Sympathetic adaptations to one-legged training

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Ray, Chester A. Sympathetic adaptations to one-legged training. J. Appl. Physiol. 86(5): 1583–1587, 1999.—The purpose of the present study was to determine the effect of leg exercise training on sympathetic nerve responses at rest and during dynamic exercise. Six men were trained by using high-intensity interval and prolonged continuous one-legged cycling 4 day/wk, 40 min/day, for 6 wk. Heart rate, mean arterial pressure (MAP), and muscle sympathetic nerve activity (MSNA; peroneal nerve) were measured during 3 min of upright dynamic one-legged knee extensions at 40 W before and after training. After training, peak oxygen uptake in the trained leg increased 19 ± 2% (P < 0.01). At rest, heart rate decreased from 77 ± 3 to 71 ± 6 beats/min (P < 0.01) with no significant changes in MAP (91 ± 7 to 91 ± 11 mmHg) and MSNA (29 ± 3 to 28 ± 1 bursts/min). During exercise, both heart rate and MAP were lower after training (108 ± 5 to 96 ± 5 beats/min and 132 ± 8 to 119 ± 4 mmHg, respectively, during the third minute of exercise; P < 0.01). MSNA decreased similarly from rest during the first 2 min of exercise both before and after training. However, MSNA was significantly less during the third minute of exercise after training (32 ± 2 to 23 ± 3 bursts/min; P < 0.01). This training effect on MSNA remained when MSNA was expressed as bursts per 100 heartbeats. Responses to exercise in five untrained control subjects were not different at 0 and 6 wk. These results demonstrate that exercise training prolongs the decrease in MSNA during upright leg exercise and indicates that attenuation of MSNA to exercise reported with forearm training also occurs with leg training.

muscle sympathetic nerve activity; microneurography; muscle reflexes; exercise

A REDUCTION in muscle sympathetic nerve activity (MSNA) at rest and during exercise may contribute importantly to training-induced reductions in arterial pressure at rest and increases in vascular conductance during exercise. However, little information exists concerning training-induced adaptations of MSNA. Exercising MSNA responses after training indicate an attenuation in sympathetic outflow (12, 15–17). However, these studies have exclusively examined forearm exercise. Furthermore, most of these studies have examined mainly responses to isometric exercise (12, 15, 17) with only one study examining MSNA responses to dynamic exercise (16). Whether these training adaptations in sympathetic outflow during arm exercise can be extrapolated to dynamic leg exercise is unclear. This concern is particularly relevant because we have previously shown that arm and leg exercise can elicit markedly different MSNA responses (9, 10). Moreover, it is well recognized that isometric contractions performed at the same intensity and duration as dynamic contraction produce greater MSNA responses (11, 19).

Additionally, training adaptations on resting MSNA remain equivocal. Cross-sectional studies indicate no effect (13, 18) or an increase (8, 16) in resting MSNA after training, whereas longitudinal studies have reported increases (15), decreases (5), and no change in resting MSNA (14, 17, 18). Thus a secondary goal of this study was to examine the effect of dynamic leg training on resting MSNA.

METHODS

Subjects

We studied 11 healthy, untrained, male volunteers, aged 19–23 yr. Written informed consent was obtained from all subjects, and the study was approved by the Institutional Review Board of the University of Iowa.

Experimental Design

MSNA, heart rate, and mean arterial pressure (MAP) were measured at rest and during 3 min of dynamic one-legged knee extensions (DKE) at 40 W in the sitting position before and after 6 wk of a one-legged exercise conditioning paradigm. One-legged peak oxygen uptake (VO2peak) was also determined before and after training.

Training Protocol

The subjects were trained by using one-legged cycling in the sitting position for a total of 6 wk. Each subject attended four exercise sessions per week. During two sessions, the subject performed unloaded cycling for 3 min and then cycled for 5 min at a work rate that elicited 90–100% of VO2peak. This pattern was repeated five times. During the other two sessions, the subject cycled for 40 min at a work rate that could be maintained throughout the exercise period (~70% of VO2peak). The work rate was adjusted as the subject’s physical work capacity improved so that a constant heart rate was maintained during the training bouts. Five subjects did not train and served as experimental control subjects.

Measurements

Microneurography. Multifiber recordings of MSNA were made with a tungsten microelectrode inserted in the peroneal nerve at the head of the fibula of a resting leg. A reference electrode was placed subcutaneously 2–3 cm from the recording electrode. Adjustments of the recording electrode were made until sites were found in which clear spontaneously occurring sympathetic bursts were recorded. The criteria for acceptable recordings of MSNA were as reported previously.
The nerve signal was amplified (40,000–80,000 times), fed through a band-pass filter with a bandwidth of 700–2,000 Hz, and passed through a resistance-capacitance integrating network with a time constant of 0.1 s to obtain a mean voltage display of the nerve activity. The mean voltage neurograms were displayed together with the electrocardiogram, arterial pressure, respiratory pattern, and force output from arm exercise on a chart recorder (Gould ES2000) at a paper speed of 5 mm/s and an online computer. The nerve traffic was also routed to a storage oscilloscope and a loudspeaker for monitoring during the study.

Heart rate was derived from an electrocardiogram and arterial pressure was measured continuously by a finger cuff (Finapres, Ohmeda, Englewood, CO). To ensure that subjects avoided respiratory maneuvers that may affect sympathetic activity during interventions, respiratory patterns were monitored with the aid of a strain gauge strapped around the chest.

VO₂peak was measured via a metabolic cart (Medical Graphic 2001) that was calibrated with known gases before all tests. The same testing protocol was used before and after training. Initially, the subjects cycled for 2 min at ~40% of an estimated VO₂peak. Then the subjects cycled for 2 min at a work rate estimated to elicit ~70% VO₂peak and for 2 min at a work rate estimated to elicit 100% of VO₂peak. After 5 min of recovery, the subjects cycled for as long as possible at a work rate 24 W greater than they attained at the final work bout. If the increase in oxygen uptake was ~150 ml/min above the maximal value obtained on the graded test, an additional work bout was conducted after a 5-min recovery period.

Data Analysis

Records of MSNA were divided into 1-min periods for statistical analysis. Sympathetic bursts were identified by inspection of the mean voltage neurogram. The significance of difference among means for the measured variables at rest and during DKE was evaluated with a two-way [exercise (time) and training (before and after)] within-subject repeated-measures ANOVA. When a significant interaction was found, simple-effect tests were performed at each time point. A significance level of P < 0.05 was used for all tests. Values are presented in text and Figs. 1 and 2 as means ± SE.

RESULTS

The one-legged training regimen elicited a 19 ± 2% increase VO₂peak in the trained leg. VO₂peak increased from 2.36 ± 0.1 to 2.78 ± 0.1 l/min. Heart rate was lower at rest after training (77 ± 3 to 71 ± 6 beats/min; P < 0.01; Fig. 1). However, MAP and MSNA were unchanged at rest after training (Fig. 1). Training resulted in a significantly lower heart rate and MAP during DKE (Fig. 1). During the final minute of DKE, heart rate was 12 beats/min lower and MAP was 13 mmHg lower after training than before. Before training, MSNA was significantly decreased from baseline during the first minute of DKE (29 ± 3 to 22 ± 2 bursts/min; P < 0.01) followed by a return to baseline during the remaining 2 min (Fig. 1). After one-legged training, MSNA decreased during the first minute of DKE as before training (28 ± 1 to 19 ± 1 bursts/min; P < 0.01; Fig. 1). However, unlike before training, MSNA did not return to baseline during the final 2 min of DKE but remained significantly below baseline (23 ± 1 and 22 ± 3 bursts/min for second and third minute, respectively; Fig. 1). The results for MSNA were unchanged when expressed as bursts per 100 heartbeats. The only significant difference remained during the third minute of exercise (29 ± 2 and 23 ± 2 bursts/100 heartbeats for before and after training, respectively). Figure 2 shows recordings of MSNA before and after 6 wk of one-legged cycle training from one subject. There were no significant changes (main
effects or interaction) for any cardiovascular variables in the control group. VO_{2peak} was also unchanged in the control group (2.58 ± 0.1 to 2.57 ± 0.1 l/min, respectively).

**DISCUSSION**

The present study examined the effect of dynamic leg training on resting and exercising MSNA. The results of the study indicate that endurance training does not alter resting MSNA but does attenuate increases in MSNA during dynamic leg exercise. The present study is unique in that MSNA responses to training were measured during dynamic leg exercise. Until this time, all training studies examining MSNA have used forearm exercise. However, the most common mode of endurance (cardiovascular) training uses the legs (i.e., running, jogging). This study supports the concept that endurance training can attenuate MSNA responses to exercise and extends it to leg exercise and training.

**MSNA Responses to DKE Before Training**

The pattern of decline in MSNA during this sitting DKE model is similar to that reported in an earlier study by our group (10). In this previous report, we presented evidence suggesting that DKE in the upright position increased central filling pressure and activated the cardiopulmonary baroreflex (10). The decrease in MSNA was not related to the engagement of the arterial baroreflex because DKE performed in the supine position elicited a comparable arterial pressure response but with no decrease in MSNA (10). Similarly, because identical work rates were used in both the upright and supine positions, central command would have been expected to be similar and not have contributed to the decrease in MSNA.

The increase in MSNA during the third minute of DKE appears to be related to the activation of muscle reflexes (i.e., muscle metaboreflex) that override the inhibitory effects of the cardiopulmonary reflex. This assumption is based on the time delay of the increase in MSNA during DKE. It might be argued that central command contributed to the increase in MSNA during the third minute of DKE because muscular fatigue becomes more evident and greater volitional effort is needed. However, central command is generally not believed to play a major role in increasing MSNA during exercise with the possible exception of very high-intensity exercise (20). It should be recognized that this conclusion is based on small-muscle-mass exercise (i.e., forearm exercise). The effect central command on MSNA during large muscle mass exercise is not known.

**MSNA Response to DKE After Training**

MSNA responses were similar during the first 2 min of DKE after training. However, MSNA remained suppressed during the third minute of DKE after training, unlike the increase in MSNA observed before training. One possible explanation for the attenuation in MSNA is decrease activation of muscle reflexes. Decreased activation of the muscle metaboreflex after training has been demonstrated by Somers et al. (17). They found that rhythmic handgrip training attenuated MSNA responses during isometric handgrip and posthandgrip muscle ischemia. Mostoufi-Moab et al. (7) found support for training-induced attenuation of the muscle metaboreflex with dynamic forearm exercise training. They found MAP responses to be attenuated during ischemic handgrip induced by positive pressure at 50 mmHg around the forearm after training. Additionally, they found lower venous lactate concentrations and muscle acidosis of the exercising forearm.

Changes to the muscle mechanoreflex may have also contributed to decrease in MSNA during DKE after endurance training. Sinoway et al. (15) found that the increase in MSNA during a 30-min bout of rhythmic handgrip at 25% maximal voluntary contraction was attenuated after 4 wk of training. In this study they concluded that the decrease was related to a desensitization of muscle mechanoreceptors. This was based on an earlier finding that showed increases in MSNA during 30 min of rhythmic handgrip were not related to the activation the muscle metaboreflex (2). Rhythmic handgrip did not lead to changes in muscle acidosis and H_{2}PO_{4}, and MSNA was not elevated during posthandgrip muscle ischemia. However, the failure for MSNA to change during the first 2 min of DKE after training makes this mechanism less viable.

It might be speculated that changes in the cardiopulmonary reflex after training might contribute to the
change in MSNA during leg exercise. DiCarlo and Bishop (3) have reported that exercise training enhances cardiac afferents’ sympathoinhibition in the rabbit (3). However, if this were the case, it would be expected that MSNA would be altered at rest and, more importantly, during the first and second minute of DKE in addition to the third minute of DKE.

Despite not having any measurement of volitional effort, it could be argued that central command was less after training on the basis of reports from subjects that the exercise bouts were much easier to perform. A lower central command after training may have contributed to the suppression of MSNA during the third minute of DKE. However, as stated earlier, central command is not expected to have an effect during DKE.

Effect of Training on Arterial Pressure

Increase muscle oxidative capacity is associated with endurance training (4, 6). The attenuated blood pressure response to DKE after training may be related to an increase oxidative capacity of the quadriceps muscle after training. Wilson et al. (22) found a decreased pressor response to isometric contraction with the gastrocnemius after 21 days of low-frequency electrical stimulation of the tibial nerve. Chronic electrical stimulation in that study greatly enhanced the oxidative capacity of the muscle as measured by increased citrate synthase and succinate dehydrogenase activity. The lower MAP during DKE, particularly during the third minute, may be related to the lower MSNA that resulted from a decrease in metabosensitive muscle afferent activity after training. Moreover, decreased muscle afferent discharge from both group III and IV afferents may occur during dynamic exercise after training. Support for this concept comes from the work of Adreani and Kaufman (1). They found that the discharge of both group III and IV muscle afferents during dynamic exercise increased when arterial flow was occluded. They concluded that both group III and IV muscle afferents are sensitive to some unspecified substance produced by the muscle during dynamic exercise. If exercise training attenuates the production of this unknown substance, group III and IV muscle afferent activity would be expected to decrease and attenuate MSNA and blood pressure.

Effect of Training on Resting MSNA

Longitudinal training studies report increases (15), decreases (5), and no change (5, 14, 16–18) in resting MSNA. Most of these studies have used dynamic exercise as the training mode. One-legged training in the present study produced a significant increase in VO$_2$peak (19%) in the trained leg but failed to alter resting MSNA. The lack of a change in resting MSNA may be due to the limited muscle mass used in the training regimen. Grassi et al. (5) reported a significant decrease in resting MSNA after 10 wk of running. MSNA decreased from 21 to 14 bursts/min after training. Training elicited a 16% increase in maximal oxygen uptake. However, Sheldahl and co-workers (14) and Svedenhag et al. (18) reported no change in resting MSNA after 8–12 wk of two-legged cycle training that elicited a ~17 and ~7% increase in VO$_2$peak, respectively. These two studies would argue against muscle mass being a factor. It appears likely that longer aerobic training periods (e.g., >1 yr) are needed to consistently decrease resting MSNA. It should be noted that long-term resistance training may produce an increase in resting MSNA on the basis of greater resting MSNA in bodybuilders compared with sedentary controls (15).

In summary, 6 wk of dynamic one-legged training failed to alter resting MSNA but did prolong the decrease in MSNA during leg exercise. It appears that the continued suppression of MSNA during DKE after training is related to an attenuation of the muscle metaboreflex that, subsequently, prevents it from overriding the sympathoinhibitory effect of the cardiopulmonary baroreflex. The present study indicates that attenuation of MSNA to exercise reported with forearm training also occurs with leg training.

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