Influence of age and sex on the pressor response following a spontaneous burst of muscle sympathetic nerve activity

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Vianna LC, Hart EC, Fairfax ST, Charkoudian N, Joyner MJ, Fadel PJ. Influence of age and sex on the pressor response following a spontaneous burst of muscle sympathetic nerve activity. Am J Physiol Heart Circ Physiol 302: H2419–H2427, 2012. First published March 16, 2012; doi:10.1152/ajpheart.01105.2011.—The sympathetic nervous system is critical for the beat-to-beat regulation of arterial blood pressure (BP). Although studies have examined age- and sex-related effects on BP control, findings are inconsistent and limited data are available in postmenopausal women. In addition, the majority of studies have focused on time-averaged responses without consideration for potential beat-to-beat alterations. Thus, we examined whether the ability of muscle sympathetic nerve activity (MSNA) to modulate BP on a beat-to-beat basis is affected by age or sex. BP and MSNA were measured during supine rest in 40 young (20 men) and 40 older (20 men) healthy subjects. Beat-to-beat fluctuations in mean arterial pressure (MAP) were characterized for 15 cardiac cycles after each MSNA burst using signal averaging. The rise in MAP following an MSNA burst was similar between young men and women (+2.64 ± 0.3 vs. +2.57 ± 0.3 mmHg, respectively). However, the magnitude of the increase in MAP after an MSNA burst was reduced in older compared with young subjects (P < 0.05). Moreover, the attenuation of the pressor response was greater in older women (+1.20 ± 0.1 mmHg) compared with older men (+1.72 ± 0.2 mmHg; P < 0.05). Interestingly, in all groups, MAP consistently decreased after cardiac cycles without MSNA bursts (nonbursts) with the magnitude of fall greatest in older men. In summary, healthy aging is associated with an attenuated beat-to-beat increase in BP after a spontaneous MSNA burst, and this attenuation is more pronounced in postmenopausal women. Furthermore, our nonburst findings highlight the importance of sympathetic vasoconstrictor activity to maintain beat-to-beat BP, particularly in older men.

THE PREVALENCE OF HYPERTENSION increases with age in both sexes; however, postmenopausal women are at the greatest risk (23, 26, 28, 47, 49). The underlying mechanisms for this increased risk and differential age effect in men and women remain incompletely understood. Although structural (25, 36) and hormonal (43, 44, 49) factors likely contribute, an age-related increase in sympathetic nerve activity (SNA) has also been implicated as a key factor (20, 28, 29).

The sympathetic nervous system and its ability to modulate vascular tone are paramount for the regulation of arterial blood pressure (BP). Studies using systemic pharmacological blockades (3, 20, 35) or correlational analyses (15, 28, 29) have indicated both age and sex differences in the regulation of resting muscle SNA (MSNA) and BP. However, findings are inconsistent and limited data are available in older postmenopausal women. An important caveat in these studies is the degree to which spontaneous bursts of MSNA actually cause a rise in BP. In this regard, Wallin and Nerhed (46) reported a peak rise in BP of 2 to 3 mmHg occurring ~5.5 s following a spontaneous burst of MSNA. However, these initial analyses were performed on a heterogeneous group of subjects without consideration for the potential influence of aging or sex on the transduction of MSNA into a change in arterial BP. Surprisingly, to date, no studies have investigated how age and sex affect the ability of the sympathetic nervous system to regulate BP on a beat-to-beat basis. Importantly, an augmentation in the beat-to-beat oscillations in BP has been demonstrated with age (39), and this increased variability is suggested to be associated with end organ damage (27, 32–34). However, the cause of these fluctuations is not completely understood.

With this background in mind, the purpose of the current study was to provide a comprehensive examination of beat-to-beat changes in BP evoked by individual bursts of MSNA in healthy young and older men and women. This was accomplished by directly recording MSNA from the peroneal nerve along with beat-to-beat BP and applying signal averaging to compare the magnitude of the rise in BP following a spontaneous burst of MSNA. Given previous studies demonstrating greater sympathetic support of BP and increased BP variability with age (20, 39), we hypothesized that the magnitude of the increase in BP following a burst of MSNA is augmented in older compared with younger subjects. Furthermore, considering the hormonal changes associated with menopause and also epidemiological data showing a higher prevalence of hypertension in women with age (26, 47), we further hypothesized that the augmentation of the pressor response is more pronounced in older women compared with older men.

METHODS

Subjects. Forty young (20 men) and 40 older (20 men) healthy subjects participated in this study. Studies were performed in a clinical research laboratory at the Mayo Clinic [n = 56; 30 young (16 men) and 26 older (13 men) subjects] and at the University of Missouri [n = 24; 10 young (4 men) and 14 older (7 men) subjects]. The records used were retrospectively analyzed from previous (13–15, 50) and ongoing studies in the respective laboratories. Of note, all data were taken during an initial baseline period before any type of intervention. The subjects were nonsmokers with no history of cardiovascular or other chronic diseases and none were using prescribed or over-the-counter medications. To minimize the effects of reproductive hor-
mones on autonomic control of cardiovascular function, all the young women were studied in the early follicular phase of the menstrual cycle or in the low hormone phase of oral contraceptive use. In addition, all older postmenopausal women were not using hormone replacement therapy. Participants were instructed to abstain from caffeinated beverages and food for at least 12 hours and alcohol for 24 hours before the study. After receiving a detailed verbal and written explanation of the intended experimental protocol and measurements, each subject provided written informed consent. All experimental procedures and protocols conformed to the Declaration of Helsinki and were approved by the Mayo Clinic Foundation and the University of Missouri Health Sciences Institutional Review Board.

**Experimental measurements.** On arrival to the laboratory, the subjects rested in the supine position during instrumentation. Arterial BP was measured either by direct arterial catheterization ($n = 54$) or finger photoplethysmography (Finometer; Finapres Medical Systems BV, Arnhem, The Netherlands; $n = 26$). Previous studies have reported similar beat-to-beat changes in BP measured by Finometer and arterial line (11, 38). For arterial catheterization, local anesthesia with 2% lidocaine was applied and a 5-cm, 20-gauge catheter was inserted into the brachial artery of the non-dominant arm, using aseptic techniques. The catheter was connected to a pressure transducer and interfaced with a personal computer to monitor beat-to-beat arterial BP. For finger photoplethysmography absolute Finometer values were validated with an automated sphygmomanometer. Heart rate (HR) was continuously monitored using a lead II electrocardiogram. Respiratory movements were monitored using a strain gauge pneumobelt placed around the subject’s abdomen. Multiunit recordings of post-ganglionic MSNA were obtained by inserting a unipolar tungsten microelectrode percutaneously through the intact skin and positioned into muscle nerve fascicles of the peroneal nerve near the fibular head. The nerve signal was processed by a pre-amplifier and an amplifier (Dept. of Bioengineering, University of Iowa, Iowa City, IA), band-pass filtered (bandwidth 700–2,000 Hz), rectified, and integrated (time constant, 0.1 s) to obtain a mean voltage neurogram. Muscle SNA recordings were identified by their characteristic pulse-synchronous burst pattern and increased neural activity in response to an end-expiratory apnea or Valsalva maneuver, without any response to arousal stimuli or stroking of the skin (31, 42, 50).

Experimental protocol: comparing beat-to-beat changes in BP following a spontaneous burst of MSNA in young and older men and women. While the subject rested quietly in the supine position in a dimly lit room, a minimum of 5 min ($9.3 \pm 0.7$ min) of baseline data were continuously recorded. Symphathetic bursts in the integrated neurogram were identified using a custom-built automated analysis program; burst identification was then corrected via visual inspection by a single observer (L. C. Vianna). Sympathetic activity was quantified using standard measures, including burst frequency (in bursts/min) and burst incidence (in bursts/100 heart beats). The relationship between each individual spontaneous burst of MSNA and the ensuing changes in mean arterial pressure (MAP) were characterized by using a signal-averaging technique, as described in detail elsewhere (46). Briefly, MAP measured during the cardiac cycle in which a sympathetic burst occurred was utilized to calculate changes of MAP from that value in the succeeding 15 cardiac cycles. This procedure was repeated for all cardiac cycles associated with a sympathetic burst, and the resulting mean changes of MAP were then calculated for each subject. MAP was used as the primary endpoint for this analysis; however, analyses were also performed for systolic and diastolic BP. We also repeated this procedure for those cardiac cycles that were not associated with a sympathetic burst (i.e., nonbursts). In addition, to understand the potential influence of variations in burst size on the pressor responses following a sympathetic burst, each subject had their sympathetic bursts divided into quartiles according to the height of the burst. To do this, the average height of the three highest bursts in the baseline segment was assigned a value of 100 (arbitrary units), and all other bursts within a trial were normalized with respect to this value. Beat-to-beat changes in BP following a MSNA burst were then put into quartiles based on the relative height of the burst.

Beat-to-beat changes in cardiac output (CO) and total vascular conductance (TVC) were also calculated and characterized for the 15 cardiac cycles following a burst of MSNA. Briefly, stroke volume was estimated from the arterial BP waveform (resampled at 100 Hz) using the Modelflow method through Beatscope (TNO-TPD; Biomedical Instrumentation, Amsterdam, The Netherlands), which incorporates age, sex, weight, and height adjustments. Modelflow is a nonlinear three-element model that uses the arterial input impedance, the compliance of the aorta, and total peripheral resistance to describe the relationship between aortic flow and pressure and thus compute stroke volume, as described in detail previously (18, 19, 48). This method has been shown to provide accurate beat-to-beat changes in CO (22, 48). TVC was calculated from the ratio of CO and MAP. MAP was calculated from the integral of the arterial pressure waveform.

**Statistical analysis.** Statistical analyses were conducted using the SPSS statistical software package for Microsoft Windows (version 19.0; SPSS, Chicago, IL). For resting cardiovascular variables, a univariate ANOVA was performed with two independent factors (age × sex). Beat-to-beat data were compared using a three-way repeated measures ANOVA followed by Bonferroni post hoc tests. Reproducibility of the MAP changes following MSNA bursts in each group was calculated by comparing the first and the second half of each subject’s baseline record using Intraclass Correlation Coefficients (ICC). Coefficient of variation for BP was calculated as the standard deviation divided by the mean. All tests were two-sided, and a $P$ value $<0.05$ was considered statistically significant. Group data are presented as means ± SE. For presentation purposes, all figures are displayed using 10 rather than all 15 cardiac cycles following an MSNA burst.

**RESULTS**

**Resting neural and cardiovascular variables.** Subject characteristics and the average resting neural and hemodynamic variables in young and older men and women are presented in Table 1. Body mass index was slightly but significantly greater in older subjects. MAP and systolic BP were significantly higher in older compared with young subjects ($P = 0.002$ and $P = 0.003$, respectively), whereas diastolic BP was similar between groups. No sex differences were observed in resting BP. HR was significantly higher in young and older women compared with the young and older men ($P = 0.026$). These differences in HR between groups were not dependent on age. MSNA was higher in older compared with young subjects expressed as burst frequency ($P < 0.001$) and burst incidence ($P < 0.001$). No sex differences were observed in resting MSNA. Respiratory rate (in breaths/min) was not different among the groups ($13.4 \pm 0.6$ young men, $13.3 \pm 0.5$ young women, $12.4 \pm 0.7$ older men, and $12.6 \pm 0.8$ older women; age, $P = 0.263$; sex, $P = 0.952$; interaction, $P = 0.732$). BP variability measured using coefficient of variation (in percentage) for MAP was also not affected by age or sex ($3.5 \pm 0.3$ young men, $3.6 \pm 0.2$ young women, $4.2 \pm 0.4$ older men, and $3.3 \pm 0.2$ older women; age, $P = 0.423$; sex, $P = 0.152$; interaction, $P = 0.052$).

**Beat-to-beat changes in BP following a spontaneous burst of MSNA in young and older men and women.** Examples of signal averaging for a young and older man (Fig. 1A) and a young and older woman (Fig. 1B) are shown in Fig. 1. Figure 2A shows the beat-to-beat increases in MAP for young and older men and women following a burst of MSNA. There was no difference in
the magnitude of the peak rise in MAP between young men and women (Fig. 2B). However, the magnitude of the increase in MAP following a MSNA burst was reduced in older compared with young subjects (+1.46 ± 0.1 mmHg older vs. +2.60 ± 0.2 mmHg young; \( P < 0.001 \)). In addition, the attenuation of the pressor response was more pronounced in older women compared with older men (+1.20 ± 0.1 mmHg older women vs. +1.72 ± 0.2 mmHg older men; \( P = 0.04 \)). Similar age and sex differences were observed when analyses were performed with systolic and diastolic BP (data not shown). The ICC for changes in MAP following MSNA bursts between the first and second half of each subject’s baseline record were high and significant (\( P < 0.001 \)) in all groups, indicating reproducible and reliable measurements: young men (ICC = 0.86, 95% CI of 0.65 to 0.95), young women (ICC = 0.82, 95% CI of 0.51 to 0.93), older men (ICC = 0.88, 95% CI of 0.69 to 0.95), and older women (ICC = 0.92, 95% CI of 0.78 to 0.97). After a spontaneous MSNA burst the latency to the peak increase in MAP was significantly longer (\( P < 0.001 \)) in the older (7.2 ± 0.5 s men vs. 7.1 ± 0.6 s women) compared with young group (5.6 ± 0.4 s men vs. 5.4 ± 0.3 s women), with no significant sex effect in either group.

The beat-to-beat changes in MAP for those cardiac cycles that were not associated with a sympathetic burst are presented in Fig. 3A. In all groups, MAP consistently decreased following cardiac cycles without MSNA bursts (Fig. 3). However, the

**Table 1. Subject characteristics and resting neural cardiovascular variables**

<table>
<thead>
<tr>
<th></th>
<th>Age, years</th>
<th>Body Mass Index, kg/m²</th>
<th>Blood Pressure, mmHg</th>
<th>Heart Rate, beats/min</th>
<th>Burst Frequency, bursts/min</th>
<th>Burst Incidence, bursts/100 beats</th>
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<tbody>
<tr>
<td><strong>Young</strong></td>
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<tr>
<td>Men</td>
<td>26 ± 1</td>
<td>25 ± 1</td>
<td>131 ± 3</td>
<td>73 ± 2</td>
<td>92 ± 3</td>
<td>59 ± 2</td>
</tr>
<tr>
<td>Women</td>
<td>25 ± 1</td>
<td>23 ± 1</td>
<td>127 ± 2</td>
<td>72 ± 1</td>
<td>92 ± 1</td>
<td>65 ± 2</td>
</tr>
<tr>
<td><strong>Older</strong></td>
<td></td>
<td></td>
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<tr>
<td>Men</td>
<td>61 ± 1</td>
<td>27 ± 1</td>
<td>138 ± 3</td>
<td>72 ± 4</td>
<td>98 ± 2</td>
<td>60 ± 2</td>
</tr>
<tr>
<td>Women</td>
<td>60 ± 2</td>
<td>25 ± 1</td>
<td>139 ± 3</td>
<td>71 ± 2</td>
<td>98 ± 2</td>
<td>63 ± 2</td>
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<table>
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<tr>
<th>( P ) value</th>
<th>Age</th>
<th>Sex</th>
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<tr>
<td></td>
<td>&lt;0.001</td>
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<td>0.891</td>
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<td></td>
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<td>0.781</td>
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Values are means ± SE.

Fig. 1. Examples of the signal averaging for a young and older man (A) and a young and older woman (B) illustrating the changes in mean arterial pressure (MAP) following spontaneous bursts of muscle sympathetic nerve activity (MSNA). The dashed lines represent the average MAP response for 10 MSNA bursts, and the thick line represents the mean MAP response for all MSNA bursts in the baseline segment.
magnitude of fall in MAP was greatest in older men (Fig. 3B; $P < 0.001$). Similar age and sex differences for cardiac cycles without bursts were observed when analyses were performed with systolic and diastolic BP (data not shown).

**Beat-to-beat changes in TVC and CO following a spontaneous burst of MSNA in young and older men and women.** Along with increases in MAP, TVC decreased following a MSNA burst in all groups (Fig. 4A). When compared with young men and women, the magnitude of decrease in TVC was attenuated in the older men and women ($P < 0.001$). When cardiac cycles without an MSNA burst were taken into consideration, TVC was increased in all groups (Fig. 4B). However, increases in TVC were greater in older compared with young subjects ($P < 0.001$). There was also a sex effect in which men exhibited greater increases in TVC compared with women (Fig. 4B; $P < 0.001$). In regards to CO, beat-to-beat changes following a MSNA burst did not reveal any sex differences ($P = 0.376$), but there was an age effect ($P < 0.001$) with smaller changes in the older subjects, particularly the older women (Fig. 5A). Importantly, CO appeared to contribute mainly to the initiation of the pressor response since at the time of the peak MAP response CO was near or below baseline in all groups. The changes in CO for cardiac cycles without an MSNA burst were minimal, although a sex effect was observed (Fig. 5B; $P = 0.006$).

**DISCUSSION**

A major novel finding of this study is that the magnitude of rise in BP following a spontaneous burst of MSNA was significantly reduced in older subjects, an effect that was more marked in postmenopausal women. Moreover, when no burst of MSNA occurred, a fall in BP was observed in all groups demonstrating the importance of SNA for the beat-to-beat maintenance of BP. Notably, the older men had the largest fall in BP following cardiac cycles without a burst, whereas older women responded similarly to young men and women. These
data suggest older men are highly reliant on SNA for the beat-to-beat maintenance of BP and may help explain the greater resting MSNA in this group. In contrast, the small increase in BP following a MSNA burst combined with the slight fall when no bursts were present suggests that SNA has minimal influences on resting beat-to-beat fluctuations in BP in older women. Collectively, these findings provide novel insight into underlying age and sex differences in the sympathetic control of beat-to-beat BP in healthy individuals.

Several studies have shown that the sympathetic nervous system plays an important role in the development of hypertension (7, 9, 12); however, this is not a universal finding (21). Although it is clear that resting MSNA is elevated with age (15, 20, 28, 29), the degree to which the increase in MSNA...
contributes to hypertension remains unclear. Importantly, in contrast with our hypothesis, we found an attenuated rise in BP following MSNA bursts in older subjects. These data suggest that at least on a beat-to-beat basis the sympathetic nervous system is not contributing to greater increases in BP with age, particularly in older women. However, the larger fall in BP in older men when no bursts of MSNA were present suggests a greater sympathetic vasoconstrictor tone under resting conditions that appears selective to this group. Given the known attenuation of α-adrenergic receptor responsiveness in older men (5, 6), these data suggest higher resting MSNA burst frequency is somewhat compensating and providing a greater sympathetic constrictor support of BP. Interestingly, this effect is not present in older women. Although limited studies have been performed in postmenopausal women, a recent study (13) indicates that α-adrenergic sensitivity may also be attenuated in this group. Nevertheless, our findings demonstrate, for the first time, a greater sympathetic support of beat-to-beat BP in older men that is not present in older women.

In young subjects, we found no difference between men and women in the rise in BP following a spontaneous MSNA burst. These data were somewhat surprising given findings that forearm vasoconstrictor responses to α-agonists are blunted in young women compared with men (10). In general agreement, following systemic ganglionic blockade, young women have been shown to exhibit lower tonic autonomic nervous system support of arterial BP (3). Furthermore, a positive relationship between resting MSNA and total peripheral resistance has been reported in young men but not young women (14). In contrast, our findings indicate no sex differences in the beat-to-beat control of BP via MSNA. The reason for these differing results is unclear but several possibilities warrant discussion. First, there are differences in the temporal resolution of data analyses between studies. Indeed, we are assessing spontaneous beat-to-beat changes over a discrete period (i.e., 15 s), whereas previous studies have primarily used pharmacological interventions and examined time-averaged responses from longer term steady-state periods ranging from 30 s to 5 min (10, 12, 14). In addition, when pharmacological blockade is used, drugs are administrated in the luminal side of the blood vessel, whereas when MSNA is assessed, nerve fibers are releasing norepinephrine on the abluminal side. Finally, we are using BP as our main end point, whereas previous studies have relied on local or systemic vascular changes only. In this regard, we also see clear reductions in TVC following spontaneous MSNA bursts that are of similar magnitude in young men and women. These findings for beat-to-beat sympathetic transduction to TVC are consistent with the lack of a sex difference in the beat-to-beat rise in BP following a MSNA burst in the young subjects.

Fig. 6. Summary data showing beat-to-beat changes in MAP following a MSNA burst when taking burst size into consideration for young and older men and women. Each subject had their sympathetic bursts divided into quartiles according to the height of the burst. Values are means ± SE.
In a closed loop system, the control of resting MSNA and beat-to-beat BP is a dynamic process with MSNA not only driving BP responses but also being evoked by changes in BP (12, 21). Indeed, although several studies have shown that sympathetic vascular transduction is paramount for the regulation of BP (i.e., peripheral arc), the arterial baroreflex control of MSNA (i.e., neural arc) represents a critical component for the maintenance of BP (1, 8, 14, 16, 30). Interestingly, Hart et al. (17) have recently shown that MSNA responsiveness to changes in BP via the arterial baroreflex (spontaneous sympathetic baroreflex sensitivity) is associated with resting MSNA in young and older men and postmenopausal women but not in young women. Thus the sex effect present in young women is lost with age and likely due to the loss of sex hormones with menopause. On the other hand, the data from the present study highlight the importance of MSNA as a driver of beat-to-beat BP fluctuations, and this can be influenced by both age and sex. Collectively, these data suggest that in the investigation of age and sex effects on BP control it is not only important to consider the afferent side of the baroreflex (neural arc) but also the efferent transduction side (peripheral arc).

In agreement with the current findings, Sugiyama et al. (41) also suggested a diminished BP response to MSNA bursts in older men. Importantly, we have extended these results by including young and older women, demonstrating a clear age effect in that postmenopausal women exhibit an attenuated pressor response following a burst of MSNA when compared with young women. In fact, as noted above, the older women had the smallest increases in BP of any group studied including the older men. To further investigate potential age and sex effects on MSNA control of beat-to-beat BP, we examined the potential influence of variations in burst size on the BP responses following each MSNA burst. We observed a graded effect of burst size with the smallest bursts evoking the smallest increase in BP, whereas the largest MSNA bursts were associated with the greatest rises in BP. This was consistent for all groups. Importantly, in general, taking into account burst size reinforced the significant blunting of the BP response following MSNA bursts with age and sex. Although these findings cannot establish strict causality, they strongly implicate sympathetic activity in producing these transient elevations in BP.

Although the mechanisms for the age-related decrease in BP responses to a given MSNA burst are unclear, several possibilities require discussion. First, it is reasonable to suggest that the decreased effectiveness of MSNA to elicit increases in BP in older subjects may be due to reduced α-adrenergic sensitivity (5, 6, 13). Alternatively, older subjects may have a reduction in norepinephrine release (4) per burst of MSNA; however, this remains unknown. In either case, a compensatory response of increased resting MSNA with age may be required to support BP (12, 15, 16, 20, 29). Because respiration can exert potent effects on MSNA and BP (2, 24, 37), we monitored respiratory excursions in all subjects. However, we did not observe any differences in respiratory rate between groups, suggesting that the frequency of respiration likely does not account for the observed differences in BP responses to MSNA bursts. Nonetheless, future studies with more comprehensive assessments of respiratory function may provide additional insight into respiratory-sympathetic coupling and its effects on the transduction of MSNA into beat-to-beat BP changes.

**Perspectives.** Little information is available regarding how the sympathetic nervous system regulates BP on a beat-to-beat basis in humans. In the early 80s, Wallin and Nerhed (46) reported a consistent transient rise in BP of ~2.5 mmHg following a MSNA burst in a heterogeneous group of subjects. To our surprise, no studies have followed up on these initial findings. Thus we extended these findings by examining how age and sex affect the ability of the sympathetic nervous system to regulate beat-to-beat BP. We demonstrate that the increase in BP following a spontaneous burst of MSNA was remarkably attenuated in older individuals, an effect that was most marked in postmenopausal women. Moreover, when no burst of MSNA occurred, older men had the largest fall in BP, whereas older women responded similarly to young women and men. Thus age-related effects cannot be generalized, and sex must be considered. The extent to which hormone replacement therapy influences the MSNA-BP relationships in postmenopausal women remains to be determined.

When compared with women, as men age it appears that MSNA becomes increasingly more important for the maintenance of beat-to-beat BP. Importantly, older men exhibit a large fall in BP when no bursts of MSNA are present, suggesting an augmented reliance upon MSNA to maintain resting BP. Indeed, although a fall in BP for cardiac cycles without an MSNA burst was seen in all groups, it was ~132% greater in older men. Thus, despite the fact that aging is associated with increased synthesis and action of vasoconstrictors (4, 40, 45), such as endothelin, and angiotensin II, our results highlight the importance and necessity of higher sympathetic outflow to the skeletal muscle vasculature in older men to regulate and maintain beat-to-beat BP. Of note, the larger falls in BP may be expected to contribute to greater BP variability in older men (39), which has been suggested to be associated with end organ damage (27, 32–34). However, we did not observe any differences in the coefficient of variation of BP between the older men and any of the other groups, suggesting that the overall distribution of BP is comparable. Nevertheless, it appears that older men may be more reliant on MSNA for maintaining BP beat-to-beat.

**Conclusions.** Healthy aging is associated with attenuated beat-to-beat changes in BP following a spontaneous burst of MSNA. Of note, this attenuation is more pronounced in postmenopausal women. Furthermore, our nonburst findings highlight on a beat-to-beat basis the importance of sympathetic vasoconstrictor activity to maintain BP, particularly in older men. Collectively, these findings provide novel insight into underlying age and sex differences in the sympathetic control of beat-to-beat BP in healthy individuals.

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**DISCLOSURES**

No conflicts of interest, financial or otherwise, are declared by the author(s).
AUTHOR CONTRIBUTIONS


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