749 ± 0.095
REE (kcal/d)	2000 ± 359	1933 ± 241	1934 ± 339

* $p < 0.001$ vs. baseline; † $p < 0.01$ vs. baseline; ‡ $p < 0.05$ vs. CHO; § $p < 0.05$ vs. baseline.
Mean ± SD.
SBP, resting systolic blood pressure; DBP, resting diastolic blood pressure; RER, respiratory exchange ratio.

ambulatory monitoring is reproducible and free of placebo effect (23). Within the 24-hour evaluation, three periods were assessed: 1) 24 hours, 2) daytime period defined as 8:00 AM to 8:00 PM, and 3) night-time period defined as 12:00 AM to 6:00 AM. The separation into daytime and night-time was arbitrary. We have decided to divide the 24-hour Holter recordings into diurnal and nocturnal periods because 1) sudden death occurred often at night, 2) the study design enabled us to look at the metabolic rate and thermogenesis data during the 24-hour period, 3) diurnal and nocturnal measurement are well recognized in other fields such as hypertension (24-hour monitoring blood pressure assessment), and 4) it allowed for the possible evaluation of changes in circadian rhythms of HRV and thermogenesis. Using frequency domains, power in the very-low frequency (VLF; 0.0033–0.04 Hz), which may be an index of parasympathetic activity and neuroendocrine and thermogenesis stimulus (24–26), low frequency (LF; 0.04 to 0.15 Hz), which is an index of both sympathetic and parasympathetic activity, and high frequency (HF; 0.15 to 0.4 Hz), which is an index of solely parasympathetic activity, was calculated. LF/HF ratio is the power in LF divided by the power in HF. Using time domains, the SD of the RR intervals (SDNN), the square root of the mean squared differences of successive RR intervals (rMSSD), and the SD of the average RR intervals calculated over 5-minute periods (SDANN) were determined. pNN50 is the proportion of interval differences of successive NN intervals >50 ms. rMSSD and pNN50 are indices of parasympathetic modulation. NN intervals are the normal-to-normal intervals that include all intervals between adjacent QRS complexes resulting from sinus node depolarizations in the entire 24-hour electrocardiogram recording. The complete signal was carefully edited using visual checks and manual corrections of individual RR intervals and QRS complex classifications as previously described (27).

Statistical Analysis

The data are presented as mean ± SD unless otherwise specified. Comparison among the three groups of subjects for various parameters was carried out by one-way repeated-measures ANOVA and the post hoc Tukey test for multiple comparisons. When normality and/or equal variance testing conditions were not met, the Kruskal-Wallis rank test and/or the Dunn test for multiple comparisons were used, respectively. Pearson's linear correlation coefficients were calculated for pairs of continuous variables. Logarithmic transformation was used for variables not normally distributed. All p values were two-tailed, and $p < 0.05$ was considered statistically significant.

Results

Table 1 shows metabolic characteristics of subjects at baseline and on the HC and the HIF diet regimens. After the
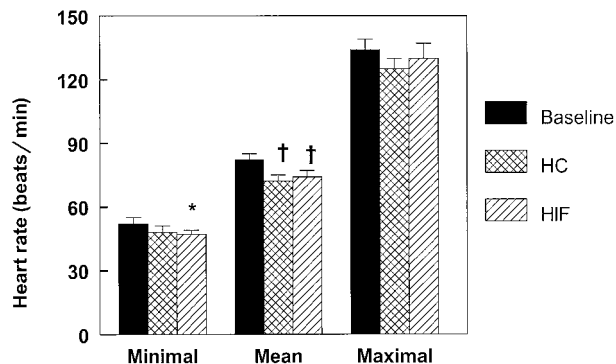
Figure 1: Holter measurements at baseline and on the HC and the HIF diet regimens. Mean ± SE: *$p < 0.05$ vs. baseline; †$p < 0.001$ vs. baseline.

Table 2. HRV indices in the frequency domains at baseline and on the HC and the HIF diet regimen

	Weight-reduced state		
	Baseline	Carbohydrate	Fat
24 hour			
VLF (ms^2)	6.7 ± 0.7	7.4 ± 0.6*	7.2 ± 0.7†
LF (ms^2)	6.0 ± 0.8	6.9 ± 1.0†	6.6 ± 0.9‡
Ratio LF/HF	3.3 ± 1.4	2.8 ± 0.9	3.0 ± 1.8
Daytime			
VLF (ms^2)	6.4 ± 0.7	7.4 ± 0.9†	7.0 ± 0.7‡
LF (ms^2)	5.7 ± 1.0	6.9 ± 1.2†	6.5 ± 1.0‡
Ratio LF/HF	4.4 ± 1.3	3.4 ± 0.9	3.1 ± 1.2‡
Night-time			
VLF (ms^2)	7.0 ± 0.7	7.4 ± 0.5	7.4 ± 1.0‡
LF (ms^2)	6.3 ± 0.8	6.8 ± 0.8	6.6 ± 1.1
Ratio LF/HF	2.3 ± 1.7	2.1 ± 1.7	3.0 ± 2.7

* $p < 0.001$ vs. baseline; † $p < 0.01$ vs. baseline; ‡ $p < 0.05$ vs. baseline.
Mean ± SD.
Frequency domain indices are log-transformed.

hypocaloric diet phase, there was a 10% decrease in weight compared with baseline. Whereas subjects presented a significantly lower weight and BMI in the HC and the HIF diet phases compared with baseline ($p < 0.001$), there were no changes in systolic and diastolic blood pressure, glucose, insulin, total cholesterol, LDL-C, high-density lipoprotein-cholesterol, respiratory exchange ratio, and REE between experiments. Triglyceride levels were lower during the HC ($p < 0.001$) and the HIF diet phases ($p = 0.003$) compared with baseline, whereas glycerol levels were lower during only the HC diet compared with baseline ($p = 0.035$). FFA levels were lower at baseline than during the HC diet ($p = 0.004$) and lower during the HC diet than during the HIF diet ($p = 0.019$).

Figure 1 summarizes the results from the Holter-derived measurements at baseline and during the two diet (HC and HIF) experiments. Mean heart rate derived from 24-hour Holter monitoring was lower after weight loss in both diets (HC and HIF) compared with baseline ($p < 0.001$). Although minimal heart rate was lower during the HIF diet compared with baseline ($p = 0.023$), there were no changes in maximal heart rate. Median number of PVCs during 24 hours were also not different among experiments: baseline 207 (range, 0 to 995), HC 196 (range, 0 to 1064), and HIF 101 (range, 0 to 473).

Frequency Domains

Indices of HRV using frequency domains are depicted in Table 2 and Figure 2. During the whole 24-hour recording, there was an increase in the HF power during the HC diet ($p = 0.004$) and the HIF diet ($p = 0.028$) compared with baseline (Figure 2), suggesting an increased cardiac vagal modulation after weight loss. LF power was also increased after weight loss during the HC diet ($p = 0.002$) and the HIF diet ($p = 0.023$) compared with baseline (Table 2). Consequently, there were no significant differences in the LF/HF ratio between experiments. VLF power was also increased

after weight loss in the HC diet ($p < 0.001$) and the HIF diet ($p = 0.009$) compared with baseline (Table 2).

During daytime, HF power increased after weight loss in both diet experiments compared with baseline ($p < 0.01$; Figure 2). VLF and LF power increments were less in the HIF diet ($p < 0.05$) vs. the HC diet ($p = 0.002$) compared with baseline (Table 2). In contrast to the 24-hour data, the LF/HF ratio was lower in the HIF diet compared with baseline ($p < 0.05$).
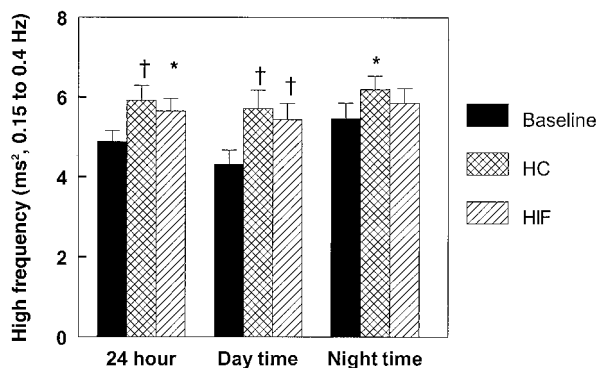

Figure 2: High-frequency power (ms^2) at baseline and on the HC and the HIF diet regimens. Mean ± SE: *$p < 0.05$ vs. baseline; †$p < 0.01$ vs. baseline.

Table 3. HRV indices in the time domains at baseline and on the HC and the HIF diet regimen

	Weight-reduced state		
	Baseline	Carbohydrate	Fat
24 hour			
Mean NN			
(ms)	735 ± 69	848 ± 108*	829 ± 111†
SDNN (ms)	116 ± 32	152 ± 31*	145 ± 36†
SDANN (ms)	100 ± 32	124 ± 31‡	120 ± 36‡
Daytime			
Mean NN			
(ms)	685 ± 64	798 ± 113†	764 ± 100‡
SDNN (ms)	89 ± 20	123 ± 38†	113 ± 32
SDANN (ms)	73 ± 20	88 ± 24	86 ± 25
Night-time			
Mean NN			
(ms)	814 ± 109	975 ± 128*	955 ± 166*
SDNN (ms)	97 ± 33	118 ± 32	102 ± 33
SDANN (ms)	67 ± 29	76 ± 28	56 ± 11

* $p < 0.001$ vs. baseline; † $p < 0.01$ vs. baseline; ‡ $p < 0.05$ vs. baseline.
Mean ± SD.

Figure 3: Parasympathetic indices in the time domains at baseline and on the HC and the HIF diet regimens. Mean ± SE: *$p < 0.05$ vs. baseline; †$p < 0.01$ vs. baseline.

During the night, HF power increased in only the HC diet compared with baseline ($p = 0.022$; Figure 2), whereas VLF power was significantly different in only the HIF diet ($p < 0.05$) compared with baseline (Table 2). There was no change in LF and in the LF/HF ratio between experiments.

Time Domains

In the time domains during 24 hours, SDNN and SDANN were significantly increased in both diets compared with baseline (Table 3). rMSSD and pNN50 were significantly increased in only the HC diet ($p = 0.004$) compared with baseline (Figure 3). In accordance with heart rate, mean NN was significantly longer in the HC diet ($p < 0.001$) and the HIF diet ($p = 0.002$) compared with baseline.

During the daytime, whereas there were no changes in the HIF diet compared with baseline, SDNN ($p = 0.009$), rMSSD ($p = 0.006$), and pNN50 ($p = 0.01$) indices were higher in the HC diet compared with baseline (Table 2; Figure 3). Again, NN was longer in both diets compared with baseline ($p < 0.05$).

During the night-time, there were no changes in SDNN and SDANN (Table 3). Indices of parasympathetic modulation, rMSSD ($p = 0.003$) and pNN50 ($p = 0.002$), increased in the HC diet compared with baseline (Figure 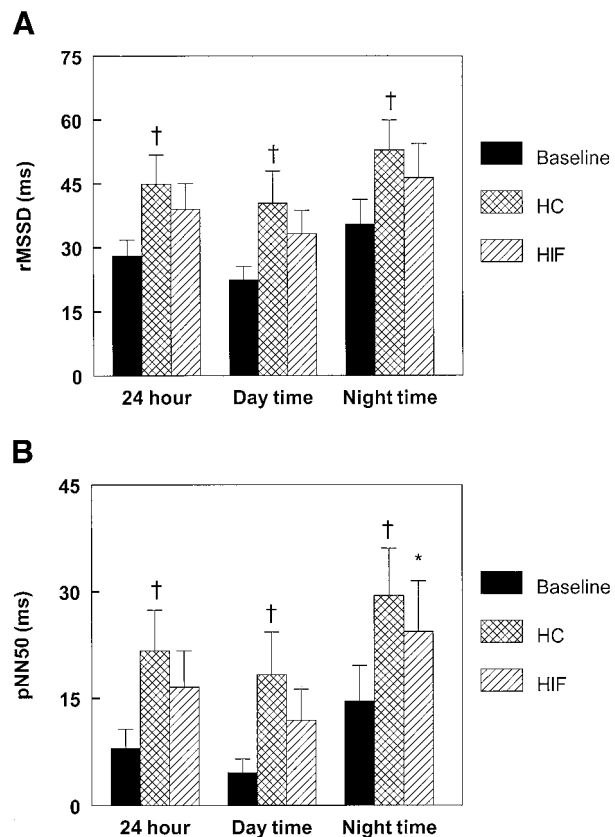3). pNN50 was also higher during the HIF diet compared with baseline ($p < 0.05$). Again, NN was longer in both diets compared with baseline ($p < 0.001$; Table 3).

To determine the impact of cardiac autonomic nervous system modulation on energy balance, several correlations were evaluated. There was a positive association between cardiac sympathovagal balance (LH/HF ratio) and total calories ($r = 0.448$, $p < 0.03$) and cardiac sympathovagal balance and CHO oxidation during the day ($r = 0.440$, $p < 0.04$). Not surprisingly, indices of parasympathetic activity were inversely correlated with energy expenditure during the day (HF: $r = -0.497$, $p < 0.015$; and rMSSD: $r = -0.470$, $p < 0.025$). Energy balance was also negatively associated with cardiac sympathovagal balance during the day ($r = -0.468$, $p < 0.025$), but it was positively related to indices of parasympathetic activity (HF: $r = 0.56$, $p < 0.005$; and rMSSD: $r = 0.480$, $p < 0.02$). Interestingly, there was a trend toward a relation between VLF (an index of thermogenesis) and protein oxidation during the night ($r = 0.383$, $p = 0.065$) with an inverse relation with fasting insulin levels ($r = -0.382$, $p = 0.066$). RMR REE was positively associated with night VLF ($r = 0.445$, $p < 0.03$) and night cardiac sympathovagal balance ($r = 0.508$, $p <$

0.015). Finally, LDL-C levels were inversely associated with heart sympathovagal balance ($r = -0.646$, $p < 0.0001$).

Looking at specific diets, there was a high association between cardiac sympathovagal balance on HIF diet and fat oxidation ($r = 0.903$, $p < 0.0003$), whereas there was no association between cardiac sympathovagal balance on HC or baseline diet and fat or CHO oxidation during the night.

Discussion

Fluctuation of heart rate around mean heart rate, which is called HRV, provides valuable information on the activity of the cardiac autonomic nervous system. The major findings of this study demonstrated that a 10% weight loss in severely obese patients is associated with significant improvement in autonomic nervous system cardiac modulation. This translates into decreased heart rate and an increased HRV, mainly through an increment in the cardiac parasympathetic modulation (HF, rMSSD, pNN50). This is of importance because higher heart rate is associated with increased mortality (8,9), and decreased HRV is associated with increased cardiac mortality independent of ejection fraction (28). In contrast to short-term diet protocols comparable to ours (29,30) in weight-stable individuals, we did not find any statistically significant differences in heart rate between diets; however, we found statistically significant increments in NN intervals, which supports the notion that heart rate decreased after weight loss. There were relations between HRV indices and energy expenditure, energy balance, and protein oxidation, emphasizing the link between heart function and energy balance through common autonomic nervous system mechanisms (31).

Analysis of daily fluctuations in HRV showed that significant improvement after weight loss occurred mainly during the daytime period. In accordance with this finding, obese subjects showed ameliorations in cardiac autonomic abnormalities after a weight-reducing gastroplasty procedure (with a mean weight loss of 32 kg). Indeed, vagal activity was significantly improved after 1 year of follow-up (7). As reported recently in a group of moderately obese Japanese subjects following a very-low-calorie diet, we found an increase in RR interval (mean NN), SDNN, SDANN indices, and LF and HF components after weight loss (32). Consistent with a previous report (32), our data depicted a reciprocal pattern of greater sympathetic activity in the daytime and greater parasympathetic activity at night, which was diminished during the HIF diet phase. The increment in parasympathetic modulation during night-time during the HC diet compared with the HIF diet may potentially be protective from cardiac arrhythmias. The fact that the HC diet was associated with the best cardiovascular autonomic modulation may be an important observation that did not reach significant levels because of the small number of subjects.

We found an inverse correlation between LDL-C levels and cardiac autonomic nervous system modulation. This is in accordance with a study reporting an inverse relationship between plasma levels of LDL-C and cardiac parasympathetic activity in young normocholesterolemic subjects free of clinical heart disease (33). In contrast to Kupari et al. (33), we found an inverse correlation between insulin levels and indices of parasympathetic activity. The subjects in the study of Kupari et al. were lean, with a BMI of 24 kg/m^2, and had a low probability of being insulin resistant. Although statistical associations do not necessarily indicate a chain of biological causation, it is interesting to emphasize that insulin increases sympathetic activity (34), but sympathetic overactivity may not necessarily be a consequence of hyperinsulinemia (34). This may reflect common intricate mechanisms. Indeed, higher LDL-C may reduce arterial distensibility and impact the baroreceptor modulation, influencing the reflex control of HRV (35,36).

Even if FFAs are the main metabolic fuel for the heart at rest (37), it has been suggested that elevated plasma FFA concentrations may play a role in arrhythmogenesis (11–13). The findings of this study do not support a deleterious impact of a HIF diet preceded by weight loss on autonomic cardiac modulation and the occurrence of arrhythmias. In contrast to previous data, there was no correlation in our study between FFA concentrations and the number of PVCs (14). It is important to emphasize that the present cohort included obese patients without other cardiovascular comorbidities, which have been demonstrated to impact heart response in the presence of FFAs (11,12). Interestingly, there was a high association between cardiac sympathovagal balance on HIF diet and total body fat oxidation, whereas the HC diet did not impact cardiac sympathovagal balance in terms of association with substrate oxidation. Short-term dietary modification, independently of changes in body weight, can impact the cardiac autonomic nervous system. A 2-week lower-fat diet (~25% of fat), in comparison with a higher-fat diet (~40% of fat), increased vagal modulation in normal weight women (38). Dietary fat intake alters cardiovascular reactivity without changes in basal noradrenaline metabolism (30) by altering cardiac function and contractility (39). Indeed, this study supports the notion that cardiac sympathovagal balance may be modulated by specific diet. However, it is important to differentiate the acute effect of a meal (40) from the chronic impact of a specific dietary regimen on cardiac autonomic nervous modulation (38). Although physiological interpretation of VLF components of HRV is still controversial, our findings support the notion that the VLF component may mirror neuroendocrine and thermoregulatory influences to the heart (24–26,41). Indeed, there was a significant association between REE and night-time VLF, which, in contrast to daytime, reflects mostly energy activity during rest.

There may be gender differences in terms of HRV responses. Unfortunately, the small number of subjects did not allow us to separate the HRV responses between men and women. Nevertheless, HF power increased significantly in women ($p < 0.002$) and tended to increase in men ($p = 0.167$), emphasizing similar responses between genders. Another issue is the influence of the menstrual cycle on HRV. Unfortunately, no information is available concerning the menstrual cycle of the women in our study. Although sympathovagal balance may be a controversial issue (42), the LF/HF ratio has been shown to be useful in the population studied herein. It has been emphasized that respiration is an important determinant of HF spectral power (42). However, it is important to note that the HF component of HRV is reproducible mainly with controlled breathing frequency in contrast to the natural breathing used in our study design (43). Although the LF/HF ratio may be a matter of dispute according to some authors (42), the conclusions drawn from the concept of sympathovagal balance are attractive and reinforced by the measurements in the time domains. Accepting that a raised LF/HF ratio is related to a higher relative sympathetic activity, and thus a higher susceptibility toward life-threatening cardiac arrhythmias, and that higher relative vagal activity exerts a cardioprotective effect, our findings (24-hour, daytime, and night-time data) are physiologically sound. Finally, even if the interpretation of VLF is still unclear in the literature, as was emphasized and referenced in Research Methods and Procedures, our study design may shed some light and may provide more evidence on the implication of thermogenesis in future interpretation of VLF.

In conclusion, these data indicate that functional impairment of the cardiac autonomic nervous system in obese subjects is improved after weight reduction and that neither a short-term HC nor short-term HIF diet further influences HRV significantly in the new weight-reduced state. However, the enhanced parasympathetic modulation during the HC diet regimen observed during the nocturnal period may indicate a beneficial impact of this particular diet compared with the HIF diet.

Acknowledgments

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