Muscle sympathetic nerve responses to passive and active one-legged cycling: insights into the contributions of central command

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INTRODUCTION

The existence of a feedforward central mechanism involved in regulating the neural response in anticipation of exercise has been known for over 100 years (23). In contrast, the involvement of these higher brain regions, termed central command, during exercise has been more difficult to isolate because of the concomitant influence of peripheral afferent reflexes (i.e., exercise pressor reflex, baroreflexes, chemoreflexes) (12). The methods used to quantify the neural contribution of central command have involved 1) neuromuscular blockade to reduce motor output and group III/IV muscle afferent feedback while increasing perception of effort (38, 44, 45), 2) comparison of similar-intensity voluntary and electrically evoked contractions (4, 8, 25) or passive and active zero-load exercise (31, 32, 40) (i.e., the same mechanical stimulus with or without central command), or 3) augmentation of central perception of effort through hypnosis (29, 47).

Data from these studies have consistently demonstrated an important role of central command in mediating the increase in heart rate during exercise (27, 32, 47) primarily through parasympathetic withdrawal (27). In contrast, the contribution of central command to the peripheral vasoconstrictor response is less clear. Studies using neuromuscular blockade have demonstrated that central command has minimal impact on muscle sympathetic nerve activity (MSNA), a direct measure of central sympathetic outflow, during low- to moderate-intensity static handgrip (44) but can increase MSNA during intense intermittent static handgrip (45). The inability of central command to augment MSNA at low to moderate intensities was also confirmed under sensory nerve blockade during static handgrip (38). In contrast, low-intensity electrically stimulated (involuntary) static bicep contractions increased MSNA, whereas similar-intensity voluntary contractions decreased MSNA, suggesting a potential sympathetic inhibitory role of central command at low intensities (25). Examination of the anticipatory period before leg cycling (and any peripheral afferent feedback) has also demonstrated reductions in MSNA (5).

An important limitation of prior microneurographic studies investigating central command is the reliance on primarily static, small-muscle mass, handgrip exercise that may not be comparable to dynamic large-muscle mass exercise more commonly associated with activities of daily living. Indeed, low- to moderate-intensity static handgrip and dynamic leg exercise produce divergent responses in MSNA (25, 37), with the
The subject completed a 20- to 30-W/min ramped cycle ergometer protocol to determine the workrate for 24 h. During the first study visit, participants were asked to abstain from caffeine and alcohol consumption and were separated by a 48-h washout period. An orientation visit, participants were asked to complete two self-assessment questionnaires for evidence of chronic disease, and not taking chronic medications with the exception of oral contraception (21, 25), and not taking chronic medications with the exception of oral contraception (21, 25).

Methods

Participants. Twenty-five healthy young men (n = 13) and women (n = 12) were recruited to complete the study. All were non-smokers, nonsmoking, in sinus rhythm, free of known cardiovascular or metabolic disease, and not taking chronic medications with the exception of oral contraception (n = 2). All procedures were approved by the University of Guelph Research Ethics Board.

Procedures and protocol. After completing written informed consent and an orientation visit, participants were asked to complete two study visits separated by 48 h. Before each study visit, participants were asked to abstain from caffeine and alcohol consumption and strenuous exercise for 24 h. During the first study visit, participants completed a 20- to 30-W/min ramped cycle ergometer protocol to peak effort to determine peak O₂ consumption (VO₂; Moxus Modular Metabolic System, AEI Technologies, Pittsburgh, PA). The starting resistance and magnitude of incremental increases were individualized based on exercise training status and daily physical activity levels, so that each participant reached maximum effort between 8 and 14 min. Peak VO₂ was represented as a percentage of that predicted by fitness.

The second study visit, each participant entered the laboratory after voiding and was seated in a comfortable chair with his/her left leg elevated on an ottoman and right leg strapped to a modified cycle ergometer secured to the floor (Rehab Trainer 881E, Monark Exercise, Vansbro, Sweden). After instrumentation, participants completed a 10-min quiet baseline session, with resting hemodynamic and neural variables acquired during the final 7 min. Subsequently, participants completed a 2-min baseline followed by 2 min of passive cycling, during which an investigator moved the right leg through the cycling motion at 50 revolutions/min. Investigators provided verbal reminders to all participants to avoid muscle contraction or aid in any way during the passive cycling motion. After 8–10 min of recovery to allow all hemodynamic and neural variables to return to baseline, participants completed another 2-min baseline followed by 2 min of active zero-load cycling at 50 revolutions/min.

Measurements. Absolute discrete minute-to-minute blood pressure was measured from the left arm by an automated sphygmomanometer (BPTru Medical Devices, Coquitlam, BC, Canada) while continuous beat-to-beat blood pressure was obtained via finger photoplethysmography (Finometer MIDl, Finapres Medical Systems, Enschede, The Netherlands) from the middle finger of the right hand. Heart rate data were collected from lead II of the electrocardiogram (AD Instruments, Bella Vista, NSW, Australia) while respiratory rate and depth (percent change from baseline) were monitored with a piezo-electric transducer belt (Pneumotrace II, UFA, Morro Bay, CA). Multiunit recordings of postganglionic MSNA were obtained using a 2-mΩ unipolar tungsten electrode (Frederick Haer, Brunswick, ME) inserted percutaneously into a muscle-nerve fascicle of the left peroneal (fibular) nerve, as previously described (26, 34, 35). The microelectrode was adjusted until bursts of spontaneous multiunit sympathetic activity were detected from the background noise. A ground electrode was placed ~2 cm away. The MSNA signal was amplified (×75,000), bandpass filtered (0.7–2.0 kHz), rectified, and integrated using a 0.1-s time constant to obtain the mean voltage neurogram (Nerve Traffic Analyzer, model 662C-4, Absolute Design and Manufacturing Services, Salon, IA). Muscle sympathetic activity was confirmed by reflexive increases in response to an end-expiration breath hold and lack of responsiveness to unexpected clapping. We have previously demonstrated the ability to collect and maintain microneurographic recordings during low- to moderate-intensity one-legged cycling (33).

To ensure no alteration in microelectrode position throughout each exercise and recording period, the neural signal was monitored both visually and audibly. If a shift in the neurogram was detected, the protocol was stopped and restarted after an 8- to 10-min recovery period. All continuous signals were collected at 1 kHz, with the exception of the raw neurogram, which was sampled at 10 kHz (PowerLab, AD Instruments).

Data analysis. MSNA was analyzed using a semiautomated custom LabVIEW program (National Instruments, Austin, TX) (26, 33–35). Determination of a sympathetic burst was based on a minimum 3:1 signal-to-noise ratio and alignment with the time-shift cardiac cycle. From the integrated neurogram, MSNA burst frequency (bursts/min) and burst incidence (bursts/100 heartbeats) were calculated. Total MSNA was calculated as the product of burst frequency and mean burst area and expressed as percent change from baseline, whereas MSNA burst amplitude was normalized to the tallest burst from the baseline period.

Spontaneous arterial sympathetic BRS was determined at rest and during each 2-min exercise period using the sequence technique (LabChart v8, AD Instruments). Briefly, we identified three consecutive and concurrent increases in heart rate and mean arterial pressure and R-R interval with minimum threshold changes of 1 mmHg and 6 ms, respectively (36). A zero lag between systolic blood pressure and R-R interval was used for heart rate < 75 beats/min, whereas a one-beat lag was used for heart rates > 75 beats/min (9). Previous analysis has shown that lag parameters can impact the number of identified sequences but produce comparable cardiac BRS (9). All sequences were carefully reviewed, and cardiac BRS was quantified by plotting R-R interval over systolic blood pressure for each identified series and averaging the slope of all up sequences, all down sequences, and the average of all sequences. Sequences were deemed acceptable to use if the regression coefficient (r) was > 0.8 and a minimum of three up and three down sequences were identified; five participants did not meet these criteria.

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Table 1. Baseline characteristics of participants

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean ± SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, men/women</td>
<td>9/9</td>
<td></td>
</tr>
<tr>
<td>Age, yr</td>
<td>22 ± 3</td>
<td>18–28</td>
</tr>
<tr>
<td>Height, cm</td>
<td>172 ± 10</td>
<td>153–184</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>66 ± 12</td>
<td>46–88</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>22 ± 3</td>
<td>18–28</td>
</tr>
<tr>
<td>Peak VO₂, ml/kg·min⁻¹</td>
<td>53 ± 12</td>
<td>28–76</td>
</tr>
<tr>
<td>Predicted peak VO₂, %</td>
<td>126 ± 28</td>
<td>90–181</td>
</tr>
<tr>
<td>Heart rate, beats/min</td>
<td>60 ± 10</td>
<td>49–83</td>
</tr>
<tr>
<td>Blood pressure, mmHg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>104 ± 11</td>
<td>87–123</td>
</tr>
<tr>
<td>Diastolic</td>
<td>64 ± 6</td>
<td>52–72</td>
</tr>
<tr>
<td>MSNA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Burst frequency, bursts/min</td>
<td>25 ± 6</td>
<td>15–39</td>
</tr>
<tr>
<td>Burst incidence, bursts/100 heartbeats</td>
<td>44 ± 13</td>
<td>22–72</td>
</tr>
</tbody>
</table>

VO₂: O₂ consumption; MSNA, muscle sympathetic nerve activity.

pressure bins) was included in the assessment of sympathetic BRS (17, 18). For sympathetic baroreflex control of burst occurrence, the slope of the line was accepted as valid if \( r \) was \( \geq 0.5 \); three participants failed to meet this criterion during the exercise periods. However, as previously demonstrated (22), a weaker relationship exists between diastolic blood pressure and MSNA burst strength; therefore, all slopes were included regardless of the \( r \) value. To confirm that the use of all slopes did not confound our data, we also examined only slopes with \( r \geq 0.5 \) and observed that the interpretation of results was unchanged.

Statistical analysis. The change in hemodynamic and neural variables during the first and second minute of passive and active zero-load cycling was compared using two-way repeated-measures ANOVA (GraphPad Software, La Jolla, CA). Significant main effects and interactions were probed using Bonferroni’s post hoc tests to assess differences between means. Two-way repeated-measures ANOVAs were used to examine the changes in cardiac and sympathetic BRS during passive and active cycling. Paired \( t \)-tests were used to compare the two baseline periods. To probe the effects of participant fitness, the median percent predicted peak VO₂ was calculated for men and women separately (to ensure equal balance in the groups). The baseline characteristics between normal- and high-fit groups were assessed with unpaired \( t \)-tests. \( P < 0.05 \) was considered statistically significant, and all data are presented as means ± SD unless otherwise stated.

RESULTS

Twenty-five participants were recruited to complete the study; of these, seven participants were excluded: two participants because of the inability to locate a microneurographic recording site at baseline and five participants because of the inability to maintain microneurographic recordings during voluntary exercise periods. Baseline characteristics of participants with complete MSNA data (\( n = 18 \), 9 men) are shown in Table 1. Representative 30-s MSNA recordings from one participant at rest and during passive and active zero-load one-legged cycling are shown in Fig. 1.

As expected, the absolute resting levels of all variables were similar during passive and active baseline periods (all \( P > 0.05 \)), although heart rate was elevated slightly during the active baseline (62 ± 11 vs. 64 ± 11 beats/min, \( P = 0.007 \)). The effects of passive and active zero-load cycling on hemodynamic and respiration responses are shown in Table 2. Blood pressure, stroke volume, and respiration depth increased during exercise (time effect, \( P < 0.0001 \)) but were not different between passive and active cycling (\( P > 0.05 \)). In contrast, the increases in heart rate, cardiac output, total vascular conductance, and respiration rate were greater during the first and second minute of active zero-load cycling (all \( P < 0.01 \)). MSNA burst frequency and incidence decreased during passive and active zero-load cycling (time effect, \( P < 0.0001 \)), but no differences were detected between exercise modes (both \( P > 0.05 \); Fig. 2). However, the reductions in total MSNA were attenuated during the first (\( P < 0.0001 \)) and second (\( P < 0.001 \)) minute of active zero-load cycling (Fig. 2). MSNA burst amplitude was also higher during the first (\( P < 0.05 \)) and second (\( P < 0.01 \)) minute of active zero-load cycling (Fig. 2).

Cardiac BRS was similar between baseline periods (17 ± 9 vs. 15 ± 5 ms/mmHg, \( P > 0.05 \)) but lower during active than

### Table 2. Mean change in hemodynamic variables during the first and second minute of passive (involuntary) and active (voluntary) zero-load cycling

<table>
<thead>
<tr>
<th>Variable</th>
<th>Passive Cycling</th>
<th>Active Cycling</th>
</tr>
</thead>
<tbody>
<tr>
<td>First minute</td>
<td>Second minute</td>
<td>First minute</td>
</tr>
<tr>
<td>Heart rate, beats/min</td>
<td>3 ± 4</td>
<td>2 ± 4</td>
</tr>
<tr>
<td>Blood pressure, mmHg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>4 ± 4</td>
<td>5 ± 3</td>
</tr>
<tr>
<td>Diastolic</td>
<td>1 ± 2</td>
<td>3 ± 2</td>
</tr>
<tr>
<td>Stroke volume, ml</td>
<td>4 ± 4</td>
<td>4 ± 5</td>
</tr>
<tr>
<td>Cardiac output, l/min</td>
<td>0.5 ± 0.5</td>
<td>0.4 ± 0.4</td>
</tr>
<tr>
<td>Total vascular conductance, ml·min⁻¹·mmHg</td>
<td>3.7 ± 4.9</td>
<td>2.2 ± 3.9</td>
</tr>
<tr>
<td>Respiration rate, breaths/min</td>
<td>2 ± 2</td>
<td>3 ± 2</td>
</tr>
<tr>
<td>Respiration depth, %</td>
<td>24 ± 28</td>
<td>27 ± 25</td>
</tr>
</tbody>
</table>

Values are means ± SD. *\( P < 0.01 \) vs. passive cycling at the same time point.
passive cycling (17 ± 9 vs. 11 ± 5 ms/mmHg, P = 0.0002). Similarly, the sensitivity of arterial baroreflex control of MSNA burst occurrence was comparable during baseline periods (P > 0.05) but lower during active zero-load cycling (P = 0.01; Fig. 3). In contrast, there were no differences in the sensitivity of arterial baroreflex control of MSNA burst area at rest or during exercise (P > 0.05; Fig. 3).

Effects of fitness. Eight individuals (4 men and 4 women) were allocated to the normal-fitness group and 10 (5 men and 5 women) to the high-fitness group. Age and height were matched between the groups (both P > 0.05), although body weight (61 ± 10 vs. 71 ± 11 kg, P = 0.05), body mass index (21 ± 2 vs. 24 ± 2 kg/m²), peak V\textsubscript{O\textsubscript{2}} (2.8 ± 1.0 vs. 4.2 ± 1.0 l/min), and predicted peak V\textsubscript{O\textsubscript{2}} (99 ± 11 vs. 150 ± 13%) were higher in the high-fitness group (all P < 0.01). Resting blood pressure was similar between groups (both P > 0.05; data not shown), although the high-fitness group exhibited a trend for lower resting heart rate (66 ± 12 vs. 58 ± 7 beats/min, P = 0.08). Resting MSNA burst frequency and incidence were similar between normal- and high-fitness groups (both P > 0.05; data not shown). Mean group changes in hemodynamic and MSNA variables during passive and active zero-load cycling are shown in Table 3. There were no between-group differences in blood pressure, stroke volume, cardiac output, or respiratory responses (all P > 0.05), whereas increases in heart rate (P < 0.002) and total vascular conductance (P = 0.06) during active cycling were (or tended to be) larger in the high-fitness group. No significant group or interaction effects were detected for MSNA burst frequency, burst incidence, total MSNA, burst amplitude, or sympathetic BRS (all P > 0.05). In contrast, the high-fitness group exhibited a trend toward a greater decrease in cardiac BRS during active cycling (−1 ± 4 vs. −6 ± 5 ms/mmHg, P = 0.09).

DISCUSSION

The present study examined the contributions of central command to the regulation of central sympathetic outflow to skeletal muscle during dynamic one-legged cycling exercise. The principal finding was that reductions in MSNA burst occurrence (frequency or incidence) were similar between passive (involuntary) and active (voluntary) zero-load cycling but that reductions in total MSNA were attenuated and MSNA burst amplitude was higher during active cycling. In concert,
the sensitivity of arterial baroreflex control of MSNA burst occurrence was attenuated with active cycling, whereas arterial baroreflex control of MSNA burst strength was unaltered. These results demonstrate that central feedforward mechanisms are involved primarily in modulating the strength, but not the occurrence, of a sympathetic burst during dynamic exercise, consistent with the proposition that sympathetic activity is modulated at two distinct sites controlling strength and occurrence (22). Furthermore, central command appears to be involved in resetting the sensitivity of arterial baroreflex control of heart rate and MSNA burst occurrence during dynamic exercise. Preliminary subgroup analyses affirmed that changes in MSNA burst occurrence and total MSNA during passive and active cycling were not impacted by cardiorespiratory fitness level.

The modulation of peripheral sympathetic activity by central command during exercise has been difficult to isolate and is based primarily on models of handgrip exercise (12, 44, 45). In contrast to consistent increases in MSNA during low- to moderate-intensity static handgrip (25), similar-intensity dynamic exercise decreases MSNA secondary to the engagement of the sympathoinhibitory cardiopulmonary baroreflex (20, 37). Given that afferent input may modulate central command (1, 46), we sought to characterize these central contributions to the sympathetic response to dynamic exercise by comparing passive and active zero-load one-legged cycling. Although this method does not permit examination across varying exercise intensities, our model has the advantage of not requiring pharmacological blockade or electrically evoked muscle contractions. Furthermore, stroke volume and blood pressure responses were comparable between passive and active cycling, limiting differences in arterial baroreflex stimulation; respiratory depth was also similar between exercise modes. The novel finding was that MSNA burst frequency and incidence decreased similarly during passive and active cycling while reductions in total MSNA were attenuated (and MSNA burst amplitude increased) during active cycling. The effects of central command on total MSNA and burst amplitude (i.e., differences between passive and active cycling) were consistent at ~20% and ~7%, respectively, during the first and second minute of active zero-load cycling.

A number of studies have demonstrated the capacity to differentially control MSNA burst occurrence and strength (burst area or amplitude) in response to a stress (15, 43). For example, peripheral chemoreflex activation with hypoxia is associated with MSNA burst amplitude but not frequency (43), whereas the application of mental stress using the color-word test can alter total MSNA without impacting burst frequency (15). Comprehensive examination of sympathetic neuron firing patterns supports differences in recruitment strategies between neural pathways (24, 42); baroreflex unloading increases primarily the firing frequency of already discharging neurons (24), whereas chemoreflex activation recruits larger previously silent neurons (42). These findings build on earlier work showing that the arterial baroreflex exerts a strong influence over the firing of a multunit MSNA burst (as demonstrated by the strength of the relationship between diastolic blood pressure and MSNA burst incidence) but only a weak association with MSNA burst strength (10, 22). From these data, it was proposed that the arterial baroreflex serves as the principal regulator of whether a burst occurs or not (gating) but that the strength of a burst is determined by the integration of all peripheral and central inputs (22). Our results are consistent with this hypothesis, as central command modulated sympathetic outflow primarily through changes in the strength, but not the occurrence, of a MSNA burst.

It is now widely appreciated that during exercise the arterial baroreflex is reset rapidly to a higher operating pressure by feedback from group III/IV skeletal muscle afferents and feedforward input from central command, enabling proper coordination of neural outputs and regulation of cardiovascular responses (11). Similar to the present results, the sensitivity of arterial baroreflex control of MSNA burst occurrence has been reported to be reduced across a wide range of leg-cycling intensities, without a change in the sensitivity of arterial baroreflex control of MSNA burst strength (16). Our results extend these observations by suggesting that 1) muscle mechanoreflex activation using passive exercise does not impact sympathetic BRS, 2) the reduced sympathetic BRS of MSNA burst occurrence during active cycling is attributable primarily to the engagement of central command, and 3) central command has limited influence on arterial baroreflex control of MSNA burst strength. It is important to acknowledge also that differences in cardiopulmonary baroreflex loading during passive and active cycling could contribute to the modulation of sympathetic BRS. It has been reported that head-down tilt or saline infusion, stimuli that increased central venous pressure by ~2 mmHg, reduced sympathetic, but not cardiac, BRS, although both loading conditions also increased systolic blood pressure (7). However, given that blood pressure and stroke volume responses were similar between passive and active conditions, cardiac BRS was attenuated during active cycling, and the intensity of our one-legged-cycling model was mild, we do not believe that differences in loading conditions contributed to our results. Nevertheless, future studies are needed to examine the interaction between central command and the cardiopulmonary baroreflex on sympathetic BRS.

### Table 3. Mean change in hemodynamic and MSNA variables during passive (involuntary) and active (voluntary) zero-load cycling in normal- and high-fitness participants

<table>
<thead>
<tr>
<th>Variable</th>
<th>Normal Fitness (n = 8)</th>
<th>High Fitness (n = 10)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Passive</td>
<td>Active</td>
</tr>
<tr>
<td>Heart rate, beats/min</td>
<td>1 ± 2</td>
<td>6 ± 3</td>
</tr>
<tr>
<td>Blood pressure, mmHg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>4 ± 3</td>
<td>8 ± 4</td>
</tr>
<tr>
<td>Diastolic</td>
<td>1 ± 2</td>
<td>4 ± 3</td>
</tr>
<tr>
<td>Stroke volume, ml</td>
<td>4 ± 4</td>
<td>8 ± 7</td>
</tr>
<tr>
<td>Cardiac output, l/min</td>
<td>0.4 ± 0.2</td>
<td>1.0 ± 0.9</td>
</tr>
<tr>
<td>Total vascular conductance, ml^-1·mmHg</td>
<td>3.0 ± 2.9</td>
<td>8.1 ± 8.0</td>
</tr>
<tr>
<td>Respiration rate, breaths/min</td>
<td>2 ± 2</td>
<td>3 ± 1</td>
</tr>
<tr>
<td>Respiration depth, %</td>
<td>15 ± 9</td>
<td>27 ± 15</td>
</tr>
<tr>
<td>MSNA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Burst frequency, bursts/min</td>
<td>−5 ± 5</td>
<td>−3 ± 5</td>
</tr>
<tr>
<td>Burst incidence, bursts/100</td>
<td>−7 ± 7</td>
<td>−6 ± 7</td>
</tr>
<tr>
<td>heartbeats</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total, %</td>
<td>−28 ± 16</td>
<td>−8 ± 16</td>
</tr>
<tr>
<td>Burst amplitude, %</td>
<td>2 ± 5</td>
<td>5 ± 11</td>
</tr>
</tbody>
</table>

Values are means ± SD; n, number of participants. MSNA, muscle sympathetic nerve activity. *P < 0.05 and †P < 0.01 vs. normal fitness during the same exercise mode.
**Influence of fitness.** Prior evidence that unilateral exercise training can attenuate diastolic blood pressure and heart rate responses to voluntary, but not electrically evoked, static contractions in the untrained limb suggests that central command can be modified by training status (13). Similarly, trained sprinters demonstrate attenuated heart rate responses to the onset of both passive and voluntary exercise compared with untrained participants (40). We investigated the effects of fitness by segregating our data into “normal”- and “high”-fitness groups based on median predicted peak VO_2_. Although no hemodynamic differences were found between fitness groups during passive cycling, a greater increase in heart rate and total vascular conductance was observed in the high-fitness group during active zero-load cycling. Endurance exercise training is associated with increases in cardiac vagal modulation (41), which could enable greater parasympathetic withdrawal during activation of central command (32). The trend toward a larger attenuation in cardiac BRS during active cycling in the high-fitness group may support this concept. As MSNA did not differ between the normal- and high-fitness groups, the greater increase in total vascular conductance may be associated with enhanced endothelium-dependent smooth muscle function, or functional sympatholysis (28, 30). Future work is required to prospectively test the influence of exercise training on central command and its influence on MSNA responses.

**Methodological considerations.** First, because of difficulties in maintaining a microneurographic recording site during dynamic muscle contractions, MSNA was collected from the contralateral resting leg. Preliminary evidence has supported similar patterns of sympathetic discharge between resting and active limbs during static contractions with ischemia (14). More recently, MSNA has been measured from the exercising leg during static dorsiflexion (3, 4). The frequency of cardiac synchronized sympathetic spikes increased during low-intensity voluntary static dorsiflexion but was unchanged during comparable electrically stimulated contraction, suggesting a sympathoexcitatory role of central command (4). Unfortunately, this prior study (4) did not differentiate between the percentage of cardiac cycles with a sympathetic spike (occurrence) and the number of spikes per cardiac cycle (strength), although secondary analysis showed that the proportional increase from baseline in multiunit MSNA burst amplitude (Δ48%) was larger than burst frequency (Δ22%) during voluntary static dorsiflexion. Second, in the present study, the order of passive and active cycling modes was not randomized in an effort to reduce the risk of carryover effects from active voluntary exercise. However, as anticipated, the absolute rest- and exercise pressor reflex (21, 27) would blunt the reductions in MSNA and could underestimate the impact of central command. However, no differences were observed in systolic or diastolic blood pressure responses, suggesting a similar recruitment of the exercise pressor reflex in both exercise modes. Fifth, spontaneous methods for quantifying cardiac and sympathetic BRS do not provide the temporal resolution to examine dynamic changes in arterial baroreflex resetting, which may occur at the onset of cycling (2). Finally, our study population was limited to young healthy individuals with normal or above-average exercise capacity. Older adults have been shown to rely more heavily on central command to reset the cardiac baroreflex during moderate-intensity static calf exercise (6), which could impact the relative contribution to the MSNA response.

**Conclusions.** The present study is the first to investigate the contribution of central command to the regulation of MSNA during dynamic exercise. In contrast to our hypothesis, MSNA burst frequency and incidence responses to passive and active zero-load cycling were similar, suggesting no impact of central command. However, comparison of total MSNA and burst amplitude responses did reveal a sympathoexcitatory role of central command. Together, these results are consistent with the concept that sympathetic burst occurrence and strength can be regulated independently (22). In addition, central command was involved in attenuating the sensitivity of cardiac BRS and sympathetic burst occurrence BRS but did not alter arterial baroreflex control of MSNA burst strength.

**DISCLOSURES**

No conflicts of interest, financial or otherwise, are declared by the authors.

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