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Effects of diet and exercise training on neurovascular control during mental stress in obese women

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Abstract

Since neurovascular control is altered in obese subjects, we hypothesized that weight loss by diet (D) or diet plus exercise training (D + ET) would improve neurovascular control during mental stress in obese women. In a study with a dietary reduction of 600 kcal/day with or without exercise training for 4 months, 53 obese women were subdivided in D (N = 22, 33 ± 1 years, BMI 34 ± 1 kg/m^2), D + ET (N = 22, 33 ± 1 years, BMI 33 ± 1 kg/m^2), and nonadherent (NA, N = 9, 35 ± 2 years, BMI 33 ± 1 kg/m^2) groups. Muscle sympathetic nerve activity (MSNA) was measured by microneurography and forearm blood flow by venous occlusion plethysmography. Mental stress was elicited by a 3-min Stroop color word test. Weight loss was similar between D and D + ET groups (87 ± 2 *vs* 79 ± 2 and 85 ± 2 *vs* 76 ± 2 kg, respectively, P < 0.05) with a significant reduction in MSNA during mental stress (58 ± 2 *vs* 50 ± 2, P = 0.0001, and 59 ± 3 *vs* 50 ± 2 bursts/100 beats, P = 0.0001, respectively), although the magnitude of the response was unchanged. Forearm vascular conductance during mental stress was significantly increased only in D + ET (2.74 ± 0.22 *vs* 3.52 ± 0.19 units, P = 0.02). Weight loss reduces MSNA during mental stress in obese women. The increase in forearm vascular conductance after weight loss provides convincing evidence for D + ET interventions as a nonpharmacologic therapy of human obesity.

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• Vasodilation
• Sympathetic nervous system
• Weight loss

Introduction

Neurovascular alteration in human obesity has been recently described (1). Muscle sympathetic nerve activity (MSNA) and forearm vascular resistance are increased, whereas forearm vascular conductance is significantly reduced in obese subjects (1). This scenario suggests an increased risk for cardiovascular disorders in obese persons (2,3).

The defense reaction, which can be elicited by mental stress in humans, provokes sympathoexcitation and muscle vasodilatation (4,5). Regarding obese subjects, for whom abnormal neurovascular control during sympathoexcitation has been reported (6), two obvious and clinically relevant ques-

tions emerge: 1) is it possible to improve the neurovascular control during mental stress in obese subjects? 2) If so, which is the best strategy to reverse this neurovascular abnormality? In a recent study, a hypocaloric diet plus exercise training, in contrast to a hypocaloric diet alone, significantly improved the vasodilatory responses during mental stress in obese children (7). However, that study provided no information regarding sympathetic activation in obese children.

In the present study, we report the impact of body weight reduction by a hypocaloric diet and hypocaloric diet associated with exercise training on MSNA and forearm blood flow during mental stress in obese women.

Our hypothesis was that weight loss would reduce MSNA and would increase forearm blood flow during mental stress in obese women. In addition, this improvement in neurovascular control would be increased if the hypocaloric diet were associated with exercise training.

Subjects and Methods

Study population

Fifty-three consecutive out-patient sedentary obese women from the Women Obesity Ambulatory of the Endocrinology Department, University of São Paulo Medical School, were invited to participate in the study. They were randomly divided into a group receiving a hypocaloric diet (N = 26) and a group receiving a hypocaloric diet associated with exercise training (N = 27) for 4 months. Nine obese women did not want to take part in the study, although they agreed to be studied before and after 4 months. Thus, our final sample consisted of three subgroups: 1) hypocaloric diet (N = 22, age 33 ± 1 years), 2) hypocaloric diet associated with exercise training (N = 22, age 34 ± 1 years), and 3) nonadherent to any of the two interventions (N = 9, age 35 ± 2 years). None of the individuals were taking medication or contraceptives and all were non-smokers, with no evidence of metabolic or cardiovascular disease at the time of the study. The hypocaloric diet, diet plus exercise training, and nonadherent groups were similar regarding total cholesterol (170 ± 7, 169 ± 6, and 166 ± 11 mg/dL, respectively, P = 0.94), HDL-cholesterol (39 ± 2, 39 ± 2, and 42 ± 4 mg/dL, respectively, P = 0.74), LDL-cholesterol (105 ± 6, 108 ± 6, and 105 ± 10 mg/dL, respectively, P = 0.91), triglycerides (129 ± 18, 116 ± 13, and 107 ± 6 mg/dL, respectively, P = 0.69), glucose (80 ± 2, 86 ± 3, and 85 ± 4 mg/dL, P = 0.11, respectively), and insulin levels (15.4 ± 2, 13.3 ± 1.4, and 12.5 ± 2.2 µIU/mL, P = 0.60, respectively). All subjects were in the pre-hypertensive stage according to the Seventh Report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (8). Since hormonal variability during the regular menstrual cycle may affect blood flow and vascular resistance (9), all women were studied between the first and the fifth day after the onset of menstruation. The study protocol was approved by the Human Subject Protection Committees of the Heart Institute (InCor) and University Hospital, University of São Paulo Medical School, and written informed consent was given by each subject that participated in the study.

Muscle sympathetic nerve activity. MSNA was recorded directly from the peroneal nerve using the technique of microneurography (10). Multiunit postganglionic muscle sympathetic nerve recordings were obtained using a tungsten microelectrode (tip diameter 5 to 15 µm). The signals were amplified by a factor of 50,000 to 100,000 and bandpass filtered (700 to 2000 Hz). For recordings and analysis, nerve activity was rectified and integrated (time constant, 0.1 s) to obtain a mean voltage display of sympathetic nerve activity that was recorded on paper. All MSNA recordings met previously

established and described criteria. Muscle sympathetic bursts were identified by visual inspection by a single investigator (C.E.N.), and were reported as burst frequency (bursts per minute) and bursts per 100 heart beats.

Forearm blood flow. Forearm blood flow was measured by venous occlusion plethysmography (1). The nondominant arm was elevated above heart level to ensure adequate venous drainage. A mercury-filled silastic tube attached to a low-pressure transducer was placed around the forearm and connected to a plethysmograph (Hokanson, Bellevue, WA, USA). Sphygmomanometer cuffs were placed around the wrist and upper arm. At 15-s intervals, the upper cuff was inflated above venous pressure for 7 to 8 s. Forearm blood flow (mL · 100 mL tissue^{-1} · min^{-1}) was determined on the basis of a minimum of four separate readings. Forearm vascular conductance was calculated as forearm blood flow/mean arterial pressure x 100, and is reported as 'units' [100 mL(dL tissue)$^{-1}$ · min^{-1} · mmHg^{-1}].

Blood pressure and heart rate. Blood pressure was monitored noninvasively with a finger photoplethysmograph device (FinaPress 2300; Ohmeda, Englewood, CO, USA) on a beat-to-beat basis (AT/CODAS software) at a frequency of 500 Hz. Heart rate was monitored continuously through lead II of the ECG.

Mental stress. In humans, the defense reaction can be elicited by mental challenge (11). In the present study, as well as in others, mental stress was induced by a 3-min period of the Stroop color word test (10-12). During this test, subjects were shown on a panel a series of names of colors written with ink of a different color from the color specified. The subject was asked to identify the color of the ink, not to read the word. The difficulty of the task was tailored to the ability of the subject. The subject was urged to proceed as rapidly as possible and was gently chastised for incorrect responses. The subject was asked to try her best, but the number of correct answers was not quantified. Each subject was asked to assess task difficulty on completion of the protocol using a standard five-point scale: 0, not stressful; 1, somewhat stressful; 2, stressful; 3, very stressful; 4, extremely stressful.

Hypocaloric diet

The hypocaloric diet was based on the basal energy requirements estimated by the FAO/WHO/UNU Expert Committee (13). Because under normal circumstances physical activity accounts for 15 to 30% of a person's total daily energy expenditure, the basal metabolic rate must be multiplied by 1.15 or 1.3 to calculate the daily energy expenditure (13). A 10% reduction in body weight leads to a substantial reduction in cardiovascular risk (14). In general, reductions of 500 to 1,000 kcal/day are used to reduce body weight by 0.5 to 1.0 kg per week. Because the planned reductions were of 8 to 10 kg over a period of 16 weeks, energy intake was reduced by 600 kcal/day. The diet consisted of 50-70% carbohydrate, 10-15% protein and 15-30% fat. On alternate weeks, every patient visited the clinical nutritionist for a regular check-up. On the occasion of each visit, the subjects were weighed and encouraged to record their intake to ensure adherence to the dietary protocol.

Exercise training

Exercise training consisted of three 60-min supervised exercise sessions per week over a period of four months. Each exercise session consisted of 40 min of aerobic cycling exercise, and 15-20 min of local strengthening exercises (sit-ups, push-ups, and pull-ups), and 5 min of cool down with stretching exercises. The exercise intensity was established by heart rate levels that corresponded to the anaerobic threshold up to 10% below the respiratory compensation

point obtained in a progressive cardiopulmonary exercise test. The anaerobic threshold was considered to occur at the point where there was a loss of linearity between oxygen uptake and carbon dioxide production (15), or at the point where the ventilatory equivalent for the oxygen and end-tidal oxygen partial pressure curves reached their respective minimum values and then began to rise during the progressive exercise test (16). The respiratory compensation point was determined as the point where the ventilatory equivalent for carbon dioxide was lowest before a systematic increase or where end-tidal carbon dioxide partial pressure reached a maximum value and began to decrease (17). The peak oxygen uptake was considered to occur at the end of the bicycle cardiopulmonary exercise test (ramp protocol with a 10- to 15-W increment every minute up to exhaustion), when the subject no longer maintained the bicycle velocity at 60 rpm. Compliance was assessed as percentage of exercise sessions attended. Compliance with the exercise program was very good, with the subjects attending more than 80% of the exercise sessions.

Experimental protocol

After a sleep of at least 7 h, no physical exercise for 24 h prior the study, and a light meal without caffeine, between 7:00 and 8:00 am, the subject lay down in a comfortable position on a laboratory bed. The leg was positioned for microneurography and an adequate nerve recording site was obtained. Baseline MSNA, forearm blood flow, blood pressure, and heart rate were recorded for 3 min. The Stroop color word test was performed for 4 min and MSNA and heart rate were recorded continuously during the test. Blood pressure was measured on a beat-to-beat basis. Forearm blood flow was measured each 15 s. The exercise-trained women were submitted to the experimental protocol two days after the last training section. This experimental protocol was repeated after 4 months of intervention (diet alone or diet plus exercise training).

Statistical analysis

Data are reported as means ± SEM. The similarity in demographics among the three groups was tested by one-way analysis of variance. Two-way analysis of variance with repeated measures was performed to test differences (pre- versus post-intervention) within each group at rest and during mental stress. When significance was detected, Scheffé *post hoc* comparison was performed. Probability values of <0.05 were considered to be statistically significant.

Results

Baseline measurements

Baseline body weight and body weight mass were similar for the diet, diet plus exercise training, and nonadherent groups (87 ± 2, 85 ± 2, and 87 ± 3 kg, P = 0.66, respectively, and 34 ± 1, 33 ± 1, and 33 ± 1 kg/m^2, P = 0.14, respectively). Similarly, there were no differences in baseline glucose or insulin levels among the diet, diet and exercise training, and nonadherent groups (80 ± 2, 86 ± 3, and 85 ± 4 mg/dL, P = 0.11, respectively, and 15.4 ± 2, 13.3 ± 1.4, and 12.5 ± 2.2 µIU/mL, P = 0.60, respectively). MSNA in bursts per minute and bursts per 100 heart beats did not differ among the groups studied (38 ± 1, 35 ± 1, and 38 ± 2 bursts/min, P = 0.14, respectively, and 51 ± 2, 49 ± 1, and 55 ± 3 bursts/100 heart beats, P = 0.49, respectively). There were no differences in systolic, diastolic, or mean blood pressure (133 ± 3, 137 ± 3, and 136 ± 5 mmHg, P = 0.54, respectively; 77 ± 2, 76 ± 2, and 79 ± 3 mmHg, P = 0.91, respectively, and 95 ± 2, 96 ± 2, and 98 ± 3 mmHg, P = 0.84, respectively) among groups. Heart rate was also similar for all groups studied (75 ±

2, 72 ± 2, and 72 ± 3 bpm, P = 0.46). Regarding forearm measurements, there were no significant differences in baseline forearm blood flow or forearm vascular conductance among the diet group, diet plus exercise training group, and nonadherent group (2.17 ± 0.22, 1.88 ± 0.08, and 1.82 ± 0.20 mL · 100 mL tissue^{-1} · min^{-1}, P = 0.34, respectively, and 2.25 ± 0.23, 2.02 ± 0.11, and 1.89 ± 0.24 units, P = 0.48, respectively). Peak oxygen uptake was also similar for all groups (17.7 ± 0.8, 18.5 ± 0.6, and 18.4 ± 1.0 mL · kg^{-1} · min^{-1}, P = 0.69, respectively).

Effects of diet and exercise training

Diet and diet associated with exercise training significantly reduced body weight (87 ± 2 *vs* 79 ± 2 and 85 ± 2 *vs* 76 ± 2 kg, respectively, P < 0.05). Body weight was unchanged in the nonadherent group (86 ± 3 *vs* 85 ± 3 kg). Similarly, diet and diet plus exercise training significantly reduced body mass index (34.4 ± 0.5 *vs* 31.0 ± 0.6 and 32.9 ± 0.4 *vs* 29.4 ± 0.5 kg/m^2, respectively). Body mass index was unchanged in the nonadherent group (33.2 ± 0.9 *vs* 32.6 ± 0.8 kg/m^2). Diet associated with exercise training significantly increased peak oxygen uptake (18.8 ± 0.6 *vs* 22.2 ± 0.7 mL · kg^{-1} · min^{-1}, P < 0.05). In the diet and nonadherent groups, peak oxygen uptake was unchanged (17.9 ± 0.7 *vs* 18.7 ± 0.7 and 18.3 ± 1.0 *vs* 18.9 ± 1.2 mL · kg^{-1} · min^{-1}, respectively).

Regarding task difficulty on completion of the protocol of mental stress, there were no significant differences among the diet, diet plus exercise training, and nonadherent groups pre- and post-intervention (pre = 1.3 ± 0.2, 1.5 ± 0.2, and 1.3 ± 0.3 scores, and post = 1.3 ± 0.2, 1.6 ± 0.1, and 1.3 ± 0.4 scores, P = 0.90, respectively).

Diet and diet associated with exercise training slightly decreased systolic and mean blood pressure levels at rest and during mental stress (Table 1). Diet significantly reduced diastolic blood pressure (P = 0.02), whereas diet associated with exercise training only tended to reduce diastolic blood pressure (P = 0.06). Both interventions, diet and diet associated with exercise training, slightly decreased heart rate levels at rest and during mental stress (Table 1). Systolic, diastolic, mean blood pressure, and heart rate levels were unchanged in the nonadherent group at rest or during mental stress.

Diet and diet associated with exercise training significantly reduced MSNA burst frequency (bursts/min) at rest and during mental stress, although the magnitude of the responses, analyzed by the interaction of phase and time, showed no significant difference between pre-intervention and post-intervention (Figure 1A). Similar findings were observed in pulse synchronous sympathetic activity (bursts/100 heart beats). Diet and diet associated with exercise training significantly reduced pulse synchronous sympathetic activity at rest and during mental stress, but caused no change in the magnitude of the responses of pulse synchronous sympathetic activity (Figure 1B). MSNA burst frequency and pulse synchronous sympathetic activity were unchanged in the nonadherent group.

Diet alone did not significantly change forearm blood flow at rest or during mental stress (Table 1). In contrast, diet associated with exercise training significantly increased forearm blood flow at rest and during mental stress (Table 1), although these interventions caused no change in the magnitude of the response of forearm blood flow. Similarly, diet did not change forearm vascular conductance at rest or during mental stress, whereas diet associated with exercise training significantly increased forearm vascular conductance at rest and during mental stress (Figure 1C) despite the fact that these interventions did not cause any change in the magnitude of the response of forearm vascular conductance. Forearm blood flow and forearm vascular conductance were unchanged in the nonadherent group.

Table 1. Systemic and vascular measurements during mental stress before and after interventions in obese women.

Systemic measurements		Mental stress			
		Rest	1 min	2 min	3 min
SBP (mmHg)					
D	Pre	134 ± 3	138 ± 3	142 ± 3*	142 ± 4*
	Post	130 ± 2	134 ± 2	139 ± 2*	140 ± 3*
D + ET	Pre	137 ± 3	139 ± 3	146 ± 3*	147 ± 3*
	Post	130 ± 3	134 ± 4	138 ± 4*	138 ± 4*
NA	Pre	136 ± 4	142 ± 5	144 ± 5*	143 ± 6*
	Post	136 ± 3	143 ± 4	147 ± 5*	148 ± 5*
DBP (mmHg)					
D	Pre	77 ± 2	81 ± 2*	83 ± 2*	83 ± 2*
	Post	71 ± 2+	74 ± 2+	77 ± 2*+	77 ± 2*+
D + ET	Pre	76 ± 2	78 ± 3*	80 ± 3*	81 ± 3*
	Post	69 ± 2	72 ± 2	74 ± 3*	74 ± 3*
NA	Pre	77 ± 2	81 ± 3*	85 ± 3*	86 ± 4*
	Post	79 ± 3	84 ± 3	85 ± 3*	86 ± 3*
MBP (mmHg)					
D	Pre	95 ± 2	100 ± 3*	103 ± 3*	102 ± 3*
	Post	91 ± 2	94 ± 2	98 ± 2*	99 ± 2*
D + ET	Pre	96 ± 2	99 ± 3	102 ± 3*	103 ± 3*
	Post	89 ± 2	93 ± 3	96 ± 3*	96 ± 3*
NA	Pre	97 ± 3	101 ± 4	105 ± 3	105 ± 4
	Post	99 ± 3	105 ± 4	108 ± 4	108 ± 4
HR (bpm)					
D	Pre	75 ± 2	83 ± 2*	81 ± 2*	80 ± 2*
	Post	70 ± 2	78 ± 3*	77 ± 3*	76 ± 3*
D + ET	Pre	72 ± 2	81 ± 3*	79 ± 2*	78 ± 2*
	Post	68 ± 2	79 ± 3*	75 ± 2*	74 ± 2*
NA	Pre	70 ± 3	80 ± 4	76 ± 3	75 ± 3
	Post	68 ± 2	79 ± 4*	76 ± 3	76 ± 3*
Forearm measurements					
FBF (mL 100 mL tissue^{-1} min^{-1})					
D	Pre	2.17 ± 0.22	2.72 ± 0.33	2.64 ± 0.32	2.52 ± 0.23
	Post	2.35 ± 0.19	3.07 ± 0.29*	3.01 ± 0.31*	2.90 ± 0.22
D + ET	Pre	1.88 ± 0.07	2.73 ± 0.20*	2.74 ± 0.20*	2.78 ± 0.20*
	Post	2.42 ± 0.12+	3.33 ± 0.24*	3.53 ± 0.28*+	3.30 ± 0.26*
NA	Pre	1.80 ± 0.20	2.67 ± 0.30*	2.53 ± 0.30	2.49 ± 0.30
	Post	1.80 ± 0.12	2.81 ± 0.40*	2.67 ± 0.38	2.50 ± 0.30

Data are reported as means ± SEM. D = hypocaloric diet group, D + ET = hypocaloric diet associated with exercise training group, NA = nonadherent group, SBP = systolic blood pressure, DBP = diastolic blood pressure, MBP = mean blood pressure, HR = heart rate, FBF = forearm blood flow.
*$P < 0.05$ compared to rest; +$P < 0.05$ compared to pre-intervention (two-way ANOVA for repeated measures).

Discussion

The novelty of the present study is that weight loss improves neurovascular control during mental stress in obesity. We found that weight loss decreases MSNA levels during mental stress in obese subjects. In addition, weight loss by diet associated with exercise training, in contrast to weight loss by diet alone, increased forearm vascular conductance during mental stress.

Reduction in MSNA after weight loss has been previously reported during moderate exercise (18) when sympathoexcitation is mediated by a central command, by mechanoreceptors and by chemoreceptors. The present study, however, brings about a new understanding of human obesity. Mental stress isolates the central command and may precipitate cardiac events, especially in obese subjects, in whom neurovascular alteration is the rule (6). Our results show that the central neural outflow during a stressful condition, directly measured by microneurography, was markedly reduced after weight loss. In addition, the unchanged magnitude of the increase in MSNA levels during mental stress after the interventions suggests that the lowered sympathetic activation during this physiological maneuver is a consequence of a reduction in baseline MSNA. Although the mechanisms underlying the reduction in central neural outflow are beyond the scope of the present investigation, the improvement in baroreflex control is a potential mechanism for explaining the decrease in the centrally mediated MSNA after weight loss (19). The decreased plasma leptin levels and the increased insulin sensitivity after weight loss can also be involved in the reduction of MSNA, although this physiological link still needs to be demonstrated in humans (18). Alternatively, the decrease in free fatty acids after weight loss (20) is a suggestive candidate to explain the reduction in MSNA in human obesity. Because free fatty acids coming from visceral adipose tissue or the portal vein can sensitize liver afferent nervous fibers which, in turn, centrally modulate sympathetic activity (21), it is conceivable that the reduction in plasma free fatty acid con-

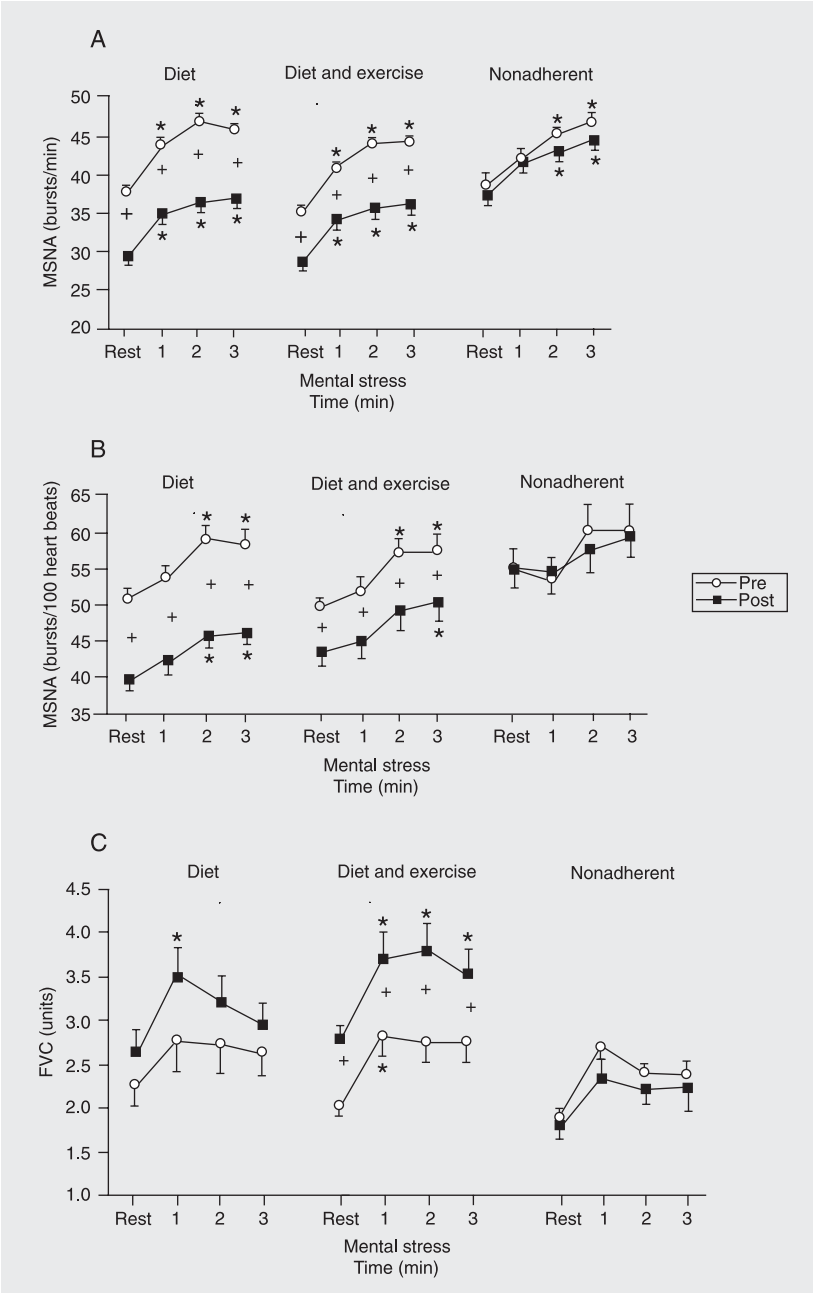

Figure 1. Muscle sympathetic burst frequency (MSNA, Panel A), pulse synchronous sympathetic activity (MSNA, Panel B), and forearm vascular conductance (FVC, Panel C) at rest and during mental stress in obese women after intervention by diet or diet associated with exercise training, and in obese women with nonadherence to either intervention. *P < 0.05 compared to rest; $^{+}$P < 0.05 compared to pre-intervention (two-way ANOVA for repeated measures).

centration after weight loss can attenuate central neural outflow in humans.

The tendency towards a decrease in heart rate during mental stress suggests that sympathoinhibition also took place at the cardiac level. Although we have not measured sympathetic activity on the heart, MSNA is highly correlated with cardiac noradrenaline spillover at rest, and changes in MSNA and cardiac noradrenaline spillover during mental stress are qualitatively similar (22). There is also the possibility that weight loss provoked an increase in the vagal activity that controls heart rate. A previous study (18) has shown that a diet and exercise regimen caused a significant reduction in heart rate during mild and moderate exercise, although no information on sympathetic or vagal functioning was provided in that study.

Even though we were not dealing with hypertensive women, but rather with prehypertensive women (8), diet and diet associated with exercise training tended to reduce diastolic blood pressure at rest and during mental stress. The effect of weight loss on blood pressure during physiological maneuvers has been recently demonstrated in obese children (7). The systolic and diastolic blood pressure levels during mental stress and exercise were significantly lowered after weight loss by diet and exercise training (7). Because high blood pressure is consistent with sympathetic activation, the question may be raised that the changes in neurovascular control changes found here were sue, at least in part, to the reduction in blood pressure.

As anticipated, weight loss increased forearm vascular conductance during mental stress. However, this vascular adaptation is only obtained when diet is associated with exercise training. These findings confer an important role on exercise in the treatment of human obesity. It is unlikely that this exercise effect reflects the decline in sympathetic activation because exercise training and diet, and diet alone equally reduced MSNA. It seems more reasonable that exercise improved endothelium function, increasing the bioavailability of nitric oxide. In fact, the benefits of exercise on endothelially mediated blood flow have been reported in adult obese subjects (23), and, more recently, in obese children submitted to diet associated with exercise training. In obese children, a hypocaloric diet plus exercise training restored muscle endothelium-mediated vasodilatory responses during mental stress and handgrip exercise (7). The effects of exercise training on endothelial function are not limited to obese individuals and skeletal muscle. A previous study has demonstrated that exercise training improves coronary flow in response to adenosine infusion in patients with ischemic heart failure (24).

The mechanisms involved in the improvement of endothelial function after exercise training are not fully understood. However, we can hypothesize that the reduction in proinflammatory mediators plays a role in this matter. It is well known that TNF-α and interleukin-6 enhance reactive oxygen species, which, in turn, increase nitric oxide degradation. Thus, exercise training, by reducing plasma and muscle TNF-α and interleukin-6 as previously demonstrated (25,26), would increase nitric oxide production in obese individuals, in whom these pro-inflammatory mediators are augmented (27, 28). Alternatively, we suggest that exercise training improves endothelial function by increasing endothelial nitric oxide synthase. A previous study demonstrated that exercise training increased endothelial nitric oxide synthase expression in dogs with heart failure (29).

Study limitations

Although body weight was substantially reduced, it did not reach normal levels. Therefore, we do not know the actual benefits of greater body weight reduction for neurovascular control. In addition, it may be possible

that more prominent benefits would be seen if our diet and exercise regimen were prolonged. Our sampling was restricted to women. This strategy avoided gender confounding, but at the same time reduced the generality of our findings. The non-adherent group included individuals who did not adhere to the diet plus exercise training or to the diet. Thus, the nonadherent group as a control group should be viewed with caution. One may argue that the decreased muscle sympathetic nerve activity in obese women after weight loss is due to the perceived exertion. This interpretation is unlikely, because the task difficulty on completion of the protocol using a five-point scale was similar across the three groups studied (data not shown).

The present study extends our knowledge by showing that weight loss reduces MSNA levels during mental stress in obese subjects as a consequence of the decrease in baseline MSNA. The improvement in muscle vascular conductance during a mental challenge depends on the weight loss strategy chosen. The increase in muscle vascular conductance during a stressful condition is achieved if a hypocaloric diet is associated with exercise training. These findings demonstrate that these two interventions should be the mandatory strategy for the nonpharmacologic treatment of human obesity.

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