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Muscle metaboreflex control is diminished in normotensive obese women

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Negrão, Carlos Eduardo, Ivani C. Trombetta, Luciana T. Batalha, Maurício Maltez Ribeiro, Maria Urbana P. Brandão Rondon, Taís Tinucci, Cláudia L. M. Forjaz, Antonio Carlos P. Barretto, Alfredo Halpern, and Sandra M. F. Villares. Muscle metaboreflex control is diminished in normotensive obese women. *Am J Physiol Heart Circ Physiol* 281: H469–H475, 2001.—There is no information about the muscle metaboreflex control in obese individuals. In 40 normotensive obese women (OW; body mass index 33.5 ± 0.4 kg/m^2, age 32.4 ± 1.1 yr) and 15 age-matched, normotensive lean women (LW; body mass index 22.7 ± 0.8 kg/m^2, age 34.4 ± 1.4 yr), we measured muscle sympathetic nerve activity (MSNA) and forearm blood flow (FBF) in the nonexercising forearm during static exercise at 10 and 30% of maximal voluntary contraction (MVC). Baseline MSNA (38 ± 2 vs. 31 ± 1 bursts/min, P = 0.001) and mean blood pressure were significantly higher in OW compared with LW. FBF was significantly lower, whereas forearm vascular resistance was significantly higher in OW. During 10% MVC, MSNA increased similarly in both groups, but during 30% MVC, MSNA was higher in LW. FBF and forearm vascular resistance responses during both 10 and 30% MVC were similar between groups. During post-handgrip circulatory arrest, MSNA remained significantly elevated compared with baseline in both groups, but this increase was significantly lower in OW (3.8 ± 0.82 vs. 9.4 ± 1.03 bursts/min, P = 0.002). In conclusion, muscle metaboreflex control of MSNA is blunted in OW. MSNA responses are not augmented during selective activation of central command/mechanoreceptors and metaboreceptors, despite increased MSNA levels in OW. Muscle vasodilatory response during graded handgrip isometric exercise is preserved in OW.

obesity; sympathetic nerve activity

PREVIOUS STUDIES HAVE DEMONSTRATED that obesity is linked to autonomic alterations. Muscle sympathetic nerve activity (MSNA) is increased in obese individuals when compared with healthy lean individuals (7, 20), which seems to be mediated by a baroreflex dysfunction (8). The reduction in body weight with a hypocaloric diet improves baroreflex control of heart rate and MSNA (8). MSNA is increased in obese individuals with sleep apnea (14). Chemoreflex responses to hypercapnia are potentiated in eucapnic obese individuals (15). However, there is no available information on functioning of muscle metaboreflex control in obesity.

In lean healthy individuals, the increase in MSNA during exercise until 10% of maximal voluntary contraction (MVC) is mediated by central command/mechanoreceptors located in the skeletal muscle (18, 21), whereas the increase in sympathetic nerve activity during exercise at 30% of MVC is mediated by central command/mechanoreceptors and metaboreceptors (18, 21). Because sympathetic nerve activity is increased in obese individuals, we hypothesized that the responses of MSNA will be augmented during selective activation of central command/mechanoreceptors and metaboreceptors in obesity.

There is consistent evidence that obese individuals have abnormal vasodilatory responses. The vasodilatory responses during euglycemic-hyperinsulinemic condition decreased in obese individuals (23). In addition, the endothelium-dependent vasodilatory response seems to be impaired in obese individuals (10). However, the muscle vasodilatory response during selective activation of central command/mechanoreceptors and metaboreceptors needs to be demonstrated in obese individuals.

There were three goals of the present investigation. The first goal tested the hypothesis that MSNA is augmented during selective activation of central command/mechanoreceptors and metaboreceptors in normotensive obese individuals. The second goal tested the integrity of the muscle metaboreflex control in normotensive obese individuals. The third goal tested the hypothesis that the vasodilatory response in the

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contralateral forearm during selective activation of central command/mechanoreceptors and metaboreceptors is reduced in obese individuals compared with healthy lean individuals.

METHODS

Study Population

After written informed consent was obtained, 40 normotensive obese women (body mass index 33.5 ± 0.4 kg/m^2, age 32.4 ± 1.1 yr) and 15 age-matched normotensive lean women (body mass index 22.7 ± 0.8 kg/m^2, age 34.4 ± 1.4 yr) participated in this study. All individuals had normal glucose tolerance, were taking no medication, and had no evidences of metabolic or cardiovascular disease at the time of the study. They had normal blood pressure levels, in accordance with The Sixth Report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure. The study protocol was approved by the Human Subject Protection Committees of the Heart Institute and Clinical Hospital, School of Medicine, University of São Paulo. Both groups of women abstained from caffeine for 24 h before the study. These studies were conducted in the postabsorptive state.

Measurements and Procedures

MSNA. MSNA was directly measured from the peroneal nerve using the technique of microneurography (17). Multiunit postganglionic muscle sympathetic nerve recordings were made with the use of a tungsten microeletrode (tip diameter 5–15 μm). The signal was amplified by a factor of 50,000–100,000 and band-pass filtered (700 to 2,000 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. MSNA was evaluated in bursts per minute.

Forearm blood flow. Forearm blood flow was measured by venous occlusion plethysmography. The arm was elevated above the heart level. A mercury-filled Silastic tube attached to a low-pressure transducer was placed around the forearm and connected to a plethysmography (Hokanson). Sphygmomanometer cuffs were placed around the wrist and upper arm. At 15-s intervals, the upper cuff was inflated above venous pressure for 7–8 s. Forearm blood flow (ml·min^{-1}·100 g of tissue^{-1}) was determined on the basis of a minimum of four separate readings. Forearm vascular resistance (units) was calculated by dividing mean arterial pressure (oscillometrically measured) by forearm blood flow.

Miscellaneous measurements. Blood pressure was monitored noninvasively from an automatic blood pressure cuff. Heart rate was monitored continuously through lead II of the electrocardiogram.

Handgrip exercise. After the MVC rate (mean of 3 trials) was obtained, handgrip isometric exercise was performed with the dominant arm by using a handgrip dynamometer. The individuals were instructed to breath normally during exercise and to avoid inadvertent performance of a Valsalva maneuver.

Experimental Protocol

Protocol 1: MSNA, forearm blood flow, mean blood pressure, forearm vascular resistance, and heart rate during 10% handgrip exercise. The purpose of this study was to determine the magnitude of change in MSNA, forearm blood flow, mean blood pressure, forearm vascular resistance, and heart rate during the activation of central command/mechanoreceptors in 40 obese individuals and 15 lean healthy individuals. All of the studies were performed in a quiet, temperature-controlled (21°C) room at approximately the same time of day. The arm was initially positioned for venous occlusion plethysmography. The leg was positioned for microneurography, and an adequate nerve-recording site was obtained. The subject then rested for 15 min. Baseline MSNA, forearm blood flow, mean blood pressure, and heart rate were recorded for 3 min. Handgrip exercise was performed for 3 min at 10% MVC. MSNA, forearm blood flow, mean blood pressure, and heart rate were recorded continuously during all handgrip exercise.

Protocol 2: MSNA, forearm blood flow, mean blood pressure, forearm vascular resistance, and heart rate during 30% handgrip exercise. The purpose of this study was to determine the magnitude of change in MSNA, forearm blood flow, mean blood pressure, forearm vascular resistance, and heart rate during the activation of central command/mechanoreceptors and chemoreceptors in 40 obese individuals and 15 lean healthy individuals. This study was started after a 15-min rest period to allow all of the physiological parameters to return to baseline. Baseline MSNA, forearm blood flow, mean blood pressure, and heart rate were recorded for 3 min. Handgrip isometric exercise was performed for 3 min at 30% MVC. MSNA, blood pressure, forearm blood flow, and heart rate were recorded continuously during all handgrip isometric exercise.

Protocol 3: MSNA, forearm blood flow, mean blood pressure, forearm vascular resistance, and heart rate during postexercise regional circulatory arrest. The purpose of this study was to determine the magnitude of change in MSNA, forearm blood flow, mean blood pressure, forearm vascular resistance, and heart rate during isolated metaboreflex activation in 40 obese individuals and 15 lean healthy individuals. Ten seconds before 30% MVC handgrip isometric exercise ended, the circulation to the exercising forearm was arrested by inflation of the upper arm occlusion cuff (240 mmHg). Postexercise regional circulatory arrest was continued for 2 min.

Statistical Analysis

Baseline data of MSNA, forearm blood flow, mean blood pressure, forearm vascular resistance, and heart rate in obese women and lean women were compared by Student's *t*-test. $P < 0.05$ was considered statistically significant. Data of MSNA, forearm blood flow, mean blood pressure, forearm vascular resistance, and heart rate are presented as means ± SE. Data during handgrip isometric exercise or during circulatory arrest were subjected to two-way analysis of variance with repeated measures. When a significant variation was found, Scheffé's post hoc comparison was performed. $P < 0.05$ was considered statistically significant.

RESULTS

Baseline Physiological Parameters

Baseline MSNA, mean blood pressure, forearm blood flow, forearm vascular resistance, and heart rate are shown in Table 1. MSNA was significantly higher in obese individuals than lean individuals ($P = 0.001$). Mean blood pressure was significantly higher in obese individuals compared with lean healthy individuals ($P = 0.0036$). Forearm blood flow was significantly lower in obese individuals ($P = 0.02$), whereas forearm

Table 1. *Baseline measurements*

	Lean, n = 15	Obese, n = 40	P
MSNA, bursts/min	31 ± 1	38 ± 2*	0.001
MBP, mmHg	91 ± 3	100 ± 2*	0.0036
FBF, ml·min^{-1}·100 g^{-1}	2.27 ± 0.15	1.90 ± 0.07*	0.02
FVR, units	43 ± 3	57 ± 3*	0.0006
HR, beats/min	66 ± 2	70 ± 2	0.16

Values are means ± SE; n, no. of female subjects. MSNA, muscle sympathetic nerve activity; MBP, mean blood pressure; FBF, forearm blood flow; FVR, forearm vascular resistance; and HR, heart rate. *P < 0.05, between-group comparisons.

vascular resistance was significantly higher in obese individuals (P = 0.0006). Heart rate was similar between the two groups (P = 0.16).

Protocol 1: mild isometric exercise. MSNA increased during mild handgrip isometric exercise in the two groups (Table 2). Despite the fact that the absolute levels of MSNA throughout the experimental protocol were significantly higher in obese individuals than in lean individuals (Table 2), the responses of MSNA during mild isometric exercise between these two groups were similar (Fig. 1*A*). Mean blood pressure increased during mild isometric exercise in obese individuals and lean individuals (Table 2). The absolute levels of mean blood pressure throughout the experiment protocol were significantly higher in obese individuals (Table 2), but no significant difference in mean blood pressure responses during mild isometric exercise between the two groups were found (Fig. 2*A*). Forearm blood flow progressively and similarly increased during mild handgrip isometric exercise in both groups (Table 2). Forearm vascular resistance decreased during mild handgrip isometric exercise in obese individuals and lean individuals (Table 2). The absolute levels of forearm vascular resistance throughout the experimental protocol were significantly higher in obese women than in lean individuals (Table 2), but the response of forearm vascular resistance was similar between the two groups (Fig. 3*A*). Heart rate progressively and similarly increased during isometric exercise in both groups (Table 2).

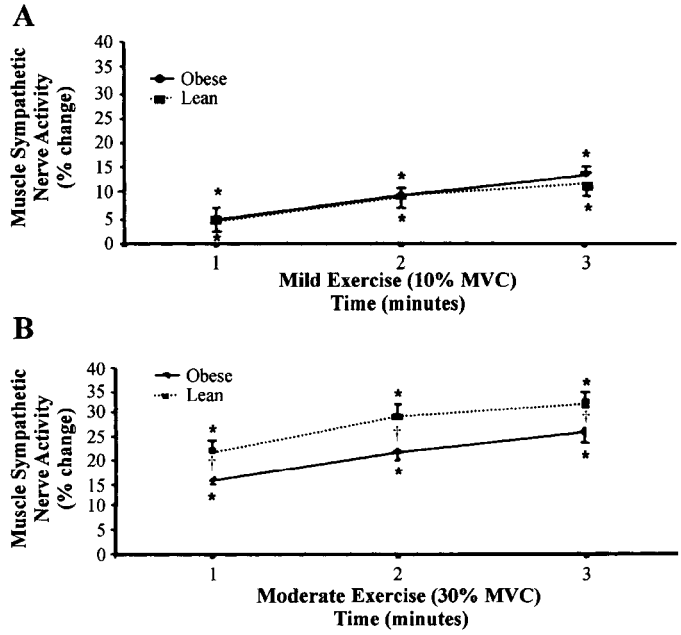

Fig. 1. *A*: responses of muscle sympathetic nerve activity during mild handgrip isometric exercise (10% maximal voluntary contraction; MVC). Muscle sympathetic nerve activity increased slightly during exercise in obese individuals and lean individuals. Muscle sympathetic nerve activity responses throughout mild handgrip isometric exercise were similar between obese individuals and lean individuals. *B*: responses of muscle sympathetic nerve activity during moderate handgrip isometric exercise (30% MVC). Muscle sympathetic nerve activity increased progressively during moderate isometric exercise in obese individuals and lean individuals. Note, however, that muscle sympathetic nerve activity responses were significantly higher throughout exercise in lean individuals compared with obese individuals. †P < 0.05, between-group comparisons. *P < 0.05, within-group comparisons vs. baseline.

Protocol 2: moderate isometric exercise. MSNA progressively and significantly increased during moderate

Table 2. *MSNA, MBP, FVR, FBF, and HR at baseline and during isometric exercise at 10 and 30% of MVC in normotensive lean women and normotensive obese women*

	Exercise at 10% MVC				Exercise at 30% MVC			
	Baseline	1 min	2 min	3 min	Baseline	1 min	2 min	3 min
MSNA, bursts/min								
Lean	31 ± 1	32 ± 2†	34 ± 1†	35 ± 2†	30 ± 2	39 ± 2†	43 ± 2†	45 ± 2†
Obese	38 ± 2*	40 ± 1*†	43 ± 2*†	45 ± 2*†	38 ± 1*	46 ± 1*†	49 ± 2*†	52 ± 2*†
MBP, mmHg								
Lean	91 ± 3	91 ± 2	93 ± 3	95 ± 4	90 ± 3	98 ± 4†	103 ± 4†	106 ± 5†
Obese	100 ± 2*	100 ± 2*	103 ± 2*	103 ± 2*	99 ± 2*	103 ± 2*†	110 ± 2*†	118 ± 2*†
FBF, ml·min^{-1}·100 g^{-1}								
Lean	2.3 ± 0.2	2.4 ± 0.2†	2.4 ± 0.2†	2.8 ± 0.2†	2.2 ± 0.1	2.7 ± 0.1†	2.9 ± 0.2†	3.1 ± 0.3†
Obese	1.9 ± 0.1	2.0 ± 0.1†	2.2 ± 0.1†	2.3 ± 0.1†	2.0 ± 0.1	2.3 ± 0.1†	2.6 ± 0.1†	2.8 ± 0.2†
FVR, units								
Lean	43 ± 3	41 ± 3	41 ± 3†	36 ± 2†	42 ± 3	38 ± 2	38 ± 3†	37 ± 4†
Obese	57 ± 3*	55 ± 3*	52 ± 3*†	49 ± 2*†	53 ± 2*	49 ± 3*	47 ± 3*†	47 ± 3*†
HR, beats/min								
Lean	66 ± 2	68 ± 3†	69 ± 3†	70 ± 2†	67 ± 2	71 ± 3†	74 ± 3†	75 ± 3†
Obese	70 ± 2	72 ± 2†	71 ± 2†	73 ± 2†	70 ± 2	75 ± 2†	79 ± 2†	82 ± 2†

Values are means ± SE. MVC, maximal voluntary contraction. *P < 0.05, between-group comparisons; †P < 0.05, within-group comparisons.

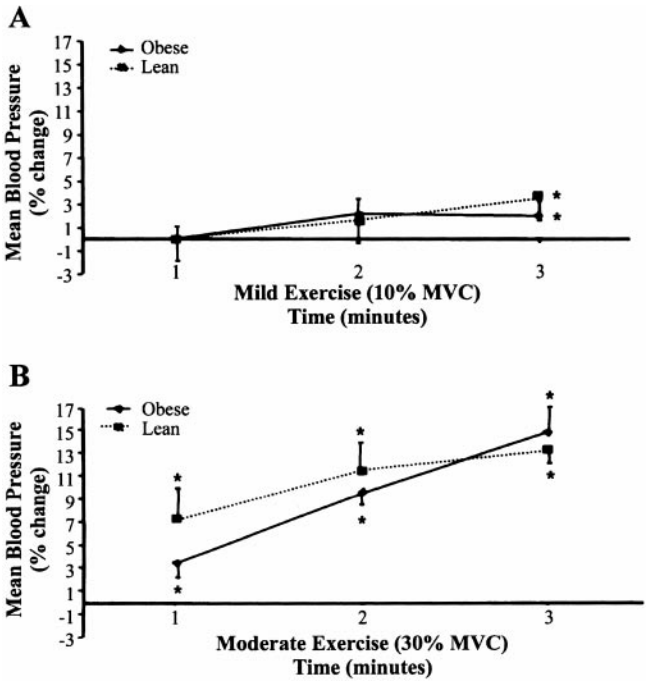

Fig. 2. *A*: responses of mean blood pressure during mild handgrip isometric exercise (10% MVC). Mean blood pressure increased slightly and similarly during exercise in obese individuals and lean individuals. *B*: responses of mean blood pressure during moderate handgrip isometric exercise (30% MVC). Mean blood pressure increased progressively and similarly during exercise in obese individuals and lean individuals. *$P < 0.05$, within-group comparisons vs. baseline.

handgrip isometric exercise in both groups (Table 2). The absolute levels of MSNA throughout the experimental protocol were significantly higher in obese individuals (Table 2). Despite this, the responses of MSNA were significantly higher in lean individuals compared with obese individuals (Fig. 1*B*). Mean blood pressure progressively and significantly increased during moderate handgrip isometric exercise in both groups. The absolute levels of mean blood pressure throughout the experimental protocol were significantly higher in obese individuals (Table 2), but no significant differences in mean blood pressure responses during moderate isometric exercise between the two groups were found (Fig. 2*B*). Forearm blood flow significantly and similarly increased during moderate handgrip isometric exercise in both groups (Table 2). Forearm vascular resistance significantly and similarly decreased during the second and third minute of the moderate handgrip exercise in both groups (Table 2). The absolute levels of forearm vascular resistance throughout the experimental protocol were significantly higher in obese individuals (Table 2). Even so, the responses of forearm vascular resistance were similar between the two groups (Fig. 3*B*). Heart rate significantly and similarly increased during moderate handgrip isometric exercise in both groups (Table 2).

Protocol 3: posthandgrip circulatory arrest. During posthandgrip circulatory arrest, MSNA remained significantly increased compared with the baseline in both lean individuals and obese individuals. Despite this, when the levels of MSNA during circulatory arrest were compared with the baseline, the responses of MSNA during the first and second minutes were significantly lower in obese women compared with lean women (Fig. 4).

To eliminate the possible influence of blood pressure levels on metaboreflex control, the responses of MSNA during circulatory arrest were studied in a subset of 17 obese individuals with similar blood pressure levels to those found in lean individuals (obese, 92 ± 1.47 mmHg vs. lean, 90 ± 1.53 mmHg). In this analysis, the decreased MSNA during circulatory arrest in obese individuals was maintained, despite the similar blood pressure levels between this subset of obese individuals and lean individuals (Fig. 5).

DISCUSSION

The novelty of the present study is the fact that normotensive obese women have lower MSNA responses during circulatory arrest when compared with normotensive lean women, which demonstrates that the metaboreflex control is reduced in obesity. In addition, we have found that MSNA responses during activation of central command/mechanoreceptors and metaboreceptors are not augmented in obese women, despite the increased baseline MSNA in these individuals. The vasodilatory response during activation of central command/mechanoreceptors and metaborecep-

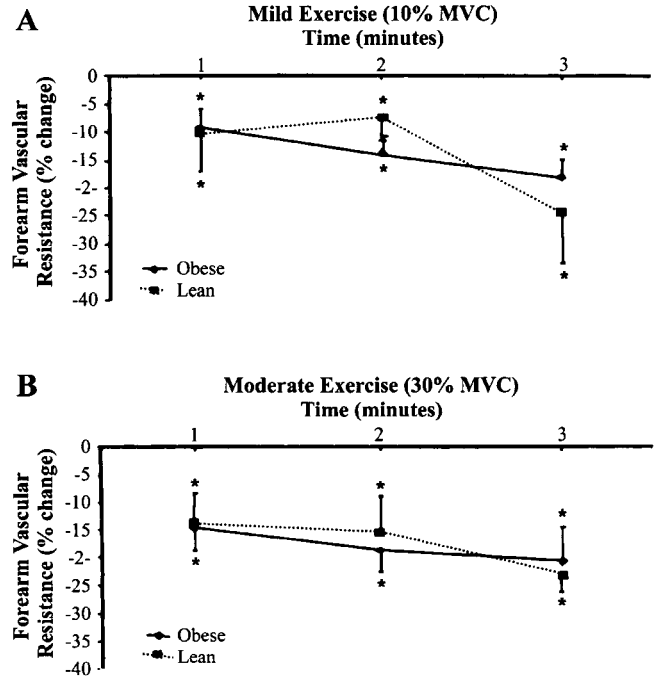

Fig. 3. *A*: responses of forearm vascular resistance during mild handgrip isometric exercise (10% MVC). Forearm vascular resistance decreased similarly during exercise in obese individuals and lean individuals. *B*: responses of forearm vascular resistance during moderate handgrip isometric exercise (30% MVC). Forearm vascular resistance decreased progressively and similarly during exercise in obese individuals and lean individuals. *$P < 0.05$, within-group comparisons.

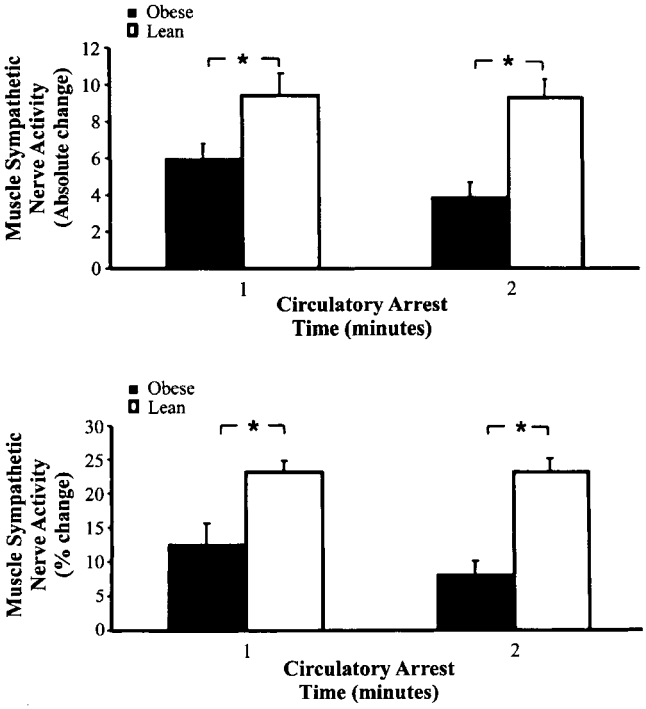

Fig. 4. Responses of muscle sympathetic nerve activity during posthandgrip circulatory arrest. During posthandgrip circulatory arrest, muscle sympathetic nerve activity remained significantly increased compared with baseline in lean individuals and obese individuals. Note, however, that the increase in muscle sympathetic nerve activity was significantly lower in obese individuals compared with lean individuals. *$P < 0.05$.

tors is preserved in normotensive obese women, despite the decreased absolute levels of forearm blood flow.

Reflex alterations have been demonstrated in humans with obesity. Baroreflex dysfunction (7) and chemoreflex responses to hypercapnia (15) have been described in obese individuals. Two pieces of information from the present study extend the knowledge about the effect of obesity in the muscle metaboreflex control. First, the reduced MSNA levels during circulatory arrest shows that the muscle metaboreflex control of MSNA is impaired in obese women. Second, the lower MSNA responses during activation of metaboreceptors (30% exercise), in contrast with the similarity of MSNA responses during activation of central command/mechanoreceptors (10% exercise), support the idea that the metaboreflex control is decreased in obesity. The metaboreflex dysfunction restricts the responses of MSNA during moderate exercise in obese women. Overall, these results demonstrate that muscle metaboreflex control of MSNA is, in fact, blunted in normotensive obese women.

Because obese women had higher blood pressure levels than lean women could suggest that obesity is not the only cause of muscle metaboreflex reduction in the present study, but both obesity and increased blood pressure levels. This does not seem to be the case because the responses of MSNA during postexercise circulatory arrest were decreased in a subset of 17 obese women compared with 15 lean women with similar blood pressure levels. These results demonstrate that obesity is, in fact, the main cause of muscle metaboreflex dysfunction.

The mechanisms underlying the reduction in metaboreflex control in obesity cannot be answered in the present study. However, we can suggest that the increased fat content in the skeletal muscle of obese individuals (6) may desensitize the metaboreceptors, reducing the metaboreflex-mediated MSNA. Alternatively, insulin resistance in obesity (1) reduces glycolysis in skeletal muscle, which, in turn, attenuates muscle acidosis during exercise in obese individuals. Thus the metaboreceptors undergo less stimulation during exercise in obese individuals. It is unlikely that the exercise force performed during handgrip exercise explains the reduction in metaboreflex control in obese women. The exercise force was adjusted to the percentage of the MVC in both groups. Besides, the maximal voluntary force was similar between these two groups (27 ± 0.7 vs. 25 ± 1.5 kg, $P = 0.118$).

We hypothesized that the responses of MSNA during selective activation of central command/mechanoreceptors and metaboreceptors would be augmented in obese individuals. Despite the increased absolute levels of MSNA at rest and during exercise in obese individuals, the responses of MSNA during activation of central command/mechanoreceptors and metaboreceptors are not augmented in normotensive obese women. During

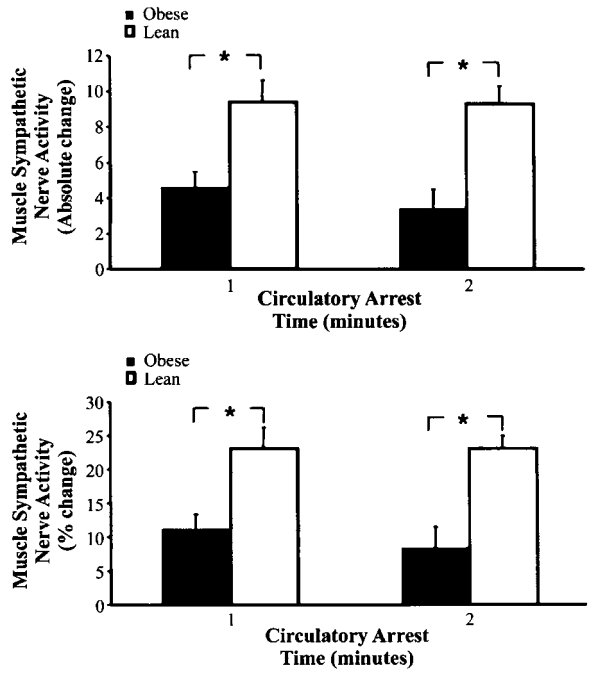

Fig. 5. Responses of muscle sympathetic nerve activity during posthandgrip circulatory arrest in obese women and lean women with similar blood pressure levels. During posthandgrip circulatory arrest, muscle sympathetic nerve activity remained significantly increased compared with baseline in lean individuals and obese individuals. Note that despite similar blood pressure levels, muscle sympathetic nerve activity during circulatory arrest was significantly lower in obese individuals compared with lean individuals. *$P < 0.05$.

10% handgrip isometric exercise, there was no difference in MSNA responses between normotensive obese women and normotensive lean women. Additionally, during 30% handgrip exercise, the responses of MSNA were higher in lean individuals. In obese women, in whom metaboreflex control is reduced, the activation of the muscle metaboreceptors during moderate exercise provokes less reflex-mediated increase in MSNA during circulatory arrest.

The findings of the present study confirm that MSNA is enhanced in obese humans (7, 20). Besides, our data extend this alteration to isometric exercise. During selective activation of central command/mechanoreceptors and metaboreceptors, the absolute levels of MSNA are increased in obese individuals. The mechanisms that increase sympathetic nerve activity in obesity are unclear. However, four convincing mechanisms seem to link the increased sympathetic nerve activity to obesity. First, besides its effect on appetite and thermogenesis control, leptin, which is augmented in obesity, increases norepinephrine turnover in brown adipose tissue (2), and increases sympathetic nerve activity to brown adipose tissue (11), kidneys, adrenal glands, and hindlimbs (11). In obese Zucker rats, in which a mutation in the leptin receptor gene is the rule, there are no sympathoexcitatory actions of leptin (13). Second, baroreflex dysfunction described in obesity (7) and obesity plus hypertension (9) seems to explain, at least in part, the increased sympathetic nerve activity in obese individuals. Because baroreceptors control sympathetic nerve activity at rest (7, 16) and during exercise (12), a baroreflex dysfunction may explain the increased levels of MSNA not only at rest, but also during 10% and 30% handgrip exercise in obese individuals. Third, obesity is a condition of insulin resistance and hyperinsulinemia (1). Forjaz et al. (5) recently described that hyperinsulinemia provokes significant increase in MSNA in humans. Also, more recently, Emdin et al. (4) demonstrated that periods of parasympathetic withdrawal and sympathetic dominance coincide with hyperinsulinemic hours in free-living obese individuals, despite the fact that these individuals have no increase in 24-h urine norepinephrine levels. It is possible that our obese individuals were studied in hyperinsulinemic state, because the experimental protocol was performed 3 h after food intake. This heterogeneity of obese state should be taken into consideration in future studies dealing with obesity. Fourth, Narkiewicz et al. (14) recently documented that increased MSNA is associated with sleep apnea in obese individuals.

The reduced forearm blood flow and the increased forearm vascular resistance at rest demonstrate a certain level of vasoconstriction in normotensive obese women. However, the vasodilatory responses during 10 and 30% handgrip exercise were preserved in obese women. Inasmuch as the increase in the contralateral forearm blood flow during exercise is, in great part, cholinergically mediated (3, 19), our results suggest that the endothelium functioning is preserved during handgrip exercise in normotensive middle-aged obese women. Although previous studies have found that the vasodilatation during hyperemia (10) or during euglycemic-hyperinsulinemic condition (22, 23) is impaired in obese individuals, the vasodilatory responses during exercise were not altered in the present study. These results favor the idea that the mechanisms underlying the reflex vasodilatory response in the nonexercising muscle during handgrip exercise are different from those involved in the vasodilatation provoked by hyperemia or euglycemic-hyperinsulinemic condition. Alternatively, the endothelium dysfunction may take place in a later stage of obesity.

In the present study, although both obese women and lean women were normotensive, blood pressure levels were higher in obese women. These increased blood pressure levels were extended to handgrip isometric exercise. The augmented absolute levels of MSNA and muscle vascular resistance seem to contribute to the increase in blood pressure levels in our obese women. These neurovascular alterations have clinical implications, because they may predispose obese individuals to additional cardiovascular risks during daily activity or exercise.

Limitations

We have included only normotensive middle-aged obese women in the present study. Therefore, our results may restrict our interpretation to this subgroup of obese individuals.

We have not evaluated the sleep status in the present study. Narkiewicz et al. (14) recently reported that MSNA is increased in obese individuals with sleep apnea but not in obese without sleep apnea. Therefore, we do not know whether sleep apnea is a confounding variable in our present study that demonstrates metaboreflex impairment in obese individuals. This is an interesting issue for future investigations.

In summary, obesity in normotensive women reduces muscle metaboreflex control of MSNA. Despite the increased MSNA levels, the responses of MSNA during selective activation of central command/mechanoreceptors are not augmented in normotensive obese women. The vasodilatory response during activation of central command/mechanoreceptors and metaboreceptors is preserved in normotensive obese women.

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