Muscle sympathetic outflow during horizontal linear acceleration in humans

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Cui, Jian, Satoshi Iwase, Tadaaki Mano, Naomi Katayama, and Shigeo Mori. Muscle sympathetic outflow during horizontal linear acceleration in humans. Am J Physiol Regulatory Integrative Comp Physiol 281: R625–R634, 2001.—To elucidate the effects of linear acceleration on muscle sympathetic nerve activity (MSNA) in humans, 16 healthy men were tested in a linear accelerator. Measurements of MSNA, electrocardiogram, blood pressure, and thoracic impedance were undertaken during linear acceleration. Sinusoidal linear acceleration with peak values at ±0.10, ±0.15, and ±0.20 G was applied in anteroposterior (±Gx, n = 10) or lateral (±Gy, n = 6) directions. The total activity and burst rate of MSNA decreased significantly during forward, backward, left, or right linear accelerations. The total activity of MSNA decreased to 50.5 ± 6.9, 52.5 ± 4.4, 71.2 ± 9.6, and 67.6 ± 8.2% from the baseline (100%) during linear accelerations with peak values at ±0.20 G in the four directions, respectively. These results suggest that dynamic stimulation of otolith organs in horizontal directions in humans might inhibit MSNA directly in order to quickly redistribute blood to muscles during postural reflexes induced by passive movement, which supports the concept that the vestibular system contributes to sympathetic regulation in humans.

Muscle sympathetic nerve activity; vestibular stimulation; microneurography

CHANGES IN MUSCLE SYMPATHETIC nerve activity (MSNA) are important for maintaining arterial blood pressure. Data from our previous study demonstrated that changes in MSNA depend on the longitudinal body component of the gravity vector from the head to legs during postural change (10) and that MSNA was suppressed during short periods of microgravity produced by parabolic flight (9).

The sympathetic nervous system is influenced by a number of reflex mechanisms. Besides arterial and cardiopulmonary baroreflexes, there is also considerable evidence that inputs from the vestibular system have direct effects on the cardiovascular system (2, 7, 12, 21, 24, 25). The neurons in the nucleus tractus solitarius, rostral ventrolateral medulla (RVLM), and parabrachial nucleus are involved in the vestibuloautonomic reflex (1, 26-30). Yates et al. (26) demonstrated that neurons in the RVLM, which is a major source of excitatory inputs to sympathetic preganglionic neurons, received vestibular inputs, and vestibular inputs to the RVLM appear to come mainly from otolith receptors. Data from animal studies have demonstrated that sympathetic outflow to renal, splanchnic, and cardiac nerves is modulated by stimulation of the vestibular system (24). MSNA from the human tibial nerve is enhanced after caloric vestibular stimulation (6, 11), whereas skin sympathetic nerve activity is suppressed and then enhanced after caloric vestibular stimulation (5). These results suggest that stimulation of horizontal semicircular canals has effects on sympathetic outflows to muscle and skin in humans. MSNA increases during sustained head-down neck flexion in humans, which suggests that sympathetic outflow is influenced by inputs from otolith organs (13, 20). Furthermore, vestibular stimulation during linear accelerations can produce responses in blood pressure and heart rate in humans (25).

Although many studies in animals have focused on the vestibuloautonomic reflex (2, 3, 13-15, 20), there are insufficient data on this reflex in humans to elucidate the response patterning. Sympathetic nerve traffic in the cat splanchnic nerve was related to the direction of the acceleration of otolith organs (29); therefore, MSNA response in humans to stimulation of otolith organs in horizontal (nasoccipital axis or interaural axis) directions may be different from that to stimulation in the cranio-caudal direction. Although preliminary data suggested that alternating forward and backward linear accelerations of 0.10 and 0.20 Gx suppress mean MSNA, an insufficient number of subjects was studied to reach definite conclusions (4). Moreover, MSNA responses to lateral linear accelerations have not been reported.

The purpose of the present study was to determine the response of muscle sympathetic outflow from the tibial nerve to dynamic stimulation of otolith organs in the forward, backward, left, or right directions in sitting humans.

METHODS

Subjects. Sixteen healthy male volunteers [age 20.8 ± 0.9 (SE) yr; height 169.8 ± 5.6 cm; weight 64.3 ± 2.2 kg] participated in the study. Written informed consent was obtained.

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from each subject. The study was approved by the Human Research Committee, Research Institute of Environmental Medicine, Nagoya University.

Experimental design. All experiments were performed with subjects seated in a linear accelerator capsule (sled) at the Research Institute of Environmental Medicine, Nagoya University. The design characteristics of the linear accelerator are as follows: 1) a magnetic levitation system is employed; 2) the maximal acceleration is 0.5 G (4.9 m/s²); 3) the experimental capsule mounted on the sled is shielded against outside light and any electromagnetic field; 4) the moving distance is limited to 18 m, and thus positive and negative acceleration occur alternately in one movement; and 5) linear acceleration in a sinusoidal or step mode can be selected.

Each subject was strapped into a chair in the capsule, and the body and head were firmly restrained with Velcro tape (Fig. 1A). The legs were extended at the knee joint in a horizontal position, and the ankles were supported at the lower part of the calves. The subjects were in a dark environment in the capsule.

Because the recording of MSNA was more stable during linear acceleration in the sinusoidal mode than during that in the step mode, linear acceleration in the sinusoidal mode was adopted with a fixed moving distance of 14 m. The acceleration was applied along the anteroposterior (±Gy, nassooccipital and occipitotonsal) direction in 10 subjects and was applied along the lateral (±Gx, interaural) direction in another 6 subjects. Forward acceleration is defined as +Gx, which tends to displace internal tissues such as eyeballs in the occipital direction (eyeballs in), and the right lateral acceleration is defined as +Gy (eyeballs left) (Ref. 8; Fig. 1B). Each stimulation had five cyclic movements with the same peak acceleration repeated continuously. There was an initial period of ~23 s before starting sinusoidal acceleration. During the initial period the sled moved to one end of the rail at a constant speed of 0.33 m/s, but subjects could feel a slight vibration and knew that the acceleration would start. Three stimulations were applied with peaks of ±0.10 G (0.98 m/s²), ±0.15 G (1.47 m/s²), and ±0.20 G (1.96 m/s²) with total periods for the five cyclic movements of 83.5, 66.5, and 58.0 s, respectively. The interval between stimulations was 5 min.

Measurements. The discharge from the postganglionic sympathetic nerve supplying the triceps surae was recorded from the right tibial nerve by using microneurography. A tungsten microelectrode with a shaft diameter of 120 μm, a tip diameter of 1 μm, and an impedance of 3–5 MΩ (26-05-1, Frederick Haer, Bowdoinham, ME) was inserted manually through the skin without anesthesia into the muscle nerve fascicle of the tibial nerve at the popliteal fossa. The sympathetic nerve signals were fed into a high impedance preamplifier (Kohno II, Kohno Instruments, Nagoya, ×20,000 in gain) and were monitored using a cathode ray oscilloscope (VC-6524, Hitachi, Densi, Tokyo, Japan) after band-pass filtering with a bandwidth of 500–5,000 Hz (E-3201A×2, NF Circuit Design Block, Yokohama, Japan). The filtered signals were rectified, amplified, and integrated in a resistance-capacitance network with a time constant of 0.1 s. The burst of MSNA was identified according to the criteria of previous studies (10, 22, 23). The main criteria for identification of MSNA were 1) pulse-synchronous spontaneous and rhythmic efferent burst discharges recorded from muscle nerve fascicle, 2) modulation by respiration, 3) increase by a fall and decrease by a rise in systemic blood pressure, and 4) enhancement by maneuvers increasing intrathoracic pressure such as Valsalva’s maneuver.

Heart rate was monitored by electrocardiography (ECG) using a bioelectric amplifier (AB-621G, Nihon-Kohden, Tokyo), and the blood pressure waveform was recorded with a Finapres 2300 (Ohmeda, Louisville, CO) at the subject’s left or right middle finger, which was fixed with adhesive tape at the level of the right atrium. Subjects were asked to control their respiratory rate at 0.25 Hz with a metronome. Respiration was recorded with a thermistor at the nose. To estimate changes in intrathoracic fluid volume, thoracic impedance was measured using impedance plethysmography (AI-601G, Nihon-Kohden) with the electrodes taped circumferentially around the neck and chest at the level of the xyphoid process. All signals were stored using a multichannel digital audio tape recorder (PC-216A, Sony Precision Technology, Tokyo). All bioamplifiers and the tape recorder were fixed in the sled (Fig. 1A). Signals were monitored in the control room simultaneously.

Data quantification and analysis. All data were digitized at 200 Hz (16 bits) by off-line processing and analyzed using LabView software (National Instruments, Austin, TX) with a computer (Power Macintosh, Apple, Cupertino, CA). Mean

Fig. 1. A: experimental setup for the recording of microneurography, blood pressure with a Finapres device, respiration with a thermistor, electrocardiography (ECG), and thoracic impedance. B: acceleration nomenclature: forward acceleration is defined as +Gx, and the right lateral acceleration is defined as +Gy, V, velocity.
arterial pressure (MAP) was calculated as the sum of the diastolic blood pressure plus one-third of the pulse pressure in each beat. Instantaneous heart rate was calculated from the R-R interval. Average values of MAP, heart rate, and thoracic impedance during 1 min just before the initial period of the sled motion served as baseline values (Fig. 2).

Figure 3 illustrates how each MSNA burst was analyzed. The computer measured the burst peak latency of the integrated neurogram from the ECG R-wave and beat-by-beat MAP simultaneously. Referring to the burst peak latency from the ECG R-wave and changes in blood pressure, the burst of MSNA was identified by manual inspection of the beat-by-beat pattern (10, 23). The burst area of the integrated neurogram was then measured (5, 6). The total activity of MSNA was defined as the burst area of the full-wave rectified and integrated neurogram with a time constant of 0.1 s (5, 6, 22). If there was no burst after a beat, a “0” would be put in the MSNA data series of beat-by-beat. The final data for the total activity of MSNA were expressed in arbitrary units by setting the sum of the burst area during the 1 min just before the initial period of the sled motion as 100%. MSNA was also expressed as burst rate (burst number per minute).

To observe dynamic responses during the five cyclic movements, the sum of the burst area of the integrated neurogram at each phase of the sinusoidal acceleration was calculated according to the time segments of the positive or negative phases of the five cyclic sinusoidal accelerations. The total activity of MSNA at each phase of the sinusoidal acceleration was calculated as MSNA% = [(sum of burst area of the phase/phase length)/(sum of burst area of baseline/60)] × 100. The algorithm is illustrated in Fig. 3. Relative changes of mean heart rate, MAP, and thoracic impedance to baseline values at each phase of the five cyclic movements were also calculated.

To observe the responses to the direction of the acceleration, the total activity of MSNA, relative changes of mean heart rate, MAP, and thoracic impedance during the sum of the periods of positive or negative acceleration were calculated, respectively, using similar methods. MSNA bursts during the total period of each direction of linear acceleration were also counted and expressed as burst number per minute (burst rate).

Cross-correlograms were used to identify whether a sinusoidal response was elicited by the sinusoidal stimulus, which were also used to observe the phase relationships between the acceleration and responses of hemodynamic parameters (5, 6, 22). After the hemodynamic beat-by-beat data series were interpolated to equidistant 1-s intervals by a cubic spline function, the cross-correlograms between the sinusoidal acceleration and MSNA, MAP, heart rate, and thoracic impedance were calculated. The responses to the five cyclic sinusoidal stimuli for each subject were averaged into a single cross-correlogram.

Values are expressed as means ± SE. We applied a one-way ANOVA to assess the changes of the variables during baseline, negative acceleration, and positive acceleration, and after acceleration. P < 0.05 was considered as significant.

RESULTS

MSNA, blood pressure, heart rate, thoracic impedance, and respiratory flow were obtained for all 16 subjects. Original recordings of thoracic impedance, respiration, instantaneous heart rate, blood pressure, and integrated MSNA from the tibial nerve during anteroposterior sinusoidal acceleration with a peak value of ±0.15 G in a representative subject are shown in Fig. 2. There was no complaint of motion sickness symptoms such as nausea, dizziness, or cold sweating in any of the subjects.

Hemodynamic responses to the four linear accelerations. A significant decrease in MSNA was observed during forward, backward, left, and right acceleration in all subjects. Figure 4 shows original recordings of integrated MSNA in six different subjects during anteroposterior sinusoidal acceleration with a peak value of ±0.15 G. Averages of burst rate of MSNA, MAP, heart rate, and thoracic impedance before and during

![Fig. 2. Representative tracings obtained for 1 subject (subject 1) during sinusoidal linear acceleration in the anteroposterior direction with peak value of ±0.15 G. The traces show the acceleration (Gx), thoracic impedance (TI), respiration (Resp), instantaneous heart rate (HR), blood pressure (BP), and integrated muscle sympathetic nerve activity (IMNSA). The average values of the variables during the 1 min just before the initial period of the sled motion were used as baseline values. Acc, total period of acceleration. First min, the 1st min after acceleration.](http://ajpregu.physiology.org/doi/10.1152/ajpregu.00223.2000)
accelerations. Heart rate increased in some individuals, whereas it decreased in others. MAP increased in some subjects, but it did not change or decreased slightly in others.

Average heart rate was not changed significantly during forward or backward accelerations with peak values of ±0.10 or ±0.15 G. Heart rate was significantly greater than baseline during forward and backward acceleration with a peak value of ±0.20 G. Average heart rate was not changed significantly during left or right accelerations with peak values of ±0.10, ±0.15, or ±20 G. There were no significant differences in heart rate between forward and backward, or left and right, linear acceleration. Average MAP during the four accelerations with peak values of ±0.10, ±0.15, or ±20 G was not significantly changed compared with baseline. There was no significant difference in MAP between forward and backward, or left and right, linear accelerations. Thoracic impedance during the period of −Gx was significantly greater than that during the period of +Gx. There was no significant difference in thoracic impedance during the periods of +Gx and −Gx. Respiratory rates were controlled successfully at 0.25 Hz in all experiments.

**Dynamic responses.** Average results of total activity of MSNA, relative changes of mean heart rate, MAP, and thoracic impedance at each phase of the sinusoidal acceleration of the five cyclic movements are shown in Fig. 6. The results in Fig. 6 were averaged responses in each positive or negative phase. Each point in Fig. 6 was calculated according to the time segments of the positive or negative phase of the sinusoidal acceleration and is expressed as the change relative to the baseline value. The method of signal processing is illustrated in Fig. 3.

During anteroposterior movement, the sinusoidal acceleration induced clear rhythmic responses in thoracic impedance, which could be observed in original recordings and averaged results. The rhythms in thoracic impedance tended to be more apparent with stronger anteroposterior acceleration. In the first cyclic movement, heart rate increased significantly (P < 0.05), while MAP did not change significantly (Fig. 6). MSNA decreased significantly (P < 0.05) in the first cyclic movement (Fig. 6).

The sinusoidal rhythms in responses of thoracic impedance, MAP, heart rate, and MSNA can be observed more clearly in cross-correlograms (Fig. 7A). The cross-correlograms show the extent of the influence of the anteroposterior sinusoidal acceleration on MAP, heart rate, and thoracic impedance and reveal the phase relationships between the stimulus and subsequent response. For the anteroposterior sinusoidal acceleration with peak of ±0.10 G, all of the correlation coefficients were between +0.5 and −0.5. For the anteroposterior acceleration with peak of ±0.15 G, the correlation coefficient between the sinusoidal acceleration and thoracic impedance had a negative peak (about −0.55) near +1 s. This result demonstrates that a fluid shift was evoked by the anteroposterior acceleration at this level. This fluid shift was delayed by −1 s relative

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**Fig. 3.** The signal processing for muscle sympathetic nerve activity (MSNA). Recordings from a subject during sinusoidal linear acceleration in the anteroposterior direction with peak value of ±0.1 G. The burst area of the full-wave rectified and integrated neurogram was measured burst by burst with a computer. The sum of the burst area during each phase of the sinusoidal acceleration was then calculated according to the time segments of positive or negative acceleration. Finally, the total activity of MSNA at each phase of the sinusoidal acceleration was calculated as [(sum of burst area of the phase/phase length)/(sum of burst area of baseline/60)] × 100. The sum of the burst area during the 1 min just before the initial period of the sled motion was used as the baseline value (100%).

forward and backward linear accelerations are shown in Table 1. The results with lateral sinusoidal accelerations are shown in Table 2. The total activity of MSNA during the four linear accelerations is shown in Fig. 5.

Burst rate and total activity of MSNA decreased significantly during forward, backward, left, or right linear accelerations at peak values of ±0.10, ±0.15, and ±0.20 G compared with baselines. The decrease in MSNA tended to be more apparent with stronger acceleration. Although there were individual differences in the extent of MSNA decrease (Fig. 4), no MSNA increase was observed in any subject. For a given stimulation level, there was no significant difference in MSNA between the forward and backward, or left and right linear accelerations. The average burst rate and total activity of MSNA recovered to the baseline level in 1 min.

There were large individual differences in responses of heart rate and blood pressure during the linear
to the acceleration of the sled. During the anteroposterior acceleration with peak of ±0.20 G, the correlation coefficient between the acceleration and thoracic impedance had a negative peak (about -0.65) near 1 s. The correlation coefficient between the acceleration and MAP had a positive peak (about +0.75) near +5 s. Although the correlation coefficient between the acceleration and MSNA was between -0.4 and +0.4 during the three levels of anteroposterior acceleration, the cross-correlograms were also in sinusoidal shapes.

Heart rate increased significantly ($P \leq 0.05$) in the first cyclic movement during the lateral acceleration with peak values of ±0.10 and ±0.15 G (Fig. 6), while MAP did not change significantly. During lateral accelerations, all of the correlation coefficients between the sinusoidal acceleration and MSNA, MAP, heart rate, and thoracic impedance were between -0.5 and +0.5. The cross-correlograms showed sinusoidal characters in the lateral direction with peak of ±0.20 G (Fig. 7B).

**DISCUSSION**

The present study was undertaken to examine sympathetic neural responses to dynamic stimulation of otolith organs in the forward, backward, left, and right directions and to elucidate the sympathetic nerve response to physiological vestibular stimulation. We em-

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**Fig. 4.** Array display of changes in MSNA during sinusoidal linear acceleration in the anteroposterior direction with peak value of ±0.15 G. Observations of MSNA suppression were made during forward and backward linear acceleration. Sub 1–Sub 6, subjects 1–6.
Table 1. Average burst rate of MSNA, HR, TI, MAP, and respiration rate before, during, and after anteroposterior acceleration

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>−Gx</th>
<th>+Gx</th>
<th>1st Min</th>
<th>2nd Min</th>
<th>3rd Min</th>
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<tr>
<td>MSNA, bursts/min</td>
<td>21.4 ± 1.4</td>
<td>18.3 ± 2.4</td>
<td>15.7 ± 2.2</td>
<td>20.3 ± 1.7</td>
<td>22.0 ± 1.4</td>
<td>20.9 ± 1.1</td>
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<tr>
<td>HR, beats/min</td>
<td>69.5 ± 3.3</td>
<td>72.1 ± 3.6</td>
<td>72.0 ± 3.6</td>
<td>72.4 ± 3.7</td>
<td>70.6 ± 3.6</td>
<td>71.0 ± 3.2</td>
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<tr>
<td>TI, Ω</td>
<td>26.2 ± 0.9</td>
<td>26.3 ± 1.0</td>
<td>26.1 ± 1.0</td>
<td>26.2 ± 0.9</td>
<td>26.1 ± 0.9</td>
<td>26.1 ± 0.9</td>
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<tr>
<td>MAP, mmHg</td>
<td>97.8 ± 2.8</td>
<td>96.7 ± 3.8</td>
<td>97.8 ± 3.5</td>
<td>98.6 ± 3.2</td>
<td>97.5 ± 2.4</td>
<td>98.6 ± 2.2</td>
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<td>Resp, min−1</td>
<td>15.1 ± 0.2</td>
<td>15.0 ± 0.2</td>
<td>14.9 ± 0.2</td>
<td>15.1 ± 0.2</td>
<td>15.0 ± 0.1</td>
<td>14.9 ± 0.2</td>
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<tr>
<td>MSNA, bursts/min</td>
<td>22.1 ± 1.7</td>
<td>14.8 ± 2.6</td>
<td>13.3 ± 2.4</td>
<td>21.8 ± 2.4</td>
<td>21.8 ± 2.5</td>
<td>21.4 ± 1.7</td>
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<td>HR, beats/min</td>
<td>72.4 ± 3.6</td>
<td>73.4 ± 4.5</td>
<td>74.3 ± 5.1</td>
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<td>68.3 ± 3.0</td>
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<td>TI, Ω</td>
<td>26.1 ± 0.9</td>
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<td>26.1 ± 1.0</td>
<td>26.1 ± 0.9</td>
<td>26.1 ± 0.9</td>
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<tr>
<td>MAP, mmHg</td>
<td>98.0 ± 2.4</td>
<td>95.9 ± 4.9</td>
<td>96.0 ± 6.6</td>
<td>98.1 ± 2.1</td>
<td>97.7 ± 1.5</td>
<td>96.9 ± 2.0</td>
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<tr>
<td>Resp, min−1</td>
<td>15.1 ± 0.2</td>
<td>15.1 ± 0.2</td>
<td>15.0 ± 0.2</td>
<td>15.1 ± 0.2</td>
<td>14.9 ± 0.2</td>
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<td>MSNA, bursts/min</td>
<td>22.1 ± 1.6</td>
<td>13.3 ± 2.2</td>
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<td>HR, beats/min</td>
<td>68.0 ± 2.7</td>
<td>70.8 ± 2.6</td>
<td>72.5 ± 2.8</td>
<td>69.9 ± 2.8</td>
<td>67.7 ± 2.6</td>
<td>70.0 ± 2.2</td>
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<td>26.4 ± 1.0</td>
<td>26.0 ± 0.9</td>
<td>26.1 ± 1.0</td>
<td>26.1 ± 0.9</td>
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<tr>
<td>MAP, mmHg</td>
<td>96.5 ± 1.8</td>
<td>96.7 ± 4.7</td>
<td>96.2 ± 4.8</td>
<td>96.6 ± 1.7</td>
<td>96.9 ± 1.2</td>
<td>94.9 ± 2.2</td>
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<tr>
<td>Resp, min−1</td>
<td>15.0 ± 0.2</td>
<td>15.0 ± 0.2</td>
<td>14.9 ± 0.2</td>
<td>15.2 ± 0.2</td>
<td>14.9 ± 0.2</td>
<td>15.1 ± 0.2</td>
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Values are means ± SE; n = 10 subjects. Average values of the variables during 1 min just before the initial period of the sled motion were used as the baselines. MSNA, muscle sympathetic nerve activity; HR, heart rate; TI, thoracic impedance; MAP, mean arterial pressure; Resp, respiration; −Gx, backward acceleration; +Gx, forward acceleration; 1st min, 2nd min, 3rd min, the 1st, 2nd, and 3rd min after the acceleration stopped (see Fig. 1); 0.10 Gx, 0.15 Gx, 0.20 Gx, the anteroposterior sinusoidal acceleration with peak values of −0.10, −0.15, and −0.20 G. *P < 0.05 vs. baseline; †P < 0.05 vs. −Gx.

Table 2. Average burst rate of MSNA, HR, TI, MAP, and respiration rate before, during, and after linear acceleration

<table>
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<tr>
<th></th>
<th>Baseline</th>
<th>−Gy</th>
<th>+Gy</th>
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<tr>
<td>MSNA, bursts/min</td>
<td>23.5 ± 2.7</td>
<td>18.6 ± 3.2</td>
<td>17.9 ± 2.9</td>
<td>21.7 ± 2.5</td>
<td>22.5 ± 2.5</td>
<td>23.0 ± 2.7</td>
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<tr>
<td>HR, beats/min</td>
<td>61.2 ± 1.8</td>
<td>64.7 ± 2.2</td>
<td>64.4 ± 2.4</td>
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<td>61.4 ± 1.8</td>
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<tr>
<td>TI, Ω</td>
<td>27.3 ± 1.1</td>
<td>27.4 ± 1.2</td>
<td>27.4 ± 1.2</td>
<td>27.3 ± 1.1</td>
<td>27.4 ± 1.1</td>
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<tr>
<td>MAP, mmHg</td>
<td>102.7 ± 1.8</td>
<td>101.5 ± 1.8</td>
<td>102.2 ± 2.7</td>
<td>101.6 ± 1.9</td>
<td>103.6 ± 1.2</td>
<td>102.1 ± 1.3</td>
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<tr>
<td>Resp, min−1</td>
<td>15.1 ± 0.3</td>
<td>15.0 ± 0.3</td>
<td>14.9 ± 0.3</td>
<td>15.2 ± 0.3</td>
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<td>24.2 ± 2.4</td>
<td>16.4 ± 2.7</td>
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<td>21.2 ± 2.5</td>
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<td>HR, beats/min</td>
<td>62.0 ± 1.7</td>
<td>64.1 ± 2.4</td>
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<td>60.3 ± 2.3</td>
<td>62.2 ± 2.6</td>
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<td>TI, Ω</td>
<td>27.4 ± 1.1</td>
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<td>27.3 ± 1.2</td>
<td>27.3 ± 1.1</td>
<td>27.4 ± 1.1</td>
<td>27.4 ± 1.1</td>
</tr>
<tr>
<td>MAP, mmHg</td>
<td>103.2 ± 2.2</td>
<td>102.1 ± 2.6</td>
<td>102.4 ± 2.1</td>
<td>104.6 ± 1.9</td>
<td>104.0 ± 1.7</td>
<td>103.7 ± 2.0</td>
</tr>
<tr>
<td>Resp, min−1</td>
<td>15.1 ± 0.3</td>
<td>15.1 ± 0.3</td>
<td>15.0 ± 0.3</td>
<td>15.1 ± 0.3</td>
<td>15.1 ± 0.3</td>
<td>14.9 ± 0.3</td>
</tr>
<tr>
<td>0.20 Gx</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MSNA, bursts/min</td>
<td>23.2 ± 2.9</td>
<td>15.7 ± 3.1</td>
<td>15.1 ± 2.9</td>
<td>23.4 ± 2.5</td>
<td>24.6 ± 2.5</td>
<td>24.9 ± 3.1</td>
</tr>
<tr>
<td>HR, beats/min</td>
<td>61.1 ± 1.9</td>
<td>63.9 ± 2.8</td>
<td>63.6 ± 3.2</td>
<td>59.1 ± 2.4</td>
<td>61.2 ± 2.5</td>
<td>62.1 ± 1.8</td>
</tr>
<tr>
<td>TI, Ω</td>
<td>27.4 ± 1.1</td>
<td>27.4 ± 1.2</td>
<td>27.5 ± 1.2</td>
<td>27.4 ± 1.1</td>
<td>27.3 ± 1.1</td>
<td>27.4 ± 1.1</td>
</tr>
<tr>
<td>MAP, mmHg</td>
<td>101.8 ± 2.0</td>
<td>97.7 ± 2.6</td>
<td>98.0 ± 2.8</td>
<td>97.9 ± 1.8</td>
<td>101.1 ± 2.1</td>
<td>102.4 ± 2.5</td>
</tr>
<tr>
<td>Resp, min−1</td>
<td>15.1 ± 0.3</td>
<td>14.9 ± 0.3</td>
<td>15.0 ± 0.3</td>
<td>15.2 ± 0.3</td>
<td>15.1 ± 0.2</td>
<td>14.9 ± 0.3</td>
</tr>
</tbody>
</table>

Values are means ± SE; n = 6 subjects. Average values of the variables during 1 min just before the initial period of the sled motion were used as the baselines. −Gy, left acceleration; +Gy, right acceleration; 1st min, 2nd min, 3rd min, the 1st, 2nd, and 3rd min after the acceleration stopped; 0.10 Gx, 0.15 Gx, 0.20 Gx, the lateral sinusoidal acceleration with peak values of −0.10, −0.15, −0.20 G. *P < 0.05 vs. baseline.
accelerations with the peak values at $0.10$, $0.15$, and $0.20$ G, whereas a significant increase in heart rate was only observed during forward and backward acceleration with the peak value of $0.20$ G; and 2) the increase of heart rate during the first cyclic movement did not induce a significant increase in MAP that could inhibit MSNA via arterial baroreflexes. The decrease in MSNA was not attributable to a change in respiration because it was controlled at $0.25$ Hz. Therefore, the suppression of MSNA could not be considered as an effect of changes in MAP, heart rate, or respiration.

The difference in thoracic impedance between the forward and backward accelerations indicates that a fluid shift between the legs and trunk was induced by anteroposterior acceleration. Moreover, the cross-correlograms between thoracic impedance and sinusoidal acceleration in anteroposterior direction showed very clear sinusoidal mode, whereas the cross-correlation coefficients were low when the acceleration was in a lateral direction. These results suggested that fluid shift could be induced even by low-level acceleration when the trunk and/or legs were in the direction of the acceleration. The sinusoidal rhythms in MAP and heart rate during anteroposterior acceleration could be considered as resulting from the fluid shift. However, the decrease in MSNA during the four accelerations could not have been caused by the fluid shift, because 1) although $+G_x$ acceleration produced a transient fluid shift into the central compartment and might

Fig. 5. Changes in total activity of MSNA during forward, backward, left, and right linear acceleration with peak values of $0.10$, $0.15$, and $0.20$ G. The total activity of MSNA during 1 min just before the initial period of the sled motion was used as the baseline value (100%). Bars: $0.10$ G, $0.15$ G, $0.20$ G, sinusoidal acceleration with peak values of $0.10$ G, $0.15$ G, $0.20$ G, respectively. Subject nos.: $n = 10$ for anteroposterior acceleration ($G_x$), $n = 6$ for lateral acceleration ($G_y$). *$P < 0.05$ vs. baseline value.

Fig. 6. Dynamic changes of the mean arterial pressure (MAP), HR, TI, and total activity of MSNA during the sinusoidal linear acceleration of anteroposterior (A) and lateral (B) direction. The variables were averaged according to time segments of the positive or negative phase of the sinusoidal acceleration. The periods for one cyclic movement with peak acceleration of $0.10$, $0.15$, and $0.20$ G were 16.7, 13.3, and 11.6 s, respectively. Average values of the variables during 1 min just before the initial period of the sled motion were used as the baseline values (100%). Graphs: $0.10$ G, $0.15$ G, $0.20$ G, the sinusoidal acceleration with peak values of $0.10$ G, $0.15$ G, $0.20$ G. Subject nos.: $n = 10$ for anteroposterior acceleration (A), and $n = 6$ for lateral acceleration (B). *$P < 0.05$ vs. baseline value.
have produced sympathoinhibition due to loading of cardiopulmonary baroreceptors, $-G_x$ acceleration produced a transient fluid shift into the legs and should have produced sympathoexcitation due to unloading of all subtype baroreceptors, which was not observed in the present study; and 2) the decrease of MSNA was also observed during left or right linear acceleration, which did not induce the fluid shift.

The correlation coefficients between the sinusoidal acceleration and MSNA were low. Because MSNA burst rates were low, there were many cardiac cycles with no MSNA burst. This low burst frequency might contribute to the low correlation coefficients. Even though the cross-correlograms between the sinusoidal acceleration and MSNA were also in sinusoidal shapes, the sinusoidal characters tended to be more apparent with stronger acceleration.

Vestibular stimulation during linear acceleration can produce cardiovascular responses in humans (25). There is also considerable evidence that stimulation of the vestibular system affects sympathetic preganglionic neurons in animals and postganglionic nerves in animals and humans (1, 2, 7, 12, 13, 20, 24, 26–30). Therefore, the decrease in MSNA during $+G_x$ or $+G_y$ acceleration in sitting subjects could be a response evoked by stimulation of otolith organs.

Linear acceleration in a sinusoidal mode, used in the present experiments, was a dynamic stimulation which would induce postural reflexes through the vestibular input in wakeful subjects. The skeletal muscle pump may be enhanced during the passive reciprocating movement, but average thoracic impedance and average MAP did not change significantly, unlike those caused by light dynamic and static exercise (16–18). It is possible that the dynamic stimulation of otolith organs in the horizontal direction might inhibit MSNA directly. The physiological significance for the decrease of MSNA during the passive movement might result in a quick redistribution of blood to muscles. A suppression of MSNA induced by vestibular stimulation would decrease the peripheral resistance and increase the blood flow to muscles that are involved in postural reflexes. The suppression of MSNA by vestibular stimulation during passive movement might be a type of feedforward regulation, as hypothesized by Yates and Miller (29). The contribution of this pathway to cardiovascular regulation would be expected to be smaller than that of the baroreflex. The individual differences in hemodynamic responses might be related to intersubject variability in postural reflexes.

Characteristics of MSNA responses to dynamic stimulation of otolith organs. The decrease in MSNA observed in the present study was different from the MSNA responses that were enhanced after a delay of 30–60 s after the onset of nystagmus induced with caloric vestibular stimulation (6, 11). Because caloric vestibular stimulation has an effect on the unilateral semicircular canals and evokes motion sickness symptoms, the enhancement of MSNA in previous experiments (6) could be considered as vestibulosympathetic responses related to motion sickness, caused partly by an imbalance between the bilateral semicircular canals. Linear acceleration stimulated bilateral otolith organs, and no motion sickness symptoms were observed. This MSNA decrease can be considered a physiological vestibulosympathetic response in sitting humans during horizontal movements. Thus the moderate horizontal linear acceleration applied to sitting subjects.
induce different MSNA responses than those induced by caloric vestibular stimulation.

Our finding of a decrease in MSNA in sitting subjects during sinusoidal acceleration in horizontal directions is different from the significant increase in MSNA found by Ray et al. (13, 20) during sustained passive head-down neck flexion in a prone position in humans. These differences may be explained by three hypotheses: 1) the utricular afferents were likely altered in the present experiments, whereas saccular and utricular afferents should be altered by the head-down neck flexion (19); 2) dynamic stimulation might cause different responses from sustained stimulation; and 3) the changes in acceleration on otolithic organs during the static head-down neck flexion should have been stronger than those in our experiments.

In summary, we found that MSNA was suppressed significantly during moderate sinusoidal linear acceleration in the forward, backward, left, or right directions in sitting human subjects. The findings support the concept that otolithic organs contribute to sympathetic regulation in humans.

Perspectives

Data from the present and previous studies have demonstrated that vestibular inputs, especially from otolithic organs, affect the sympathetic nervous system, which supports the hypothesis that the vestibular inputs are involved in the regulation of the cardiovascular system. Different directions of linear acceleration activate different populations of vestibular receptors. However, the present data show that MSNA recorded in tibial nerves in humans was suppressed during linear acceleration in the four directions. MSNA suppression during linear acceleration may help to redistribute blood to muscles that are involved in postural reflexes. Because postural reflexes will be induced when one slips and falls in any of the four directions, and the muscles in lower legs and feet will be used in the postural reflexes, the responses of sympathetic outflow to the muscles in legs and feet should be similarly suppressed during activation of any group of utricular receptors. However, the responses of sympathetic outflow to other muscle groups might be different from that recorded from tibial nerves during horizontal linear acceleration, which could be identified in further experiments.

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