Impairment of vestibular-mediated cardiovascular response and motor coordination in rats born and reared under hypergravity

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We recently reported that hypergravity environment induces the plastic alteration of the vestibulo-cardiovascular reflex (1, 20). The vestibular-mediated arterial pressure (AP) response is attenuated in rats reared in a 3-G environment. This effect is evident at the age of 8–10 wk when the vestibular system is considered completely developed. The vestibular organ in rats develops between embryonic day 8 and postnatal day 15 (P15), while efferent innervation is completely developed by P21 (5). Vestibular nuclear neurons are fully formed by P30 (P15), while efferent innervation is completely developed by P30 (P15).

Abe C, Tanaka K, Awazu C, Morita H. Impairment of vestibular-mediated cardiovascular response and motor coordination in rats born and reared under hypergravity. Am J Physiol Regul Integr Comp Physiol 295: R173–R180, 2008. First published May 21, 2008; doi:10.1152/ajpregu.00120.2008.—It is well known that environmental stimulation is important for the proper development of sensory function. The vestibular system senses gravitational acceleration and then alters cardiovascular and motor functions through reflex pathways. The development of vestibular-mediated cardiovascular and motor functions may depend on the gravitational environment present at birth and during subsequent growth. To examine this hypothesis, arterial pressure (AP) and renal sympathetic nerve activity (RSNA) were monitored during horizontal linear acceleration and performance in a motor coordination task in rats born and reared in 1-G or 2-G environments. Linear acceleration of ≥1 G increased AP and RSNA. These responses were attenuated in rats with a vestibular lesion, suggesting that the vestibular system mediated AP and RSNA responses. These responses were also attenuated in rats born in a 2-G environment. AP and RSNA responses were partially restored in these rats when the hypergravity load was removed, and the rats were maintained in a 1-G environment for 1 wk. The AP response to blood pressure (BP) in which is mediated independently of the vestibular system, did not change in the 2-G environment. Motor coordination was also impaired in the 2-G environment and remained impaired even after 1 wk of unloading. These results indicate that hypergravity impaired both the vestibulo-cardiovascular reflex and motor coordination. The vestibulo-cardiovascular reflex was only impaired temporarily and partially recovered following 1 wk of unloading. In contrast, motor coordination did not return to normal in response to unloading.

We recently reported that hypergravity environment induces the plastic alteration of the vestibulo-cardiovascular reflex (1, 20). The vestibular-mediated arterial pressure (AP) response is attenuated in rats reared in a 3-G environment. This effect is evident at the age of 8–10 wk when the vestibular system is considered completely developed. The vestibular organ in rats develops between embryonic day 8 and postnatal day 15 (P15), while efferent innervation is completely developed by P21 (5). Vestibular nuclear neurons are fully formed by P30 (15). Thus our previous studies indicated that different gravitational environments influence the sensitivity of the vestibular system, even in rats whose vestibular system has completely developed.

Hubel and Wiesel (12) originally suggested that environmental stimulation is important for the proper development of sensory function. Subsequent research has validated this concept via investigations of the relationships between light environment and visual sensation, odor environment and olfactory sensation, and tactile environment and somatic sensation (21, 24, 25). With regard to the gravitational environment, Walton et al. (32, 33) demonstrated that the normal 1-G environment is required for the development of motor function. The microgravity environment alters surface righting and swimming behavior in a time-dependent manner. Motor function is permanently altered in rats exposed to microgravity for 16 days (P14–P30), but is transient in rats exposed to microgravity for 9 days (P15–P24). Different gravitational environments may affect the development of the gravity sensor and the vestibular system; this may, in turn, influence vestibular-mediated motor function.

These concepts led us to hypothesize that exposure to different gravitational environments during development of the vestibular system may permanently modify vestibular-mediated cardiovascular responses. To address this hypothesis, we divided rats born and reared in different gravitational environments into three groups: 1) the usual 1-G environment; 2) a 2-G environment; and 3) a 1-G environment after 9 wk of 2-G load. We then examined the vestibular-mediated AP and renal sympathetic nerve responses to linear acceleration in these rats. Furthermore, to examine the vestibular-mediated motor function, we investigated rotarod skill in these rats. The rotarod task is used to examine vestibulo-motor coordination in rats (6, 9).

METHODS

Animals used in the present study were maintained in accordance with the “Guiding Principles for Care and Use of Animals in the Field of Physiological Science” set by the Physiological Society of Japan. The experiments were approved by the Animal Research Committee of Gifu University. The age and number of rats in each group in the present study are summarized in Fig. 1. In brief, six rats at gestation day 14, their male pups (n = 33), and 10-wk-old male rats (n = 10, for vestibular lesion [VL]) were used. An additional 12 male rats were used for short-term 2-G load during vestibular mature period (8–10 wk of age).

Of the six pregnant rats, three were maintained in individual cages (50 cm width × 50 cm length × 25 cm height) set in a 2-G environment; the environment was induced by centrifugation using a custom-made gondola-type rotating box (Shimadzu, Kyoto, Japan). The pregnant rats delivered and reared pups in the 2-G environment. To clean the cages and refresh food and drinking water, centrifugation was ceased for 15 min every day. Rats were fed ad libitum, the cages were maintained on a 12:12-h light-dark cycle, and the room temperature was maintained at 24 ± 1°C. The other three pregnant rats were maintained in individual cages, but in the usual 1-G environment (1-G rats). They delivered and reared pups in the 1-G environment. At 4 wk
Grip strength of the 1-G, 2-G, andUnload rats was measured using a custom-made grip strength meter (IMADA, Toyohashi, Japan). Each rat was held by the tail just over the bar of the grip-strength meter; the rat reached out and grasped the bar with its forepaws. The rat was then pulled away from the grip-strength meter by its tail in one smooth motion until the grip was released. In this manner, the grip-strength meter measured the maximum force (in grams) at the instant before the bar was released. The maximum value obtained from five trials was used as individual data.

After the rotarod and grip-strength experiments, all of the rats were anesthetized with pentobarbital sodium (50 mg/kg ip), and a polyethylene catheter (PE-50; Becton Dickinson, Sparks, MD) was inserted into the abdominal aorta via the left femoral artery to measure AP. The catheter was exteriorized from the back of the neck. For recording the renal sympathetic nerve activity (RSNA), the postganglionic renal sympathetic nerve was isolated through a right or left flank incision, and two stainless-steel electrodes (AS633; Cooner Wire, Chatsworth, CA) were placed around it. The nerve and electrodes were covered and fixed with silicone gel (Semicosil 932 A and B; Wacker Chemie, Munich, Germany), and the electrodes were exteriorized at the back of the neck. The same implantations were also conducted on other 10-wk-old rats with VL (n = 10). Sodium arsanilate solution (100 mg/ml) was injected into the bilateral middle ear cavities (50 μl/ear). In 1-G, 2-G, andUnload rats, a sham operation was performed using the same procedure as that for the VL, except that saline was injected instead of sodium arsanilate. All of the rats were maintained in individual cages to allow recovery from the surgery until the linear acceleration experiment.

At 1 day after the surgery, each rat was placed in a small box (6 cm width × 20 cm length × 6 cm height) that loosely restricted movement to prevent the rats from turning around. The rats were trained to stay in the box. Training was employed twice before the surgery and once before the linear acceleration experiment; each session lasted 20 min. The catheter was connected to a pressure transducer (MP5200; Baxter, Deerfield, IL) placed at the cardiac level. The signal from the transducer was transmitted to an amplifier (MEG-6108; Nihon Kohden, Tokyo, Japan). The electrodes for RSNA recording were connected to an amplifier (MEG-1200; Nihon Kohden, Tokyo, Japan) equipped with a 50- to 1,000-Hz band-pass filter. The output from the amplifier was passed through a gate circuit to subtract baseline noise, and it was rectified by an absolute value circuit. A gravity sensor (MTS-050; Mitec, Hiroshima, Japan) was placed on the stage of the linear accelerator (LSA-S10HS; IAI, Shizuoka, Japan). All signals were recorded using an analog-to-digital converter (PowerLab; AD Instruments, New South Wales, Australia) at a rate of 1,000 Hz.

The box containing the rat was covered with a copper box to minimize electrical noise, visual cue, and wind during the linear acceleration. This box was placed on the stage of the linear accelerator. The G level (±1 G), stroke (2,000 mm), and interval (30 s) were programmed using computer software (SSEL; IAI, Shizuoka, Japan). Linear acceleration was employed in four directions: from tail to nose (tail-nose), from nose to tail (nose-tail), from left to right (left-right), and from right to left (right-left). Figure 1, bottom, shows the G profile of the rat that moves in the tail-nose or left-right direction. The G force directed to the tail or the left direction indicates −1 G, whereas that directed to the nose or the right indicates +1 G. The G profile during movement in the tail-nose or left-right directions is also shown. The G value decreased and was maintained at −1 G until the speed reached 2,500 mm/s, and at 0 G after the speed reached 2,500 mm/s; the G force was applied in the opposite direction for deceleration. 1-G, rats reared under 1 G; 2-G, rats reared under 2 G; Unload, rats reared under 1 G after 9 wk of 2-G load; VL, rats with vestibular lesion.
single pulse (1-s duration) of compressed air (23 g/mm²) aimed at the forehead was applied from a 1-mm opening at the front of tube.

All of the data are presented as means ± SE. For the data in Table 1, Fig. 3, bottom, and Fig. 7, right, a one-way ANOVA was applied. Repeated-measures two-way ANOVA was used for the data presented in Fig. 2, Fig. 3, top, Fig. 4, and Fig. 6. If the F ratio indicated statistical significance, the Student-Newman-Keuls post hoc test was applied for intergroup comparison. For the post hoc test, the significance level was set at P < 0.05.

RESULTS

Table 1 shows the mean baseline AP and heart rate data of all of the groups. AP in the 2-G rats was significantly lower than that in the 1-G and Unload groups and rats with VL. The heart rate in the 2-G rats tended to be higher; however, the difference was statistically significant.

Figure 2, top, shows the daily variation in body mass from 4 to 10 wk in the 1-G, 2-G, and Unload rats. In all groups, body mass increased daily. Body mass differed between the groups [group effect: F(2,30) = 45.187, P < 0.001], and differences in body mass were dependent on time [interaction effect: F(82, 1,230) = 33.489, P < 0.001]. The body mass of the 2-G and Unload rats was significantly lower than that of the 1-G rats (P < 0.001), whereas body mass was similar in the 2-G and Unload rats. The daily gain in body mass was presented separately for weeks 4–9 and weeks 9–10 (Fig. 2, bottom). This gain was calculated by dividing the increase in body mass for each individual rat by the number of days for both periods. The gain during weeks 4–9 in the 1-G rats was significantly greater than that in the 2-G and Unload rats. Compared with the gain during weeks 4–9, the gain during weeks 9–10 was significantly smaller in the 1-G and 2-G rats. In contrast, the Unload rats gained body mass at a consistent rate. Furthermore, the gain during weeks 9–10 in the Unload rats was significantly greater than that in the 2-G rats. At the beginning of the 10th wk, the body mass (means ± SE) was 289 ± 6 g in the 2-G rats, 307 ± 6 g in the Unload rats, and 366 ± 5 g in the 1-G rats.

Figure 3, top, shows the duration for which the rats could hold themselves on the rotating rod during the first, second, and third trials of the rotarod experiment. In the 1-G rats, this duration increased significantly with each trial; however, this improvement did not occur in the 2-G or Unload rats. All of the 2-G rats could remain on the rod when the rod was static; however, they could not walk on the rod once the rod started to

Table 1. Baseline data for AP and HR

<table>
<thead>
<tr>
<th>Direction of Acceleration</th>
<th>Group</th>
<th>AP, mmHg</th>
<th>HR, beats/min</th>
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<tbody>
<tr>
<td></td>
<td>1 G</td>
<td>114±2</td>
<td>381±10</td>
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<tr>
<td></td>
<td>2 G</td>
<td>106±1*</td>
<td>417±14</td>
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<tr>
<td></td>
<td>Unload</td>
<td>113±4</td>
<td>384±8</td>
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<td></td>
<td>VL</td>
<td>115±3</td>
<td>389±13</td>
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<tr>
<td>Nose-tail</td>
<td>1 G</td>
<td>114±2</td>
<td>378±9</td>
</tr>
<tr>
<td></td>
<td>2 G</td>
<td>106±2*</td>
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<tr>
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<tr>
<td></td>
<td>VL</td>
<td>115±3</td>
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<tr>
<td>Left-right</td>
<td>1 G</td>
<td>115±2</td>
<td>378±9</td>
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<tr>
<td></td>
<td>2 G</td>
<td>108±2*</td>
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<td></td>
<td>Unload</td>
<td>113±5</td>
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<tr>
<td></td>
<td>VL</td>
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<tr>
<td>Right-left</td>
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<td>VL</td>
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Values are means ± SE. AP, arterial pressure; HR, heart rate; VL, vestibular lesion. See METHODS for explanation of groups. The baseline AP in the 2-G rats was significantly lower than that in the 1-G, Unload, and rats with VL in all directions (*P < 0.05 vs. 1 G, Unload, and VL).
rotate. Hence, the 2-G rats remained on the rod for an extremely short duration (2 ± 1 s in all three trials). This duration did not increase after unloading of gravity for 1 wk. We believe that the inability to walk on the rotating rod was not due to muscle weakness, as there was no difference in grip strength among groups (Fig. 3, bottom). The rats with VL were unable to maintain their position on the rod; consequently, we did not conduct the rotarod experiment with these rats. The 2-G environment during the vestibular mature period also impaired rotarod skill (Fig. 4). However, this impairment was not permanent, but recovered by 1 wk of unloading. Furthermore, the improvement of duration with each trial was not observed in the 2W-2G rats; however, this duration was significantly increased with each trial in 2W2G-Unload rats.

Figure 5 shows the typical recordings of gravity, AP, and RSNA in response to tail-nose linear acceleration in 1-G, 2-G, Unload, and VL rats. In a 1-G rat, RSNA transiently increased at the onset of acceleration, followed by a transient increase in AP. The AP increased from 111 mmHg to a peak value of 136 mmHg at 1.7 s after the onset of acceleration. At this time, RSNA was suppressed. Although the tendendencies of the AP and RSNA responses in a 2-G rat, an Unload rat, and a VL rat appeared identical to those in a 1-G rat, the magnitudes of the responses were smaller in these groups.

The mean data for AP (left) and RSNA (right) responses used for intergroup comparisons are shown in Fig. 6. AP response was calculated as the difference between the 4-s average of AP just before the induction of acceleration, and the 1-s average of the peak AP value. RSNA response was calculated by dividing the 4-s average just before the induction of acceleration by the 0.45-s average observed during acceleration. In the 1-G rats, AP increased by 24 ± 1 mmHg in the tail-nose direction, by 19 ± 1 mmHg in the nose-tail direction, 20 ± 1 mmHg in the left-right direction, and 21 ± 1 mmHg in the right-left direction. A direction-specific response was observed in the tail-nose and nose-tail accelerations, but not in the left-right and right-left accelerations. The pressor response in the tail-nose direction was significantly greater than that in the 2-G rats in the nose-tail and left-right directions. RSNA in the 1-G rats increased to 777 ± 77% in the tail-nose direction, 600 ± 44% in the nose-tail direction, 731 ± 65% in the left-right direction, and 619 ± 87% in the right-left direction. The RSNA response was significantly attenuated in 2-G and rats with VL; however, RSNA did not differ significantly between the 1-G and Unload rats. A direction-specific RSNA response was observed in the 1-G rats in the tail-nose and nose-tail accelerations, but not in the left-right and right-left accelerations.

Figure 7, left, shows the typical recordings of AP and RSNA in response to compressed air in a 1-G rat. RSNA transiently increased when compressed air was applied, followed by a transient increase in AP. AP increased from 113 mmHg to a peak value of 133 mmHg at 1.5 s after compressed air was applied. At this time, RSNA was suppressed. The mean data for the pressor response to compressed air are shown in Fig. 7, right. The presessor response was calculated as the difference between the 4-s average of AP just before application of compressed air and the 1-s average of the peak AP value. The RSNA response was calculated by dividing the 4-s average of RSNA just before the application of compressed air by the 1-s average of the duration for which compressed air was applied. In contrast to the linear acceleration experiment, the pressor response and RSNA did not differ between the groups in response to the application of compressed air.

DISCUSSION

The major findings of the present study are as follows. First, the 2-G environment attenuated the daily gain in body mass, in addition to the AP and RSNA responses to linear acceleration. One week of unloading reversed these effects. Second, the 2-G environment impaired coordinated movement, but not grip strength. This effect did not change after 1 wk of unloading. Third, the 2-G environment during vestibular mature period also impaired coordinated movement, although this impairment was recovered by 1 wk of unloading.

Daily body mass was recorded from the 4th to 10th wk. In the 1-G rats, the gain in body mass during weeks 4–9 was 7.4 ± 0.1 g/day, significantly higher than the gain in body mass in the 2-G and Unload rats. The decrease in the body mass of the 2-G and Unload rats observed in the present study is consistent with the findings of previous studies (1, 18, 31), in which hypergravity was applied to adult rats for 2 wk. This decrease is probably due to the high-energy expenditure during a hypergravity load and transient decrease in food intake (18, 31). Before sexual maturity (40–60 days), rapid growth occurs; subsequently, the gain in body mass slows (13). In the 1-G and 2-G rats, the rate of gain in body mass decreased from 4–9 wk to 9–10 wk. The rate of gain during 9–10 wk in the 2-G rats was also lower than that in the 1-G rats; however, this age-related slowing of weight gain did not occur in the Unload rats. The gain in body mass during weeks 9–10 in Unload rats was significantly greater than that in the 2-G rats and comparable with that in the 1-G rats. We believe that unloading of gravity from 2 to 1 G reduced energy expenditure, as the gravitational body mass was reduced by one-half after unloading. This decrease in energy expenditure may lead to increased...
body mass, if we consider that food intake was not affected by the unloading of gravity.

A recent study performed in our laboratory demonstrated that vertical gravitational change induces the vestibular-mediated pressor response (1, 7, 19, 20, 29). In the present study, we applied linear horizontal accelerations in four directions, and we also observed the pressor response. VL attenuated this pressor response, indicating that the vestibular system is a key factor mediating AP during horizontal linear acceleration. Therefore, we used horizontal acceleration to evaluate the vestibular-mediated AP and RSNA responses in the present study.

A direction-specific pressor response was observed in the 1-G, 2-G, and Unload rats; the pressor response in the tail-nose direction was significantly greater than that in the nose-tail direction. Since the rats with VL did not respond in this manner, the direction specificity may depend on the direction of input to the vestibular organ. Hess and Angelaki (10) also reported asymmetry of the vestibulo-ocular reflex during transient forward and backward motion. Specifically, they noted that the vestibular-mediated ocular velocity gain is greater with the forward motion than with the backward motion. They proposed that this difference may result from functional adap-

![Fig. 5. Typical recordings illustrating the arterial pressure (AP) and renal sympathetic nerve activity (RSNA) in the 1-G, 2-G, Unload, and VL rat groups in response to tail-nose acceleration.](image)

![Fig. 6. Top left: changes in the AP (ΔAP) during movement in the tail-nose (solid bars) and nose-tail (open bars) directions in the 1-G, 2-G, Unload, and VL rat groups. Bottom left: ΔAP during movement in the left-right (solid bars) and right-left (open bars) directions. ΔAP was calculated as the difference between the 4-s average of AP just before the induction of acceleration and the 1-s average of the peak AP value. Top right: responses of the RSNA to tail-nose (solid bars) and nose-tail (open bars) accelerations in the 1-G, 2-G, Unload, and VL rat groups. Bottom right: RSNA responses to the left-right (solid bars) and right-left (open bars) accelerations. The RSNA response was expressed as the percentage calculated by dividing the 4-s average of RSNA just before the induction of acceleration by the 0.45-s average of RSNA in the first acceleration. P < 0.05 vs. *1-G rats, †tail-nose direction (solid bars), and ‡2-G rats.](image)
tation of the vestibular system to the most commonly experienced forward movements.

The pressor responses to linear acceleration in the 2-G rats were significantly attenuated compared with those in the 1-G rats; however, the pressor response to compressed air, which is not mediated via the vestibular system, was not attenuated in the 2-G rats. Therefore, the 2-G environment suppressed the vestibular-mediated AP response, but did not influence the nonvestibular-mediated AP response. In the Unload rats, the pressor responses tended to be greater than those in the 2-G rats, although a significant difference was observed only in the nose-tail and left-right accelerations. Furthermore, sympathoexcitatory responses were significantly attenuated in the 2-G rats. This effect was completely reversed after 1 wk of unloading from 2G to 1G. Accordingly, in rats born and reared under a hypergravity environment, the magnitude of pressor and RSNA responses to linear acceleration was reduced; however, these responses were gradually restored when the rats were unloaded from 2 to 1 G.

In contrast to the recovery of AP and RSNA responses to linear acceleration, performance in the rotarod task did not recover following 1 wk of unloading. The rotarod task, which evaluates the ability to maintain equilibrium on a rotating rod, has been used to examine vestibulo-motor coordination in rats (6, 9). The exact mechanism underlying the impairment of the rotarod skill in the 2-G rats was not clear in the present study, but may involve motor coordination. Modification of postnatal motor coordination has been reported in rats reared under a microgravity environment (32, 33). Therefore, a hypergravity environment may modify motor coordination, which comprises many processes, including vestibular input, tactile and somatosensory clues, central nervous system, and a motor component. In the rats with VL in the present study, the vestibular system is completely destroyed, thereby preventing the rats from remaining on the rod. The 2-G and Unload rats could remain on the static rod, but could not continue walking once the rod started to rotate. They could, however, walk normally and stand up on hind paws in their own cage. This observation suggests that vestibular function, as reflected in the ability to maintain balance on the rod and in a stable place, did not deteriorate in the 2-G and Unload rats. Accordingly, the vestibular function in the 2-G and Unload rats was not completely inhibited, but might have been partially impaired.

The difference in recovery of responses to linear acceleration vs. recovery of rotarod skill might reflect differences between the two conditions with regard to compensation by the nonvestibular system. VL partially abolished the AP and RSNA responses to linear acceleration (Fig. 6). This indicates that 30–50% of the pressor and RSNA responses to linear acceleration were mediated via the nonvestibular system, probably including the somatosensory and proprioceptive systems (16, 34). Thus unloading for 1 wk may have increased the sensitivity of the nonvestibular-mediated responses. Evidence in support of this notion is that the recovery of AP control during nose-up tilt was observed in VL animals (14). In contrast, the vestibular system may exert greater influence in the rotarod skill, because the rats with VL could not remain on the rod at all. Even partial dysfunction of the vestibular system impairs performance in the rotarod task. It is possible that compensation via nonvestibular systems does not assist in completing the rotarod task.

Another finding from the rotarod experiment was that rotarod skill did not improve in the 2-G and Unload rats with each trial. In rats with an intact vestibular system, short-term improvement in the rotarod skill was observed with each trial (3), and we also observed improvement in the 1-G rats in the present study. However, in the 2-G and Unload rats, rapid motor skill acquisition was impaired. Successful performance of the rotarod task requires the vestibular system for sensing balance and self-motion, the cerebellum for improving the skill, and the hippocampus for the processing of spatial information. In combination, these functions contribute to motor learning (3, 4, 26–28). Thus short-term improvement in rotarod skill likely depends on interaction among the vestibular system, cerebellum, and hippocampus. To further understand the effect of hypergravity environment on vestibular-mediated motor coordination, future studies could focus on individual pathways, including the vestibular system, cerebellum, and hippocampus.
The hypergravity load during vestibular mature period (8–10 wk of age) also impaired rotarod skill. Thus the duration and period of hypergravity applied may not be a determinant factor of the induction of impaired rotarod skill. However, the recovery of the impaired function was depending on the period of 2-G load. The impairment that was induced by 2-G load during vestibular mature period was recovered by 1 wk of unloading. On the other hand, the impairment that was induced by 2-G load during vestibular immature period was not recovered by 1 wk of unloading. This is consistent with the concept of “critical period” (12, 32, 33).

Limitations. Richardson and Knapp (23) compared baseline AP between the 2-G rats and the 1-G control rats, which were undergone on axis centrifugation, and found that the AP in the 2-G rats (126 mmHg) was slightly higher than that in the 1-G rats (121 mmHg), but the difference was not significant. However, in the present study, the baseline AP in the 2-G rats was significantly lower than that in the 1-G rats. This discrepancy is probably due to the difference in control group, i.e., with or without centrifugation effects on control groups, and anesthetic used; they measured AP under alobarbital and urethane anesthesia. Furthermore, in the present study, all measurements were performed under the 1-G environment; a transient gravitational shift from 2 to 1 G was achieved in the 2-G rats. This transient gravitational shift might have influenced the physiological responses. Thus the decrease in the baseline AP in the 2-G rats may have occurred for two reasons. First, the 2-G load itself decreased the baseline AP. Second, the 2-G load itself did not alter the baseline AP, but acute gravitational change from 2 to 1 G decreased AP, since AP measurement was performed under the 1-G condition and 1 day after the cessation of the 2-G load. To clarify these possibilities, it is necessary to measure AP under the 2-G environment.

The 2-G load during vestibular immature period attenuated pressor and sympathoexcitatory responses to linear acceleration, and these responses were restored by the unloading of gravity for 1 wk. The gain in body mass was also reversed by unloading of gravity for 1 wk; that is, the critical period might exist in the vestibular-mediated motor function. Thus, depending on the functions, the 2-G environment induced either a transient or much longer alteration in the vestibular-mediated responses.

Perspectives and significance. Long-term exposure to hypergravity environment might have two effects on the vestibular system: one is a static increase in the vestibular input, and the other is a decrease in fluctuation of the vestibular input, since the movement activity in rats under 2-G environment was significantly suppressed compared with the 1-G rats (11). Although the mechanisms responsible for hypergravity-induced deficits are unclear in the present study, two possibilities are worth discussing. First, the increased static input to the vestibular organ might “downregulate” the receptors (30). Second, decreased fluctuation of the vestibular input may induce “disuse deterioration” of the vestibular system. In spaceflight, both static input to the vestibular system and fluctuation of the input are minimal. In elderly subjects whose daily activity is reduced, fluctuation of the vestibular input is also low. Both spaceflight and aging are known to induce orthostatic intolerance and impairment of motor coordination (8, 17, 22, 36). Since the vestibular system is considered to be important for maintaining AP upon posture transition (35), detailed studies of the plastic alteration of the vestibulo-cardiovascular reflex are required to clarify the relevant mechanisms and explore potential countermeasures against orthostatic intolerance. In particular, which is more critical, i.e., static input or amount of fluctuation, for inducing plastic alteration of the vestibular system has to be examined in future studies.

GRANTS

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