Effects of bilateral vestibular lesions on orthostatic tolerance in awake cats

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Jian, B. J., L. A. Cotter, B. A. Emanuel, S. P. Cass, and B. J. Yates. Effects of bilateral vestibular lesions on orthostatic tolerance in awake cats. J. Appl. Physiol. 86(5): 1552–1560, 1999.—Previous experiments in anesthetized or decerebrate cats showed that the vestibular system participates in adjusting blood pressure during postural changes. The present experiments tested the hypothesis that removal of vestibular inputs in awake cats would affect orthostatic tolerance. Before the lesion, blood pressure typically remained within 10 mmHg of baseline values during nose-up-pitch body rotations of up to 60° in amplitude. In contrast, bilateral peripheral vestibular lesions altered the pattern of orthostatic responses in all animals, and blood pressure fluctuated >10 mmHg from baseline values during most 60° nose-up tilts in five of six animals. The deficit in correcting blood pressure was particularly large when the animal also was deprived of visual cues indicating position in space. During this testing condition, either a decrease or increase in blood pressure >10 mmHg in magnitude occurred in >80% of tilts. The deficit in adjusting blood pressure after vestibular lesions persisted for only 1 wk, after which time blood pressure remained stable during tilt. These data show that removal of vestibular inputs alters orthostatic responses and are consistent with the hypothesis that vestibular signals are one of several inputs that are integrated to elicit compensatory changes in blood pressure during movement.

blood pressure; heart rate; cardiovascular system; exercise

CONSIDERABLE EVIDENCE collected in the cat suggests that the vestibular system influences the regulation of blood pressure during movement and changes in posture. Electrical stimulation of vestibular afferents produces changes in activity in a variety of sympathetic nerves containing vasomotor fibers (4, 6, 8, 14, 15, 19). These vestibulosympathetic responses are eliminated by increasing blood pressure to over 160 mmHg in baroreceptor-intact animals, a manipulation that selectively decreases responsiveness of sympathetic efferents innervating vascular smooth muscle but not other targets such as gastrointestinal smooth muscle (6). This finding suggests that the vestibular system influences components of the sympathetic nervous system that control blood pressure. Furthermore, selective nose-up natural stimulation of vestibular afferents, produced by rotation of the head of an animal with extensive denervations to remove nonlabyrinthine inputs that might be produced by this movement, results in changes in sympathetic nerve activity (20) and blood pressure (16). For example, a 50° nose-up head rotation elicited a mean pressor response of ~20 mmHg (16). This response pattern is appropriate to offset posturally related hypotension, because the cat has a long longitudinal axis and is susceptible to orthostasis during nose-up body rotations (but not ear-down or nose-down tilts). Thus the vestibulosympathetic reflex has been proposed as a mechanism that serves to maintain constant blood pressure during unexpected changes in posture that place the longitudinal axis parallel with the gravitational vector; such postural disturbances are common in cats during climbing maneuvers (17, 18).

These findings suggest that removal of vestibular inputs would compromise the ability of a quadruped to maintain stable blood pressure during nose-up tilt. Doba and Reis (3) demonstrated that orthostatic tolerance is impaired in anesthetized and paralyzed cats after a bilateral eighth cranial nerve transection. The hypotension was modest during 30° nose-up tilts, but 60° nose-up tilts resulted in a drop in blood pressure of ~50 mmHg from baseline values. In contrast, 60° nose-up tilt in vestibular-intact animals had only a small impact on blood pressure.

However, there is presently little information concerning the role of the vestibular system in cardiovascular control in awake animals because previous studies of vestibulosympathetic responses were conducted in anesthetized or decerebrate preparations. It is possible that peripheral vestibular lesions in conscious animals, which have a variety of sensory inputs available for determining body position in space, would have different effects on orthostatic tolerance than those Doba and Reis (3) reported in anesthetized cats. In the present study, blood pressure and heart rate were monitored during unexpected body rotations in the pitch plane in awake cats trained to lie sedentary on a tilt platform. After the changes in blood pressure and heart rate elicited by tilt were recorded over a period of several weeks, vestibular inputs were removed bilaterally, and the effects of these lesions on cardiovascular responses to whole body pitch were evaluated. We also assessed whether the effects of removal of vestibular inputs on the control of blood pressure and heart rate were transient or whether the effects persisted for up to 1 mo after the vestibular lesion.

METHODS

All of the procedures used in this study conformed to the American Physiological Society’s Guiding Principles for the Care and Use of Animals and were approved by the University of Pittsburgh’s Animal Care and Use Committee.
Overview of data-collection procedures. Data were collected from six female adult cats that had been spayed before the onset of data collection. The animals were trained to remain sedentary, with limbs fully extended, on a tilt table during nose-up whole body rotations of 20, 40, or 60° amplitude. A jacket with attached Velcro straps was placed around the animal's torso; the Velcro straps were secured to the sides of the tilt table to prevent the animal's position from shifting during testing. The animal's head was immobilized by inserting a screw into a bolt mounted on the skull (see Fig. 1A for illustration). Blood pressure was recorded during whole body tilts by using a telemetry system, including a transducer and attached transmitter (Data Sciences International, St. Paul, MN) implanted in the animal. The transducer tip was placed into the abdominal aorta, and the transmitter unit was secured in the abdomen. The radio signal generated by this transmitter was detected by using a receiver mounted to the tilt table.

Blood pressure was monitored during body tilts under two conditions, as illustrated in Fig. 1. In some trials, the animal could visualize the laboratory and thus could potentially determine body position in space by using visual information; this testing situation will subsequently be referred to as the “visual cues present” condition (see Fig. 1A). During other tilts, black cardboard panels were mounted on the front and sides of the tilt table so that the animal's visual field rotated with its body (see Fig. 1B); this testing situation will subsequently be referred to as the “visual cues absent” condition.

Data were collected during recording sessions with a duration of 30–60 min. Tilts of 20, 40, and 60° amplitude were randomly disbursed throughout the recording session so that animals could not “predict” the amplitude of the tilt at the onset of each rotation. Tilts persisted for 40–60 s and were separated by at least 1 min. Only data recorded during trials in which animals were observed to remain sedentary, with limbs fully extended, were analyzed. The tilt table was rotated manually and was secured in the tilted position by using a spring device that permitted movement to one of three predetermined amplitudes. Tilts from the horizontal to the nose-up position were performed rapidly, at a velocity of ~60°/s at all three amplitudes, to produce a sudden orthostatic challenge.

Blood pressure responses to tilt were recorded in animals with eighth nerves intact over a period of 21–134 days (see Table 1). Heart rate changes during whole body rotations were also calculated from blood pressure traces. Experimental sessions were typically conducted three or more times per week. Subsequently, the peripheral vestibular apparatus was lesioned bilaterally, and blood pressure and heart rate changes during tilt were measured in the same manner as before the lesion. The postlesion blood pressure and heart rate determinations began the day after the surgery and continued for 13–56 days (median of 21 days; see Table 1). Typically, experimental sessions were conducted daily during the week immediately after the lesion and afterward two to three times per week. During data collection, it became apparent that blood pressure and heart rate responses to tilt were altered by vestibular lesions but that these changes only remained prominent for ~1 wk. Thus, for subsequent examination, responses recorded in the first week after removal of vestibular inputs were analyzed as a separate group from those recorded at subsequent times.

Training procedures. A training period of ~2–3 mo was required for animals to learn to remain sedentary, with limbs extended, during experimental sessions. The training was done in three phases. As a first step, animals learned to tolerate body restraint in a vinyl bag that encompassed the torso. The restraint period initially lasted for only a few minutes but was gradually increased until animals remained sedentary for at least 30 min. Food was provided at the end of the testing period as a reward, and the experimental session was terminated promptly if the animal attempted to move from the restraint bag or showed any signs of distress (e.g., vocalization). The second phase of training involved teaching...
the animal to tolerate head fixation. Initially, a flexible rod that permitted some movement was used to secure the head, which was replaced over time with a solid rod. The third training phase prompted the animals to maintain the limbs in a relaxed, extended position on the tilt platform. The limbs were initially gently held in an extended position by the investigators, until this prompting was not required for animals to retain their limbs in an extended position during the testing session.

Surgical procedures. Three recovery surgeries were required for each animal. All surgeries were performed by using sterile procedures in a dedicated operating suite. The first surgical procedure was performed to secure a bolt to the skull to permit head fixation. After animals were trained to remain sedentary in the tilt apparatus during testing, the second surgical procedure was performed to implant the Data Sciences International telemetric blood pressure transducer and transmitter. The blood pressure transducer was implanted during a second surgery, because this battery-powered device has a limited life span and was functional for only a few months. Thus it was necessary to implant the transducer after the 2- to 3-mo training period was complete. The third surgery to produce a peripheral vestibular lesion was performed after initial data collection was complete.

For each surgery, animals were initially anesthetized by using an intramuscular injection of ketamine (20 mg/kg) and acepromazine (0.2 mg/kg). Subsequently, an endotracheal tube and intravenous catheter were inserted. Anesthesia was supplemented as necessary by using 1–1.5% isoflurane vaporized in O2 to maintain areflexia and stable heart rate. Ringer lactate solution was infused intravenously to replace fluid loss during the surgery, and a heating pad was used to maintain rectal temperature near 38°C.

To implant the blood pressure transducer, a small incision was made in one hindlimb to expose the femoral artery; blood flow through the artery was occluded, a small incision was made in the arterial wall, and the transducer tip was passed 3–5 cm proximally into the abdominal aorta. The incision in the arterial wall was closed by using Vetbond adhesive, and a ligature was used to secure the transducer in the artery. The transmitter unit was passed subcutaneously into the abdomen, and a small incision was made through linea alba to allow the transmitter to be placed in the peritoneal cavity. Sutures were used to attach the transmitter unit to the rectus abdominis muscle.

To eliminate vestibular inputs, the tymanic bulla on each side was exposed by using a ventralateral approach and opened to expose the cochlea. A drill was used to remove temporal bone near the base of the cochlea, thereby producing a labyrinthectomy that rendered the vestibular apparatus dysfunctional. This procedure also provided access to the internal auditory canal. The eighth cranial nerve was then transected under microscopic observation within the internal auditory canal. Thus two independent lesions affecting the vestibular system were made on both sides to ensure that vestibular inputs were removed. In no case did nystagmus or deviation in eye position occur after the surgery, suggesting that the peripheral lesions were complete (1). To ensure that animals received proper hydration and nutrition during the postsurgical period, ~100 ml of Ringer lactate solution were administered subcutaneously each day, and feeding was done by hand until the animal’s spontaneous consumption of food and water returned to presurgical levels.

Data-recording procedures. Each data recording session for a particular animal occurred at approximately the same time each day, and animals were deprived of food until after the recording session. We attempted to standardize experimental methods to minimize the risk that extraneous factors may have affected blood pressure in these experiments. The Data Sciences International telemetric blood pressure recording system produced a voltage proportional to blood pressure, which was led along with a recording of table position into a Vetter digital audio tape recorder. Subsequently, the signals were fed into a Cambridge Electronic Design (Cambridge, UK) 1401-plus data-collection system interfaced with a Macintosh Quadra 800 computer for digitization (sampling rate of 100 Hz) and storage. The Spike-2 software package (Cambridge Electronic Design) was used for data analysis. Mean blood pressure was determined at the following times relative to each tilt: 5 s before tilt onset and 0, 2, 4, 6, 8, 10, 20, and 40 s after the tilt amplitude reached its peak. In addition, heart rate was calculated over 3-s bins during the tilt cycle.

Verification of peripheral vestibular lesions. At the conclusion of data recording in three cases, animals were anesthetized with an intraperitoneal injection of pentobarbital sodium (40 mg/kg) and perfused transcardially with phosphate-buffered saline followed by the paraformaldehyde-lactogel-sodium metaperiodate fixative developed by Mcl. and Nakane (7). The head was then removed and decalified by using a solution of EDTA and hydrochloric acid. The temporal bone on each side was subsequently removed, embedded in 12% celluloid, cut in the coronal plane (30-µm thickness), and stained by using hematoxylin. The temporary bone sections were then inspected histologically to determine the extent of damage to the eighth cranial nerves and vestibular labyrinth.

Statistical analysis of data. A one-tailed ANOVA procedure in combination with a post hoc test (Tukey-Kramer) was used to compare heart rate and blood pressure measurements collected before the peripheral vestibular lesion, in the first week after the lesion, and at subsequent times. The number of experimental trials before and after the vestibular lesion in which the change in blood pressure during tilt was minimal (<10 mmHg), moderate (10–20 mmHg), or large (>20 mmHg) was also compared by using a χ2 test. All confidence intervals reported in the text represent means ± SE.

RESULTS

Table 1 summarizes the recording times and number of tilts performed in each of the six animals. Data collection was performed for 21–134 days when the eighth cranial nerves were intact and 13–56 days after vestibular inputs were removed. However, complications arose during these long-duration experiments that affected data collection in animals 2 and 6.
animal 2, a large (>30-mmHg) shift in mean baseline blood pressure occurred abruptly between the 9th and 10th days after the vestibular lesion, although the fluctuations in blood pressure related to the cardiac cycle (i.e., the pulse pressure) remained obvious. It is possible that coagulation of blood on the transducer tip produced this artifact. Because of this problem, we did not analyze changes in blood pressure during tilt after the first week after elimination of vestibular inputs in animal 2. However, changes in heart rate during tilt were examined throughout the recording period in this animal. Data collection was affected by another factor in animal 6; this animal became distressed during trials after the vestibular lesion in which visual cues regarding position in space were available. It was thus impossible to collect data during this testing situation in animal 6, and only data collected during the visual cues absent condition are available.

Effects of bilateral vestibular lesions on resting blood pressure and heart rate. Figure 2 shows the mean baseline blood pressure measured 5 s before each tilt, both before and after removal of vestibular inputs. In vestibular-intact animals, mean baseline blood pressure ranged from 86 to 114 mmHg. However, in the first week after the vestibular lesion, baseline blood pressure was significantly different from the prelesion values in all six cases. In three of the six animals, elimination of vestibular inputs resulted in a significant elevation of mean blood pressure by 10–20 mmHg. In the other three animals, however, blood pressure decreased subsequent to the vestibular lesion by 7–16 mmHg. After the first week after removal of vestibular inputs, mean blood pressure was closer to prelesion values in all cases but was still significantly different from that before the lesion in four animals.

Baseline heart rate (determined over the time interval from 6 to 9 s before each tilt) also changed significantly after the vestibular lesion. As indicated in Fig. 3, when vestibular inputs were present, the mean baseline heart rate ranged from 158 to 205 beats/min in the six animals. In the first week after removal of vestibular inputs, mean heart rate increased to 172–245 beats/min. The heart rate subsequently dropped, but in four of the six animals it still remained significantly elevated over prelesion values. It is curious that baseline heart rate increased after removal of vestibular inputs even in the animals (animals 4–6) in which resting blood pressure decreased (see Fig. 2).

Effects of bilateral vestibular lesions on blood pressure changes during 60° nose-up tilt. Figure 4A illustrates recordings of blood pressure during 60° nose-up tilt in animal 1, and Fig. 4B shows responses in animal 4. The figure depicts traces recorded both when vestibular inputs were present and in the first week after the lesion; all sweeps illustrated were obtained during the visual cues absent condition. In both prelesion examples, blood pressure remained relatively stable during tilt; in contrast, removal of vestibular inputs resulted in more unstable blood pressure during pitch rotations. In the postlesion trial illustrated in Fig. 4A, blood pressure dropped at the onset of table movement but returned to the pretilt level within 10 s. This type of blood pressure response to body rotation, characterized by an initial decrease below baseline values, will subsequently be referred to as “response pattern A.” In contrast, in the postlesion example in Fig. 4B, blood pressure increased during tilt; this response type will subsequently be referred to as “response pattern B.”

Figure 5 shows the mean change in blood pressure from baseline measured 2, 4, 6, 8, 10, 20, and 40 s after a tilt plateaued at 60° amplitude. Data collected from each of the six animals are depicted in a different panel; only responses measured during the visual cues absent condition are illustrated. When vestibular inputs were present, mean blood pressure during 60° tilt typically remained within 10 mmHg of the pretilt value in all animals. In the first week after the vestibular lesion, however, the blood pressure response to 60° nose-up tilt was significantly different in all cases from when vestibular inputs were present. In one-half of the animals (animals 1, 2, and 6), the orthostatic response was altered such that blood pressure dropped significantly more during 60° nose-up tilts than before the vestibular lesion. In animals 1 and 2, a drop in blood
pressure of ~15 mmHg occurred at the onset of tilts (response pattern A illustrated in Fig. 4). In animal 6, the orthostasis was not as severe, although blood pressure dropped significantly more than when vestibular inputs were present. In all three cases, blood pressure rebounded to pretilt levels after ~10 s. Furthermore, the hypotension during the onset of static nose-up tilt persisted for only ~1 wk. In subsequent trials, the change in blood pressure during 60° nose-up tilt was not significantly different from before the vestibular lesion. As discussed above, in animal 2 we could not determine absolute blood pressure after ~1 wk after the lesion and thus could not establish whether the tilt-related decrease in blood pressure after removal of vestibular inputs was a permanent deficit.

In animals 3–5, bilateral vestibular lesions resulted in an increase in mean blood pressure over baseline values during 60° tilt. The peak pressor response in these three animals occurred 8–10 s after the table movement plateaued at its maximal amplitude, when mean blood pressure was 12–19 mmHg higher than pretilt levels in the respective cases. The large increase in blood pressure during 60° nose-up tilt in these animals only persisted for ~1 wk after the lesion.

The effects of vestibular lesions on blood pressure stability during nose-up tilt are further illustrated in Figs. 6 and 7. These figures show the proportion of trials in which the maximal change in mean blood pressure from baseline during 60° nose-up tilt was

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**Fig. 3.** Effects of removal of vestibular inputs on baseline heart rate, which was calculated from blood pressure measurements made over time period from 6 to 9 s before each tilt. Open bars, prelesion values; solid bars, responses in first week after lesion; hatched bars, data collected subsequently. Data from each animal are shown in a different panel. Error bars, SE. *Baseline heart rates measured after vestibular lesion that were significantly different from prelesion values, \( P < 0.05 \) (1-tailed ANOVA).

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**Fig. 4.** Recordings of blood pressure during 60° nose-up tilt in 2 animals. All traces illustrated were obtained during recording condition in which the animal could not determine body position in space by using visual cues (illustrated in Fig. 1B). A: response pattern A. Blood pressure recordings in animal 1 made before (top) and in first week after (bottom) production of peripheral vestibular lesions. In this animal, removal of vestibular inputs resulted in a decrease in blood pressure at onset of nose-up tilt. B: response pattern B. Blood pressure traces collected in animal 1 before (top) and after (bottom) vestibular lesions. In this case, a pressor response occurred during nose-up body rotation after removal of vestibular inputs.

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**Fig. 5.** Mean change in blood pressure (from pretilt values) recorded 2, 4, 6, 8, 10, 20, and 40 s after rotation amplitude plateaued at 60°. Only data collected during condition in which animal could not determine position in space by using visual cues were used for this figure. Different symbols are employed to indicate responses recorded before vestibular lesion (□ or ●), in the first week after removal of vestibular inputs (○ or ●), and at subsequent times (△ or ■). Bars, SE. Solid symbols indicate postlesion values that differed significantly from those before vestibular lesions (open symbols), \( P < 0.05 \) (by 1-tailed ANOVA).
modest (<10 mmHg), moderate (10–20 mmHg), or large (>20 mmHg). Figure 6 depicts responses from each animal as separate panels, whereas Fig. 7 represents pooled responses from all animals. Responses recorded in the presence and absence of visual cues regarding body position in space are illustrated in separate rows, whereas different columns illustrate data recorded before and in the first week after the vestibular lesion. As discussed above, animal 6 could not be tested during the visual cues present situation after the vestibular lesion, as this animal vocalized during these particular trials. Thus data from animal 6 have been excluded from these figures.

When vestibular inputs were present, large maximal changes in blood pressure during 60° tilt (solid areas in the pie diagrams) were uncommon (<15% of runs). Instead, in ~50% of 60° tilts, blood pressure was altered <10 mmHg (open areas in the pie diagrams). In the first week after removal of vestibular inputs, however, moderate (hatched areas in the pie diagrams) or large changes in blood pressure during tilt became more common and are obvious in each individual case. In all animals except animal 5 (Fig. 6E), the deficit in correcting blood pressure during tilt was most obvious during the visual cues absent condition. An analysis of all visual cues absent trials conducted in all animals (Fig. 7) showed that blood pressure changed by >20 mmHg during 30% of tilts and between 10 and 20 mmHg in 54% of tilts. A χ² analysis (P < 0.05) of the pooled data from all animals confirmed both that blood pressure instability was greater after the vestibular lesion than when labyrinthine inputs were present and that the deficit was worse if the animal was also deprived of visual cues indicating body position in space.

Effects of peripheral vestibular lesions on heart rate changes during 60° nose-up tilt. Figure 8 illustrates the changes in heart rate that occurred during nose-up tilt before and after removal of vestibular signals; only results collected in the visual cues absent condition, in which vestibular lesions resulted in greater blood pressure instability during body rotation, are shown. Before the lesions in all animals, heart rate increased by 20–75 beats/min over baseline levels during 60° nose-up tilt. Such a response is required to maintain constant blood pressure during nose-up body rotation. However, removal of vestibular inputs had two patterns of effects on heart rate responses, which were correlated with the effects of lesions on changes in blood pressure during tilt. In animals in which a tilt-related decrease in blood pressure occurred after removal of vestibular inputs (animals 1, 2, and 6), the lesion had no significant effect on heart rate (1-tailed ANOVA, P > 0.05). In these cases, heart rate increased by a similar amount during tilt after the vestibular lesion than when vestibular inputs were present. Clearly, the tilt-related decrease in blood pressure that occurred in these animals after removal of vestibular inputs was not the result of a drop in heart rate. In contrast, animals 3–5 exhibited an increase in blood pressure during tilts after peripheral vestibular lesions. Paradoxically, heart rate increased less during these tilt-induced increases in blood pressure than before the vestibular lesion, when blood pressure remained stable during tilt. The difference in modulation of heart rate between animals with and without vestibular inputs occurred 9–15 s after the rotation reached 60° amplitude, when the pressor response was maximal in lesioned animals. Thus the tilt-related increase in blood pressure that occurred in
Effects of peripheral vestibular lesions on cardiovascular changes during 20° and 40° nose-up tilt. Tilts of 20° and 40° amplitude were randomly interspersed with those of 60° amplitude so that animals could not predict the amplitude of rotations at the onset of table movement and potentially learn to produce conditioned responses to the stimuli. As might be expected, 20° and 40° rotations produced smaller changes in blood pressure than did 60° tilts, including during experimental trials conducted after vestibular lesions. In most animals, mean blood pressure remained within 10 mmHg of the pretilt value throughout the period that the body was maintained nose up. Thus vestibular dysfunction only resulted in unstable blood pressure during large changes in posture that provided a substantial orthostatic challenge to an animal.

Histological confirmation of peripheral vestibular lesions. In three of the animals, a histological analysis of temporal bone sections was performed to determine whether the labyrinthectomy and eighth cranial nerve transection were complete. In all of the cases, we confirmed that the vestibular labyrinth had been opened, thereby producing a functional lesion by permitting the perilymph and endolymph to escape. Furthermore, in two of the animals, both eighth cranial nerves appeared to be completely severed. In these cases, the cut ends of the nerves were degenerated and surrounded with glial scars, and all vestibular endorgans appeared to be necrotic. In one animal, however, although one eighth cranial nerve was entirely transected, in the contralateral nerve some of the fibers may have spared. Inspection of the inner ear on this side revealed pathology in the vestibular labyrinth, but degeneration in one crista ampullaris was not as complete as in the other cases. Nonetheless, it is likely that the process of opening the labyrinth along with the partial transection of the eighth cranial nerve produced severe dysfunction of the inner ear on this side [explaining the observation that the animal exhibited no nystagmus (1)]. Thus it appears that our procedures were sufficient to remove vestibular inputs bilaterally.

DISCUSSION

The present data confirmed previous findings collected in anesthetized cats showing that blood pressure is more unstable during nose-up tilt after removal of vestibular inputs than when labyrinthine inputs are present (3). However, in conscious animals, the effects of removal of vestibular inputs on the control of blood pressure were more complex than those that have been reported in surgically reduced preparations. One major difference is that vestibular lesions in awake animals could result in either an increase or decrease in blood pressure during 60° nose-up tilt, whereas only ortho-
static hypotension routinely occurred in anesthetized animals lacking vestibular input (3). A second difference is that, in conscious animals, the availability of visual inputs indicating body position in space typically reduced the effects of vestibular lesions on maintenance of stable blood pressure during changes in posture. We also demonstrated that the deficit in control of blood pressure during nose-up tilt only persisted for ~1 wk after vestibular lesions in conscious animals; a parallel analysis of recovery of orthostatic tolerance after removal of vestibular inputs is not possible in anesthetized or decerebrate preparations.

These results support the hypothesis that multiple sensory inputs are integrated to produce stable blood pressure during changes in posture (21). Presumably, maintenance of constant blood pressure is most precise when a number of sensory cues are processed to determine the orthostatic challenge presented by a movement. When fewer inputs are available, the likelihood is higher that an error will be made in determining the correct compensatory response, and blood pressure may either drop below or rise above the target level. For example, our results showed that removal of both vestibular and visual information concerning body position in space typically resulted in larger blood pressure fluctuations during tilt than did elimination of only one of these cues. This explanation could also account for the short-term (1-wk) duration of the deficit of vestibular-lesioned animals in compensating for orthostasis; it is likely that animals learn to better "calibrate" the remaining sensory inputs over time, resulting in improved control for peripheral blood pooling.

There are, however, alternate explanations for the results of this study. For example, the vestibular system is known to elicit posturally related changes in activity of respiratory muscles (11, 12, 19), and removal of vestibular signals might be expected to have complex effects on ventilation (and secondary effects on blood pressure) during tilt. Another possibility is that body rotation after vestibular lesions could have elicited stress in animals 3–5, resulting in the tilt-related pressor response observed in these cases. However, we believe this is less likely for three reasons. First, the increase in heart rate during tilt was no larger after vestibular lesions than when vestibular inputs were present; in fact, in animals 3–5, the vestibular lesion diminished heart rate responses during 60° rotations. In contrast, a stress response during tilts should have elicited tachycardia that occurred simultaneously with the change in blood pressure (2). Second, at least in humans, motion-related anxiety and motion sickness are less common in bilateral vestibular-deficient than in vestibular-intact individuals (see Ref. 9 for review). It would thus be unexpected that motion discomfort resulted in the cardiovascular disturbances observed after vestibular lesions in the present study. Third, 20° or 40° tilts resulted in little change in blood pressure, despite the fact that the velocity of rotation was similar to that of 60° tilts. Because tilts of different amplitudes were interspersed randomly throughout an experimental session, an animal could not predict the amplitude of a rotation at its onset. Thus any "stress" produced at the onset of table movement should have been similar during body rotations of all amplitudes. Because only 60° tilt had large cardiovascular effects, it seems unlikely that the testing situation or table movement in itself (as opposed to the cardiovascular challenge produced by tilt) resulted in the changes in blood pressure observed in these experiments.

Removal of vestibular inputs also resulted in a persistent change in resting heart rate and blood pressure, which outlasted the effects of vestibular dysfunction on maintenance of stable blood pressure during tilt in some animals. However, the alterations in heart rate and blood pressure did not always occur in parallel. For example, in animals 4–6, resting blood pressure decreased, whereas heart rate increased, after the vestibular lesion. In the other animals, removal of vestibular inputs resulted in an increase in both blood pressure and heart rate. Presumably, removal of vestibular inputs from neural pathways that process multiple sensory inputs and influence the control of circulation may produce such complex cardiovascular responses. Future studies will be required to determine the identity of these pathways.

Although the deficits of vestibular-lesioned animals in correcting blood pressure during body rotations persisted for only ~1 wk, it should be considered that the testing conditions in these experiments were somewhat artificial. Because the animals could expect to be tilted quite often when restrained in the tilting device, it is possible that they were particularly vigilant during the experimental sessions. In contrast, animals may not always maintain such a high level of attention to environmental cues regarding body position in space outside of laboratory conditions. Thus vestibular dysfunction could result in a long-lasting deficit in correcting blood pressure, but this deficit only becomes apparent when the level of alertness diminishes. Further experiments will be required to examine this possibility.

It should finally be remembered that the approach of utilizing awake animals in studying the neural control of circulation has several limitations. It is impossible to control for a number of variables in this preparation, including vigilance and attention to environmental cues, baseline blood pressure, and heart rate, etc. In addition, the results of these experiments may not be directly applicable to humans. For example, the present results indicate that visual cues may be important in regulating blood pressure during movement in the cat, whereas a previous study suggested that visual information does not trigger changes in sympathetic outflow in humans (13). Nonetheless, the multisensory influences on regulation of blood pressure demonstrated here could only be detected and investigated in awake, unanesthetized animals. Thus our results indicate that a parallel use of chronic and surgically reduced preparations may be most effective in exploring the range of mechanisms that participate in the neural control of circulation.
Perspectives. The present data suggest that vestibular, visual, and other somatic signals influence cardiovascular control in conscious animals and demonstrate that elimination of vestibular inputs can lead to difficulty in maintaining stable blood pressure during unexpected movements that challenge orthostasis. The central nervous system is apparently capable of utilizing a large amount of sensory information in formulating cardiovascular responses during exercise, postural adjustments, and spatial realignment of the body. Future studies should consider the relative role of each of these sensory inputs in cardiovascular control, the neural mechanisms involved in integrating the signals, and the circuitry through which these signals impinge on the brain stem neurons that regulate blood pressure. Furthermore, because the vestibular system appears to influence sympathetic outflow in humans (10, 13), it will also be important to examine the effects of vestibular dysfunction on autonomic regulation under clinical circumstances.

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