Sympathetic neural responses to 24-hour sleep deprivation in humans: sex differences

Jason R. Carter,1 John J. Durocher,1 Robert A. Larson,1 Joseph P. DellaValla,2 and Huan Yang1

1Department of Kinesiology and Integrative Physiology, Michigan Technological University, Houghton, Michigan; and
2Center for Sleep Medicine, Androscoggin Valley Hospital, Berlin, New Hampshire

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Carter JR, Durocher JJ, Larson RA, DellaValla JP, Yang H. Sympathetic neural responses to 24-hour sleep deprivation in humans: sex differences. Am J Physiol Heart Circ Physiol 302: H1991–H1997, 2012. First published March 9, 2012; doi:10.1152/ajpheart.01132.2011.—Sleep deprivation has been linked to hypertension, and recent evidence suggests that associations between short sleep duration and hypertension are stronger in women. In the present study we hypothesized that 24 h of total sleep deprivation (TSD) would elicit an augmented pressor and sympathetic neural response in women compared with men. Resting heart rate (HR), blood pressure (BP), and muscle sympathetic nerve activity (MSNA) were measured in 30 healthy subjects (age, 22 ± 1; 15 men and 15 women). Relations between spontaneous fluctuations of diastolic arterial pressure and MSNA were used to assess sympathetic baroreflex function. Subjects were studied twice, once after normal sleep and once after TSD (randomized, crossover design). TSD elicited similar increases in systolic, diastolic, and mean BP in men and women (time, P < 0.05; time × sex, P > 0.05). TSD reduced MSNA in men (25 ± 2 to 16 ± 3 bursts/100 heart beats; P = 0.02), but not women. TSD did not alter spontaneous sympathetic or carotid baroreflex sensitivities in either sex. However, TSD shifted the spontaneous sympathetic baroreflex operating point downward and rightward in men only. TSD reduced testosterone in men, and these changes were correlated to changes in resting MSNA (r = 0.59; P = 0.04). Resting HR, respiratory rate, and estradiol were not altered by TSD in either sex. In conclusion, TSD-induced hypertension occurs in both sexes, but only men demonstrated altered resting MSNA. The sex differences in MSNA are associated with sex differences in sympathetic baroreflex function (i.e., operating point) and testosterone. These findings may help explain why associations between sleep deprivation and hypertension appear to be sex dependent.

arterial blood pressure; microneurography; hypertension; autonomic activity

Recent epidemiological studies demonstrate an association between sleep deprivation and hypertension (7, 12, 14). Moreover, a recent study examining the relations between sex, short sleep duration, and blood pressure reported that short durations of sleep were associated with hypertension in women, but not men (7). Therefore, evidence is accumulating to suggest that sleep deprivation contributes importantly to hypertension and that women may be at higher risk than men. Mechanisms underlying these potential sex differences remain unclear. Increases in sympathetic neural activity have been suggested as a potential contributor to the increased blood pressure observed after sleep deprivation, but direct evidence is lacking. In fact, 24-h total sleep deprivation (TSD) has been reported to reduce resting muscle sympathetic nerve activity (MSNA) in humans (16). Kato et al. (16) reported an increase in blood pressure and decrease in MSNA after TSD in six men and two women. Ogawa et al. (19) followed up with similar findings in six men and attributed the increase in resting blood pressure to a resetting of the sympathetic arterial baroreflex. Thus our current knowledge of the relations between sleep deprivation, hypertension, and MSNA is limited to two studies of primarily men with no insight into potential sex differences. Given the reported associations between short sleep duration and hypertension in women (7), we hypothesized an augmented pressor response to TSD that would be associated with a potentiated MSNA response in women (i.e., an increase of MSNA compared with men). Because sleep deprivation has been shown to alter sex steroids (13), we also examined the potential interactions between TSD, sex steroids, and MSNA.

METHODS

Subjects

Thirty healthy subjects (15 men and 15 women) participated in the study. All subjects were nonsmokers and had no history of autonomic dysfunction, cardiovascular disease, asthma, or diabetes. All subjects were instructed to abstain from exercise, alcohol, and caffeine for 12 h before laboratory testing. All female subjects reported regular menstrual cycles (range, 26–30 days) and were tested during their early follicular phase to diminish potential confounding hormonal effects. Subjects could not participate if they were taking oral contraceptives or other hormonal supplementations. One female subject was excluded because her estradiol and progesterone levels indicated that she was not in her early follicular phase during one of the visits. Additionally, all subjects were screened for obstructive sleep apnea by a board certified sleep physician (J. DellaValla) using the at-home ApneaLink (ResMed, San Diego, CA). One male subject was excluded because his apnea-hypopnea index was ≥10 arbitrary units. Thus our final data set included 14 men and 14 women (Table 1). Testing procedures were explained to all subjects before obtaining written informed consent and were approved by the Michigan Technological University Institutional Review Board.

Experimental Design

Subjects were tested twice: once after 24-h TSD in the laboratory and once after normal sleep (NS) at their homes. Trial order (TSD vs. NS) was randomized, and all subjects were tested ~1 mo apart to ensure female subjects were tested during their early follicular phase for both visits. Wrist actigraphy (Actiwatch-64; Respinorics, Bend, OR) was used to monitor limb movement for a minimum of three consecutive nights immediately preceding each trial. All wrist actigraphy data were analyzed by a board certified sleep physician (J. DellaValla). In the minority of nights (~10%), actigraphy data were unavailable and self-reported sleep diary data were used. The actigraphy/sleep diary data from the three nights preceding each autonomic test demonstrate that participants were getting adequate and similar

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sleep before the NS (7.3 ± 0.2 h in men and 7.2 ± 0.2 h in women) and TSD (7.6 ± 0.3 h in men and 7.4 ± 0.3 h in women) trials.

During the TSD trial, subjects were contacted at 7:30 AM the morning before the sleep deprivation night. Subjects were instructed to remain awake (i.e., no naps) and report to the laboratory at 11:00 PM where two research assistants supervised the subject throughout the remainder of the night to ensure they remained awake (continuous visual observation and periodic auditory confirmations). Participants stopped eating a minimum of 8 h before the start of laboratory testing. During the TSD trial, subjects were contacted at 7:30 AM the morning before the sleep deprivation night. Subjects were instructed to remain awake (i.e., no naps) and report to the laboratory at 11:00 PM where two research assistants supervised the subject throughout the remainder of the night to ensure they remained awake (continuous visual observation and periodic auditory confirmations). Participants stopped eating a minimum of 8 h before the start of laboratory testing. Participants were provided a controlled light breakfast (i.e., water and granola bar) during each testing day (NS and TSD) after the resting seated blood pressure measurements and blood draw were completed.

On each day of testing (NS vs. TSD), three seated resting blood pressures were taken at 7:30 AM after 5 min of quiet rest. After the blood pressure recordings, state-anxiety was measured using the State-Trait Anxiety Inventory (STAI) questionnaire for adults (28), and fasting venous blood samples were then obtained to determine state-anxiety was measured using the State-Trait Anxiety Inventory (STAI) questionnaire for adults (28), and fasting venous blood samples were then obtained to determine sexual steroids. Subjects were then situated in the supine position immediately preceding the 10-min baseline. Both seated and supine resting arterial blood pressures were measured three consecutive times (separated by ~1-min intervals) using an automated sphygmomanometer (Omron HEM-907XL; Omron Health Care). Beat-to-beat arterial blood pressure was recorded continuously by 10.220.32.246 on October 6, 2016 http://ajpheart.physiology.org/ Downloaded from

### Table 1. Subject characteristics and sex steroids

<table>
<thead>
<tr>
<th>Variable</th>
<th>NS</th>
<th>TSD</th>
<th>NS</th>
<th>TSD</th>
<th>Condition</th>
<th>Sex</th>
<th>Condition × Sex</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>22 ± 1</td>
<td>–</td>
<td>22 ± 1</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Height, cm</td>
<td>176 ± 2</td>
<td>–</td>
<td>165 ± 2</td>
<td>–</td>
<td>–</td>
<td>&lt;0.001</td>
<td>–</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>79 ± 4</td>
<td>79 ± 4</td>
<td>62 ± 4</td>
<td>63 ± 3</td>
<td>0.65</td>
<td>&lt;0.001</td>
<td>0.27</td>
</tr>
<tr>
<td>STAI, arbitrary units</td>
<td>28 ± 2</td>
<td>35 ± 2</td>
<td>27 ± 2</td>
<td>32 ± 2</td>
<td>&lt;0.01</td>
<td>0.43</td>
<td>0.36</td>
</tr>
<tr>
<td>Standard</td>
<td>42 ± 2</td>
<td>49 ± 2</td>
<td>40 ± 2</td>
<td>44 ± 2</td>
<td>&lt;0.01</td>
<td>0.18</td>
<td>0.21</td>
</tr>
<tr>
<td>Percentile STAI,%</td>
<td>26 ± 6</td>
<td>48 ± 7</td>
<td>21 ± 6</td>
<td>33 ± 7</td>
<td>&lt;0.01</td>
<td>0.24</td>
<td>0.18</td>
</tr>
<tr>
<td>Estradiol, pg/ml</td>
<td>25 ± 2</td>
<td>20 ± 1</td>
<td>36 ± 8</td>
<td>29 ± 3</td>
<td>0.13</td>
<td>0.07</td>
<td>0.79</td>
</tr>
<tr>
<td>Progesterone, ng/ml</td>
<td>2.2 ± 0.2</td>
<td>1.8 ± 0.2*</td>
<td>2.1 ± 0.2</td>
<td>1.3 ± 0.1†</td>
<td>&lt;0.01</td>
<td>0.20</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Testosterone, ng/dl</td>
<td>589 ± 67</td>
<td>480 ± 54†</td>
<td>46 ± 2</td>
<td>44 ± 4</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Values are means ± SE; n = 14 men and n = 14 women unless otherwise noted. NS, normal sleep; TSD, total sleep deprivation; STAI, state-trait anxiety inventory. *P < 0.05, NS vs. corresponding TSD; †P < 0.01, NS vs. corresponding TSD. Estradiol/progesterone/testosterone, n = 27 (n = 14 men and n = 13 women).

### Table 2. Hemodynamic and neural responses to sleep deprivation

<table>
<thead>
<tr>
<th>Variable</th>
<th>NS</th>
<th>TSD</th>
<th>NS</th>
<th>TSD</th>
<th>Condition</th>
<th>Sex</th>
<th>Condition × Sex</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seated arterial blood pressure, mmHg</td>
<td>109 ± 2</td>
<td>113 ± 2</td>
<td>99 ± 3</td>
<td>102 ± 2</td>
<td>0.02</td>
<td>&lt;0.01</td>
<td>0.35</td>
</tr>
<tr>
<td>Systolic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diastolic</td>
<td>64 ± 2</td>
<td>68 ± 2</td>
<td>65 ± 2</td>
<td>67 ± 2</td>
<td>0.04</td>
<td>0.40</td>
<td>0.22</td>
</tr>
<tr>
<td>Mean</td>
<td>79 ± 2</td>
<td>83 ± 1</td>
<td>76 ± 2</td>
<td>78 ± 2</td>
<td>0.03</td>
<td>&lt;0.05</td>
<td>0.25</td>
</tr>
<tr>
<td>Mean arterial blood pressure, mmHg</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>109 ± 2</td>
<td>115 ± 2</td>
<td>95 ± 2</td>
<td>97 ± 2</td>
<td>0.02</td>
<td>&lt;0.01</td>
<td>0.05</td>
</tr>
<tr>
<td>Diastolic</td>
<td>58 ± 2</td>
<td>61 ± 1</td>
<td>55 ± 1</td>
<td>59 ± 2</td>
<td>&lt;0.01</td>
<td>0.12</td>
<td>0.20</td>
</tr>
<tr>
<td>Mean</td>
<td>75 ± 1</td>
<td>79 ± 1</td>
<td>68 ± 1</td>
<td>72 ± 2</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>0.35</td>
</tr>
<tr>
<td>Heart rate, beats/min</td>
<td>59 ± 2</td>
<td>62 ± 2</td>
<td>62 ± 2</td>
<td>60 ± 2</td>
<td>0.37</td>
<td>0.66</td>
<td>0.13</td>
</tr>
<tr>
<td>MSNA burst frequency, bursts/min</td>
<td>15 ± 2</td>
<td>10 ± 2*</td>
<td>8 ± 1</td>
<td>10 ± 2</td>
<td>0.17</td>
<td>0.11</td>
<td>0.03</td>
</tr>
<tr>
<td>MSNA burst incidence, bursts/100 heart beats</td>
<td>25 ± 2</td>
<td>16 ± 3*</td>
<td>14 ± 2</td>
<td>17 ± 3</td>
<td>0.16</td>
<td>0.11</td>
<td>0.02</td>
</tr>
<tr>
<td>sympBRS, burst incidence/mmHg</td>
<td>−1.4 ± 0.2</td>
<td>1.3 ± 0.2</td>
<td>−1.1 ± 0.2</td>
<td>1.4 ± 0.2</td>
<td>0.63</td>
<td>0.73</td>
<td>0.36</td>
</tr>
<tr>
<td>cVBRs up-up, ms/mmHg</td>
<td>23 ± 3</td>
<td>23 ± 2</td>
<td>25 ± 4</td>
<td>25 ± 3</td>
<td>0.92</td>
<td>0.58</td>
<td>0.97</td>
</tr>
<tr>
<td>cVBRs d-d, ms/mmHg</td>
<td>20 ± 2</td>
<td>22 ± 1</td>
<td>26 ± 4</td>
<td>24 ± 1</td>
<td>0.85</td>
<td>0.11</td>
<td>0.35</td>
</tr>
<tr>
<td>Respiration, breaths/min</td>
<td>15 ± 1</td>
<td>15 ± 1</td>
<td>16 ± 0</td>
<td>16 ± 1</td>
<td>0.25</td>
<td>0.37</td>
<td>0.23</td>
</tr>
</tbody>
</table>

Values are means ± SE; n = 14 men and n = 14 women unless otherwise noted. MSNA, muscle sympathetic nerve activity; sympBRS, spontaneous sympathetic baroreflex sensitivity; sympBRs, spontaneous baroreflex sensitivity; cVBRs, spontaneous cardiac vagal baroreflex sensitivity for up-up sequences; cVBRs d-d, spontaneous cardiovagal baroreflex sensitivity for down-down sequences. *P < 0.05, NS vs. corresponding TSD. MSNA, n = 20 (10 men and 10 women); sympBRS, n = 18 (9 men and 9 women); cVBRs up-up, n = 22 (12 men and 10 women); cVBRs d-d, n = 25 (13 men and 12 women).
throughout the 10-min baseline using the Finometer (Finapres Medical Systems, Amsterdam, The Netherlands) to allow spontaneous baroreflex assessment (described below). Three consecutive supine blood pressures were taken from the automated sphygmomanometer immediately preceding the 10-min baseline and were used to calibrate the Finometer to accurately depict absolute values. Arterial blood pressures are expressed as systolic arterial blood pressure (SAP), diastolic arterial blood pressure (DAP), and mean arterial blood pressure (MAP). Heart rate was recorded continuously via a three-lead electrocardiogram, and respiratory rate was continuously measured using a pneumobelt.

Data Analysis

MSNA. Data were imported and analyzed in the WinCPRS software program (Absolute Aliens; Turku, Finland). R-waves were detected and marked in the time series. Muscle sympathetic nerve bursts were automatically detected on the basis of amplitude using a signal-to-noise ratio of 3:1, within a 0.5-s search window centered on a 1.3-s expected burst peak latency from the previous R-wave. Potential bursts were displayed and edited by one trained investigator. MSNA was expressed as burst frequency (in bursts/min) and burst incidence (in bursts/100 heart beats). Resting MSNA was successfully recorded during both NS and TSD conditions in 20 subjects (10 men and 10 women).

Spontaneous sympathetic baroreflex sensitivity analysis. Spontaneous sympathetic function was determined using the spontaneous DAP-MSNA slope method, which examined the relations between spontaneous fluctuations in DAP and MSNA at rest (10, 29, 34). This analysis has been described in detail in previous studies (8, 17). Briefly, DAPs for each cardiac cycle were grouped into 3-mmHg intervals (bins) during baseline. Burst incidence for each DAP bin was calculated and plotted against the corresponding DAP. The slopes of these relationships were evaluated using linear regression analysis. All linear regression analyses were weighted for the number of cardiac cycles within each DAP bin. A minimum r value of 0.40 was set as the criteria for inclusion. As a result, one male and one female were excluded from the slope analysis (r ≤ 0.30). The mean coefficient values were ±0.70 for the remaining nine men and nine women. Operating points for each regression line were determined as the mean value of burst incidence versus the mean DAP for the corresponding baseline period (n = 18 as in the spontaneous slope analysis).

Spontaneous cardiovagal baroreflex sensitivity analysis. Spontaneous cardiovagal baroreflex sensitivity was determined from beat-to-beat changes in R-R interval and SAP (sequence method) as originally reported by Bertinieri et al. (5) and modified by Blaber et al. (6). Briefly, three or more beats relating to R-R intervals and progressive, spontaneous changes of SAP (lag 1) were identified as baroreflex sequences. We recorded both up-up sequences (progressive increases of SAP followed by a lengthening of the R-R interval) and down-down sequences (progressive decreases of SAP with a subsequent shortening of the R-R interval). Minimum criteria were set at 1 mmHg for SAP and 4-ms for R-R interval. Linear regression analysis was used to determine the slope of the linear relationship between the R-R intervals and SAP for each sequence. Up-up or down-down sequences within each 10-min baseline were averaged for each subject. Only sequences with linear r values >0.7 were accepted, resulting in 12 men and 10 women for up-up sequence analysis and 13 men and 12 women for down-down sequence analysis (Table 2).

Statistical Analysis

All data were analyzed statistically using commercial software (SPSS 18.0; SPSS, Chicago, IL). We used repeated-measures ANOVA with condition (NS vs. TSD) as the within-subjects factor and sex (men vs. women) as the between-subjects factor. Post hoc analysis was performed when significant condition × sex interactions were detected. Pearson correlations were used to examine the relations between MSNA and sex steroids (i.e., estradiol, progesterone, and testosterone). Results are expressed as means ± SE. Means were considered significantly different at P < 0.05.

RESULTS

Table 1 depicts subject characteristics and mean values for state-anxiety and sex steroids following NS and TSD. TSD elicited similar increases in state-anxiety in men and women (condition, P < 0.05; condition × sex, P ≥ 0.18). TSD significantly reduced testosterone in men, but not women (condition × sex, P = 0.01). Progesterone levels were reduced by TSD in both men and women, although decreases were more dramatic in women (condition × sex, P < 0.05). Estradiol was not significantly altered by TSD in either sex.

Table 2 compares the hemodynamic and neural responses to TSD in men and women. TSD elicited similar increases in SAP, DAP, and MAP in men and women (condition, P < 0.05 for all). This hypertensive response was observed regardless of body position (i.e., seated vs. supine). TSD did not alter resting heart rate in either sex. Figure 1 demonstrates that TSD decreased MSNA in men, but not women, when expressed as both burst frequency and burst incidence. TSD did not alter spontaneous sympathetic baroreflex sensitivity as determined by the spontaneous DAP-MSNA linear regression analysis in

**Fig. 1.** Muscle sympathetic nerve activity (MSNA) after a normal night of sleep (NS) and 24 h of total sleep deprivation (TSD) in men and women. TSD decreased MSNA burst frequency and burst incidence in men, but did not alter MSNA in women (condition × sex interactions; P < 0.05). *P < 0.05 vs. corresponding NS.
either sex (Table 2). However, TSD significantly reduced the operating point in men, but not women (condition × sex, \( P < 0.05 \)). This downward, rightward shift of the spontaneous sympathetic baroreflex operating point in men is illustrated in Fig. 2. Importantly, blood pressure responses to TSD in the subjects with complete MSNA recordings (\( n = 20 \)) revealed similar results to the blood pressure responses in the 28 subjects reported in Table 2. Specifically, TSD increased supine DAP in the men \((56 ± 2 \text{ to } 60 ± 2 \text{ mmHg})\) and women \((55 ± 2 \text{ to } 59 ± 2 \text{ mmHg})\), and these increases were not different between sexes (condition, \( P = 0.001 \); condition × time, \( P = 0.827 \)). Table 2 also demonstrates that TSD did not alter spontaneous cardiovagal baroreflex sensitivities in either sex.

Figure 3 depicts the relations between changes in testosterone and MSNA in response to TSD in men and women. Changes in testosterone were correlated to changes in MSNA in men, but not women. Changes in progesterone and estradiol were not correlated to changes in MSNA in either sex.

**DISCUSSION**

The present study examined the influence of TSD on neural cardiovascular control in men and women. Our results support previous findings that TSD increases resting blood pressure \((16, 19)\) and state-anxiety \((2, 26, 33)\), and we extend these previous studies by demonstrating that the TSD pressor responses subsist in both men and women. More important, the present study introduces three new and novel findings. First, MSNA responses to TSD are sex dependent. Specifically, TSD decreased MSNA in men, but did not alter MSNA in women. Second, TSD did not alter spontaneous sympathetic and cardiovagal baroreflex sensitivities in either sex. However, TSD elicited a rightward, downward shift of the sympathetic baroreflex operating point in men, but not women. Third, TSD reduced testosterone in men, and these changes were associated with changes in resting MSNA. Collectively, our findings suggest that mechanisms underlying the acute hypertensive response to TSD differ in men and women and that both neural (i.e., spontaneous sympathetic baroreflex) and non-neural (i.e., testosterone) mechanisms may be underlying these sex differences.

The effects of TSD on arterial blood pressure and catecholamines are inconsistent. Several studies report increases in arterial blood pressure following TSD \((16, 19, 25, 27)\), whereas others have demonstrated no change \((1, 22, 32, 37)\). Likewise, multiple studies report an increase in plasma or urine catecholamines after TSD \((4, 18, 27, 31)\), whereas others report no change \((1, 11, 16, 19, 23)\). Studies have also measured heart rate variability as an index of autonomic function in sleep-deprived subjects and reported an increase in sympathetic cardiac modulation \((27, 37)\). An underlying theme of these prior studies is the lack of female participants and/or emphasis on sex differences. Moreover, the use of catecholamine levels and heart rate variability as indices of autonomic function are not as direct as post-ganglionic sympathetic nerve activity (i.e., MSNA).

To date, only two studies have examined resting MSNA following TSD in humans \((16, 19)\). Kato et al. \((16)\) reported that TSD increased blood pressure and decreased MSNA in six men and two women. Similarly, Ogawa et al. \((19)\) demonstrated an increase in blood pressure and decrease of MSNA following TSD in six men. Thus to date our understanding of the effects of sleep deprivation on MSNA is limited to two studies with a total of 12 men and two women. The aim of the present study was to comprehensively examine neural cardiovascular responses to TSD in men and women. Our findings support the existing concept that TSD reduces MSNA in men. However, TSD reductions of MSNA were not observed in women, despite a similar pressor response to that of the men. Ogawa et al. \((19)\) attributed the TSD reduction of MSNA in men to a resetting of the sympathetic baroreflex. The authors support this claim by reporting a significantly elevated set point as determined by the \( x \)-intercept of the spontaneous DAP-MSNA linear regression line \((19)\). However, the \( x \)-intercept is

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Fig. 2. Mean linear regression lines and operating points (·) for MSNA burst incidence and diastolic arterial blood pressure. TSD altered the operating point in men (downward, rightward shift), but not women. TSD did not alter the burst incidence slopes, an index of sympathetic baroreflex sensitivity, in either sex. Burst incidence slopes and respective operating points were determined from 9 men and 9 women. \(* P < 0.05 \) vs. corresponding operating point.
strongly influenced by slope; thus we used the DAP-MSNA linear regression slope in conjunction with resting DAP (via the automated sphygmomanometer) and resting MSNA to determine the operating point of the spontaneous sympathetic baroreflex (20). We demonstrate that TSD did not alter spontaneous sympathetic baroreflex sensitivity in men or women, but did significantly alter the spontaneous sympathetic baroreflex operating point in men. Specifically, the operating point was shifted rightward and downward in men, but not women. We believe the response exhibited by the men was an appropriate response given the rise in arterial blood pressure during TSD. In other words, the baroreflex detected increases in arterial pressure and consequently reduced MSNA. Women, on the other hand, demonstrated a significant increase in arterial blood pressure similar to the men, but the acute hypertensive response was not accompanied by a concurrent decrease of MSNA. We conclude that TSD was associated with some degree of sympathetic baroreflex dysfunction in women compared with men. We recognize that this assumes that the baroreflex is primarily driving MSNA responses, as opposed to MSNA driving arterial blood pressure. In reality, a dynamic interaction exists between arterial blood pressure, the arterial baroreflex, and MSNA, in which MSNA can either drive or respond to changes in arterial blood pressure. Moreover, non-baroreflex factors are known to contribute importantly to the control of resting MSNA (21). Regardless, the novelty of the present study is that men and women respond differently regarding MSNA responses to TSD, as well as DAP-MSNA relations. Moreover, these findings are consistent with recent evidence that men and women have different strategies for regulating arterial blood pressure and MSNA (15). Such findings might help explain why women appear to be more susceptible to developing hypertension as a result of short sleep duration (7).

TSD has repeatedly been shown to significantly decrease testosterone levels in male rats and humans (3, 13, 36). The decreased testosterone levels in our study were correlated to reductions of MSNA in men (Fig. 3). To our knowledge, only one microneurographic study has examined the relations between MSNA and testosterone. Specifically, women with polycystic ovary syndrome demonstrated increased levels of MSNA that were positively correlated to testosterone (30). The authors suggest that testosterone modulated MSNA in women with polycystic ovary syndrome and is an important contributor to the sex difference in sympathetic outflow observed in the normal population. Our results reveal for the first time that the

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**Fig. 3.** Correlations of MSNA and testosterone in men and women. Changes in MSNA were correlated with changes in testosterone in men, but not women.
positive relation between changes of MSNA and testosterone observed in young women may also be important in young men. Thus, in addition to the role of the spontaneous arterial baroreflex in MSNA control during TSD discussed previously, we conclude that reductions of testosterone may also play a key role in reducing resting MSNA after TSD in men.

If increases in MSNA are not driving the TSD-induced hypertension, what is? Perry et al. (24) recently reported that paradoxical sleep deprivation in Wistar-Hannover male rats resulted in selective alterations of sympathetic nerve activity. Specifically, both 24-h and 96-h paradoxical sleep deprivation increased renal sympathetic nerve activity but did not alter splancnic sympathetic nerve activity (24). This preferential sympathoexcitation to the kidney was also associated with reduced plasma angiotensin II concentrations (24). Moreover, Charloux et al. (9) has demonstrated that TSD modifies the 24-h profile of aldosterone. The microneurography technique used in the present study was specific to the muscular bed of the lower leg. Wallin and colleagues (35) have reported a strong positive correlation between MSNA and renal noradrenaline spillover at rest, but it is unclear whether this strong relationship persists during interventions such as TSD. Based on the recent findings of Perry et al. (24), it may be warranted to examine the influence of TSD on renal noradrenaline spillover in humans.

Numerous studies have noted an association between anxiety and abnormal sleeping patterns; however, relatively few have examined how TSD influences state-anxiety (2, 26, 33). Numerous studies have noted an association between anxiety and abnormal sleeping patterns; however, relatively few have examined how TSD influences state-anxiety (2, 26, 33). Specific associations of short sleep duration with prevalent and incident hypertension: the Whitehall II Study. Hypertension 50: 693–700, 2007.


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GRANTS

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DISCLOSURES

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

AUTHOR CONTRIBUTIONS


REFERENCES


