J. Endocrinol. Invest. *25:* 138-142, 2002

Changes of autonomic cardiac profile after a 3-week integrated body weight reduction program in severely obese patients

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ABSTRACT. The autonomic control of the heart is abnormal in obese subjects due to a prevalence of sympathetic over parasympathetic limb of the autonomic balance. We evaluated the effects of a short-term (3 weeks) integrated body weight reduction program (consisting of energy restricted diet and high-intensity exercise training) on heart rate variability (HRV) in severely obese, normotensive patients. The HRV was evaluated both in the time and frequency domain over a 18-hour Holter recording period obtained before and at the end of the third week. Three-week body weight reduction program reduced BMI (from 41.4±4.6 to 39.5±4.3 kg/m^2, -4.6%, *p*<0.0001) and heart rate (from 77.8±8.6 to 73.6±8.7 b/min, *p*=0.0003). Significant changes in the autonomic profile were observed both in the time and frequency domain (SD of RR interval, SDRR: +16.1%; mean squared successive difference: (MSSD) +16.7%; percentage of RR intervals differing more than 50 msec from the preceding one, pNN50: +31.8%; low frequency oscillation, LF: +17.1%; high frequency oscillation, HF: ±18.2%). In conclusion, this study demonstrates that a short-term, integrated body weight reduction program is able to favorably modify the autonomic profile in a population of normotensive, severely obese subjects. The reduction of heart rate and the increase in parasympathetic activity may consistently contribute to a reduction of the risk of cardiovascular morbidity and of sudden cardiac death, still high in this patients' group.

(J. Endocrinol. Invest. *26:* 138-142, 2003)

INTRODUCTION

Several reports have recently demonstrated that the autonomic control of the heart is imbalanced in obese subjects. Heart rate variability (HRV) has been reported to be reduced in obese patients (1-4), suggesting that the sympathetic limb of the autonomic balance is prevalent over the parasympathetic one. This hypothesis has been confirmed by the fact that either plasma norepinephrine concentrations and the spillover rate of norepinephrine from sympathetic nerve terminals are increased in obese subjects compared to lean controls (5) and that the sympathetic nerve traffic is twice as large in normotensive obese compared to lean subjects (5). Weight reduction has been proven to be effective in reducing sympathetic hyperactivity (6) and in restoring both the reflex (6) and tonic (1) autonomic control of the heart, this effect being usually observed after a relevant weight reduction (>10%), obtained either with surgical bowel resection (1) or long-lasting hypocaloric diet programs (6).

Among factors known to positively affect the autonomic balance, physical training proved to be effective in modulating the autonomic tone or reflexes – examined with heart rate variability – in patients with previous myocardial infarction (7), in healthy normotensive subjects (8) and even in conditions of severely compromised autonomic profile (*i.e.* patients with congestive heart failure) (9).

Key words: Obesity, autonomic nervous system, physical training, weight reduction, cardiovascular risk.

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Accepted: September 17, 2002.

To date, few controlled studies have been performed in severely obese patients, the only data available being those obtained after energy restricted diets.

The aim of this study was to evaluate the effects of a short-term (3 weeks) integrated body weight reduction program (consisting of energy restricted diet, psychological counseling, nutritional education, associated with an individualized, low-volume and high-intensity exercise training) on the autonomic balance evaluated by heart rate variability in obese normotensive subjects, irrespective on the achievement of a large weight reduction that usually requires a longer period of time to take place.

SUBJECTS AND METHODS

Subjects

Forty obese patients (10 male/30 female, mean BMI: 41.4±4.6 kg/m^2, mean age: 30±7 yr) participated in the study, after giving their written informed consent. The study protocol was approved by the Ethical Committee of our Institute. All obese subjects were in-patients at the 3rd Division of Metabolic Diseases (Istituto Auxologico Italiano, Piancavallo, Italy), where they had been admitted for an integrated body weight reduction program; none was involved in systematic physical activity before admission.

Heart disease was excluded in all patients by careful clinical evaluation and by diagnostic procedures (ECG, X-ray, Holter recording, exercise stress testing). All subjects were normotensive at repeated BP measurements and were not taking any medication at the time of the study. Patients with liver, lung, kidney failure and overt diabetes mellitus were excluded from the study. Two patients with diabetes mellitus (previously diagnosed on the basis of a venous plasma glucose concentration after 2 h oral glucose tolerance test higher than 11.1 mmol/l) were admitted to the study due to their present fasting normoglycemia under oral agent treatment.

Body weight reduction program

Patients underwent a 3-week integrated body weight reduction program, consisting of energy restricted diet (1200-1800 kcal/day), individualized low volume and high intensity exercise, psychological counseling and nutritional education.

Diet

The amount of energy to be given with diet was calculated by subtracting approximately 500 kcal from the measurement of basal energy expenditure.

The diet, in terms of macronutrients, contained 21% proteins, 53% carbohydrates and 26% lipids; the daily estimated water content was 1000 ml, and the estimated salt content was 1560 mg Na, 3600 mg K and 900 mg Ca. Extra water intake of at least 2000 ml/day was encouraged. The subject's compliance to diet was daily evaluated by a dietician.

Exercise training

The aerobic training protocol was designed in agreement with the guidelines dictated by the American College of Sport Medicine (10). The physical activity program consisted of 5 days per week training, including aerobic exercise on cycloergometer, treadmill and armoergometer for 35 min/day at 50% of VO_2 max during the first week and at 60% of VO_2 max in the following two weeks.

Psychological counseling and nutritional education

The subjects underwent a psychological counseling program consisting of two or three sessions per week of individual and/or group psychotherapy, performed by clinical psychologists. Nutritional education consisted of lectures, demonstrations and group discussions (with or without a supervisor) and took place daily.

Measurements

Holter monitoring, ECG, exercise stress testing with the evaluation of maximal oxygen uptake (VO_2 max) and body composition were evaluated before and at the end of the integrated body weight reduction program (3rd week).

Heart rate variability

During Holter recording (18 h, from 15:00-16:00 h to 09:00-10:00 h), patients were left free to move inside and outside the hospital area. The recordings were digitized by a Marquette 8000 scanner and submitted to the standard Marquette algorithms for QRS labeling and editing. Premature atrial and ventricular complexes were automatically discarded. After the editing was performed and reviewed by a cardiologist, the HRV was evaluated over the entire recording interval. The HRV was evaluated both in the time and frequency domain over the entire recording period. The time domain variables considered in this study were: 1) the mean RR interval and its standard deviation (SDRR), 2) the mean squared successive difference (rMSSD) and 3) the percentage of RR intervals differing more than 50 msec from the preceding one (pNN50). The frequency domain analysis was performed with a FFT algorithm. The boundaries of the very low-frequency (VLF) oscillation (0-0.03 Hz), LF oscillation (0.03-0.15 Hz) and those of the HF oscillation (0.15 to 0.40 Hz) were chosen by the investigator: their value was expressed as amplitude (ms) and as normalized units (individual power/total power * 100). The ratio between LF and HF oscillations (LF/HF) was also evaluated. The LF oscillation reflects the modulation of sympathetic or parasympathetic activity by baroreflex mechanisms; HF oscillation, reflects the modulation of vagal activity, primarily by breathing; their ratio LF/HF is a useful tool to investigate the sympathovagal balance in pathophysiologic conditions.

Body composition

Body composition was measured using a tetrapolar impedance plethysmograph (Human-IM Scan, DS-Medica, Milano, Italy), according to standardized procedures (11).

Statistical analysis

Data are presented as mean ±SD. Comparison between observations before and after the physical training were made by *t* test for coupled data. Probability values of less than 0.05 were considered statistically significant.

RESULTS

Three-week body weight reduction program reduced bw (from 112.9±17.8 kg to 107.8±16.5 kg,

Table 1 - *Effects of a 3-week integrated body weight reduction program on heart rate and time domain HRV in the study group (no. 40).*

	Before	After	*p*
Heart rate (b/min)	77.8±8.6	73.6±8.7	0.0003
% bradycardia (<60 b/min)	12.5±14.4	20.8±16.7	0.0002
RR interval (msec)	777±87	822±100	0.0003
SDRR (msec)	149±45	173±48	0.0001
rMSSD (msec)	42±17	49±18	0.0016
pNN50 (%)	17.0±11.9	22.4±12.4	0.002

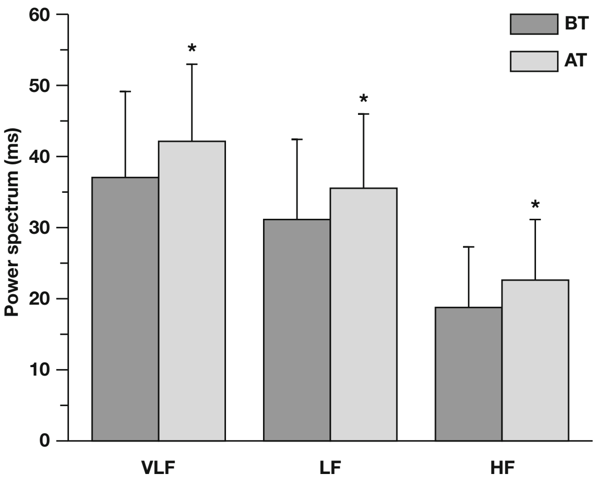

Fig. 1 - *Figure 1 - Effects of the 3-week integrated body weight reduction program on VLF: very low frequency; LF: low frequency and HF: high frequency power.*
BT = before 3-week body weight reduction program;
AT = after 3-week body weight reduction program;
**=p<0.0001, **=p<0.002, ***=p<0.005.*

p<0.0001), BMI (from 41.4±4.6 to 39.5±4.3 kg/m^2, -4.6%, *p*<0.0001) and percent fat mass (from 49.1±6.9% to 47.3±6.5%, *p*<0.0001). No significant change was observed in percent FFM (from 50.9±6.9 to 51.9±7.2%, *p*=0.23).

Resting systolic and diastolic BP significantly reduced (from 124.5±9.0 to 117.5±8.3 mmHg; from 77.3±5.4 to 74.5±5.9 mmHg, respectively, *p*<0.005). Maximal oxygen consumption (VO_2 max) during exercise stress testing increased from a mean baseline value of 22.8±5.8 up to 26.7±7.6 ml/kg/min at the end of the program (*p*<0.0001).

Three week body weight reduction program reduced mean heart rate from 77.8±8.6 to 73.6±8.7 b/min (*p*=0.0003). All the heart rate variability parameters in the time domain significantly increased after training, as reported in Table 1. The power of VLF, LF and HF components increased after training by 14.3% (*p*<0.0001), 17.1% (*p*<0.002) and by 18.2% (*p*<0.005), respectively (Fig. 1), while no changes were observed when evaluating their normalized units (Table 2). The LF/HF ratio was not modified after the 3 weeks of program (Table 2).

No relationship was found between the degree of BMI reduction and the change of HRV parameters (Fig. 2). The autonomic response to the bw reduction program was not different between males (no. 10) and females (no. 30).

No clinically relevant arrhythmias were observed. Atrial ectopic beats (>1/h) were observed in 7/40 subjects, without differences before and after the body weight reduction program; ventricular ectopic beats (>1/h) were documented in 3/40 subjects.

DISCUSSION

This study demonstrates that an intensive, short-lasting combined program of physical activity and energy restricted diet is able to favorably modify

Table 2 - *Effects of training on frequency-domain heart rate variability parameters evaluated in normalized units (nu).*

	Before	After	*p*
VLF (nu)	42.3±7.7	41±8.7	0.1
LF (nu)	36.3±5.2	36.7±6.1	0.42
HF (nu)	21.4±4.6	22.3±4.8	0.07
LF/HF	1.77±0.48	1.73±0.49	0.33

HF: high frequency; LF: low frequency; VLF: very low frequency

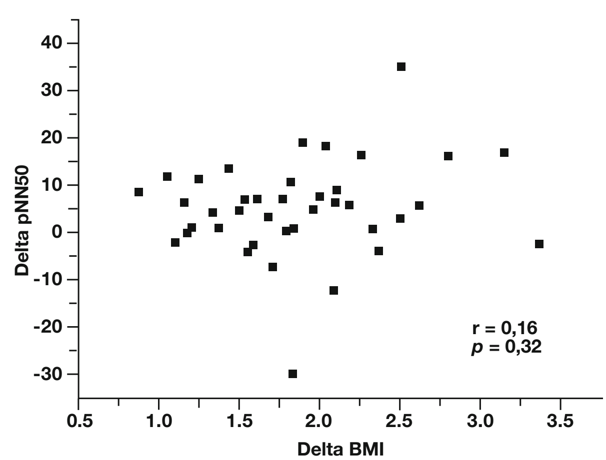

Fig. 2 - *Relationship between the degree of body mass index (BMI) reduction (kg/m^2) and the absolute change of pNN50. A similar pattern is observed for the other time-domain heart rate variability parameters.*

the autonomic profile in a population of normotensive, severely obese subjects. This effect is obtained in spite of a small, albeit significant, weight reduction.

Obesity *per se* is a condition associated with a decreased parasympathetic activity (12, 13) inherent in weight gain (14), as demonstrated in overfed normal subjects (15) and animals (16, 17) and independent from the presence of blood pressure elevation, heart disease or cigarette smoking (5). Changes in the balance between parasympathetic and sympathetic activity due to either physical conditioning or weight loss have been commonly observed by several authors in normal subjects (18, 19), obese patients (19, 20) as well as animals (21). In the present investigation, in which both exercise training was regularly performed and weight loss occurred, such a change determined a significant decrease in resting heart rate and arterial blood pressure, possibly also contributing to the improvement observed in maximum aerobic performance. Thus, patients with severe obesity appear to be very susceptible to the combined effect of exercise and weight loss. Although controlled studies concerning the combined effect of weight loss and physical conditioning on autonomic activity in obesity are scanty, the approach to the autonomic dysfunction provided by the program presently studied seems promising and probably deserves further investigation to ascertain the relative independent effect of physical exercise and of weight loss (and therefore, dietary restriction).

Previous studies evaluated changes in the autonomic balance after moderate to large weight loss obtained either with long-standing low-caloric diets, as observed by Grassi *et al*. (6) (12.6% decrease of body weight) or with surgical intervention, as observed by Karason *et al*. (1) (26.2% decrease of body weight). In our population, body mass reduction was less than 5% of the initial weight. In spite of this small reduction in BMI, subjects under study showed significant changes in the autonomic profile examined in the time domain to the combined intensive protocol of exercise and weight reduction (SDRR +16.1%, rMSSD +16.7%, pNN50 +31.8%, LF +17.1%, HF +18.2%).

A modification of the autonomic balance obtained in a very short time and besides a small BMI reduction may be due to several factors: 1) a reduction in nutrient intake may *per se* reduce sympathetic activity and increase vagal tone even when body weight remains abnormal (22); 2) the positive effect on HRV was obtained by two intervention able to modify the autonomic profile in the same direction, that is, reduced caloric intake and physical training. On one side, the reduction of body weight may decrease hyperinsulinemia, thus reversing sympathetic dominance and parasympathetic withdrawal related to the abnormal excursion in plasma insulin observed in the obese (3). On the other side, physical training may reduce sympathetic responsiveness by a decrease in β-adrenoceptors and a decrease in the adenylate cyclase activity (23-25).

A potentially puzzling finding was that frequency-domain variables were not influenced by our integrated protocol. In fact, our program was rather short and intensive (3 weeks), and therefore different from that used by Amano et al. (2), who showed a change in resting power spectral density of RR intervals variability after 12 weeks of activity in overweight subjects (mean BMI 27.3±0.4 kg/m^2) (2). A similar difference could be noticed in patients with ischemic heart disease: the frequency domain variables were influenced by long periods of rehabilitation (7) but not with a shorter period of training (26), while the total variance was more easily modulated (7, 26). It must be emphasized that the short exercise protocol scheduled for our population was able to significantly modify some cardiovascular parameters (*i.e.* increase of maximal oxygen consumption, reduction of blood pressure, both systolic and diastolic). Moreover, this approach proved effective in determining a significant reduction of some metabolic factors in obese subjects, such as blood glucose and serum cholesterol (27). Thus, one may conclude that a potentially favorable effect on the autonomic balance begins to appear after a short period of combined diet and exercise, as indicated by the changes in time domain variables. The changes in spectral variables could reflect a more profound modulation of the autonomic nervous system, and may require a longer time to appear.

In conclusion, our study demonstrates that a short-term, integrated body weight reduction program is able to favorably modify the autonomic profile in a population of normotensive, severely obese subjects. The reduction of heart rate and the increase in parasympathetic activity may consistently contribute to reduce the risk of cardiovascular morbidity and of sudden cardiac death, still high in this patients' group. Moreover, such an improvement in the autonomic profile in response to a body mass reduction obtained with a program including also exercise training is a favorable adaptation, because it contributes to reduce myocardial oxygen demands both at rest and during submaximal exercise, as well as during other forms of everyday life stress entailing physical activity.

ACKNOWLEDGMENTS

This work was partially supported by Progetti di Ricerca Corrente, Istituto Auxologico Italiano, IRCCS, Milan and Piancavallo. The Authors thank dr. A. Tibaldi and M. Resnik for the clinical monitoring of the training sessions, Mrs. F. Pera and the nursing staff at the 3rd Division of Metabolic Diseases for their appreciated professional contribution, Mr. S. Ottolini and Mr. M. Proietti for their experienced technical assistance in the physical protocol and testing and Dr. M. Massarini (Centro Studi e Ricerche Technogym, Gambettola, Italy) and Dr. P. Morini (DS-Medica, Milan, Italy) for having made available the exercise machines and the impedance plethysmograph.

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