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The Susceptibility of Rhesus Monkeys to Motion Sickness

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The susceptibility of rhesus monkeys to motion sickness was investigated using test conditions that are provocative for eliciting motion sickness in squirrel monkeys. Ten male rhesus monkeys and ten male Bolivian squirrel monkeys were rotated in the vertical axis at 150°/s for a maximum duration of 45 min. Each animal was tested in two conditions, continuous rotation and intermittent rotation. None of the rhesus monkeys vomited during the motion tests but all of the squirrel monkeys did. Differences were observed between the species in the amount of activity that occurred during motion tests, with the squirrel monkeys being significantly more active than the rhesus monkeys. These results, while substantiating anecdotal reports of the resistance of rhesus monkeys to motion sickness, should be interpreted with caution because of the documented differences that exist between various species with regard to stimuli that are provocative for eliciting motion sickness.

THE RHESUS MONKEY has not been considered a good model for motion sickness research because these animals are thought to be resistant to motion sickness (1,16). However, the resistance of rhesus monkeys to motion sickness has not been clearly documented and most of the available information on motion sickness susceptibility in these animals is anecdotal (personal communications G. H. Crampton and J. Lackner).

Apparently, the evaluations of motion sickness susceptibility in rhesus monkeys have been opportunistic rather than by design. For this reason parameters known to be important for inducing motion sickness in squirrel monkeys and other susceptible species (3,4,5,9,18) have not been examined systematically in the rhesus monkey. For instance, it is well known that head movements out of the plane of rotation produce cross-coupled accelerations which affect the efficacy of rotation as a motion sickness stimulus (15). Thus, the susceptibility of squirrel monkeys to rotation is greatly reduced when they are restrained in primate chairs (5). Similarly, head stabilization prevents or greatly reduces motion sickness in these animals (18) as well as in humans (9). While it is impossible to determine the degree to which movement was allowed in some previous investigations using rhesus monkeys, in other studies it is apparent that voluntary movements were restricted because the animals were restrained in primate chairs during testing. Therefore, previous tests of susceptibility of rhesus monkeys to motion sickness may have produced negative results due to test conditions that were inadequately provocative, rather than to the resistance of rhesus monkeys to motion sickness.

This investigation was undertaken to compare the motion sickness responses of the rhesus monkey with those of the squirrel monkey, using stimuli known to elicit motion sickness in the majority of squirrel monkeys. In all tests unrestrained voluntary movement was permitted within a test cage large enough to allow head and whole-body movements of sufficient magnitude to produce cross-coupled accelerations.

METHODS

Subjects: Ten sub-adult (approximately 4 years of age) male rhesus monkeys (*Macaca mulatta*) with no previous history of motion testing, and ten adult (approximately 7 to 10+ years of age) male Bolivian squirrel monkeys (*Saimiri sciureus*) selected randomly from a pool of animals used previously in motion sickness studies, were tested. The animals were housed in standard colony conditions and were maintained on 12:12 (rhesus monkey) and 14:10 (squirrel monkey) light:dark cycles. Food and water were available *ad lib*. On each test day the monkeys were fed fresh bananas in the experimental chamber approximately 5 min before testing began.

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The experiments were conducted at the Ames Research Center and conformed to the Center's requirements for the care and use of animals.

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Apparatus: Rhesus monkeys were exposed individually to rotation while free to move about in a stainless steel cage (60 × 60 × 60 cm) that was mounted on a Goerz Model 611 turntable. The lower half of three walls (30 cm) of the cage was formed by solid stainless steel panels, while the ceiling and the upper half of the cage were made of wire mesh. One wall of the cage had a guillotine door made of clear Plexiglas.

Squirrel monkeys were exposed individually to rotation, while free to move in a cage constructed of clear Plexiglas (52 × 23 × 30 cm) that was mounted on the turntable. To make the conditions of visual stimulation comparable for squirrel and rhesus monkeys, aluminum foil was attached to the lower half (15 cm) of three walls of this cage to simulate the visual conditions formed by the stainless steel panels of the cage used for the rhesus monkeys.

During rotation both the rhesus and squirrel monkeys could view the lighted test chamber by looking directly out through the clear walls of the cages while sitting upright, or by looking up through the upper portion of the walls or the ceiling, if in a crouched or prone position. The animals could see through the door of the cages from floor to ceiling when oriented in that direction.

Procedure: Two conditions of vertical-axis rotation were used. In the first test, "Continuous Rotation," the animals were exposed to clockwise rotation at 150°/s for a maximum duration of 45 min. In the second test, "Sudden-Stop," the animals were exposed to periods of rotation alternating with brief periods during which the cage was stopped. The second test was conducted 1.5–2 months after the first motion test. A velocity-ramp was used to drive the turntable in this Sudden-Stop Condition. The cage was accelerated at $75°/s^2$ for 2.0 s to reach the rotation velocity of 150°/s, then maintained at constant velocity for 23.6 s, and then decelerated at $88°/s^2$ for 1.7 s to 0°/s (stopped). The turntable remained stationary (stopped) for 3.1 s. This alternation of rotation with stationary periods continued for a maximum duration of 45 min (90 cycles). The direction of rotation was clockwise for the first 30 min and counterclockwise for the remaining 15 min of exposure. If an animal vomited, motion was terminated 5 min after the first vomiting episode.

The animals were observed continuously during tests, and latencies to retching and vomiting were recorded. To characterize the activity level of animals during the Sudden-Stop Condition, the duration (in s) of periods of inactivity was recorded on a printout counter using a manual switch operated by an observer. A state of "inactivity" was defined as a 5-s period during which neither head movements nor whole-body movements of the animals were observed. Small arm movements which did not affect head or whole-body orientation were ignored.

RESULTS

None (0/10) of the rhesus monkeys retched or vomited during either condition of rotation, but all (10/10) of the squirrel monkeys retched and vomited during both conditions. For the squirrel monkeys the mean latency to the first vomiting episode was significantly shorter during continuous rotation (3.6 ± 2.0 min) than during intermittent rotation (7.8 ± 3.0 min) [$t(9) = 6.87$, $p < .001$].

Voluntary movements made during the motion tests differed greatly, with some animals moving continuously and others remaining still for extensive periods. The amount of activity that occurred during the motion tests varied more among the rhesus than among the squirrel monkeys. The percentage of the test session during which the individual rhesus monkeys were active ranged from 20% to 92%, while the percentage of active time ranged from 79% to 100% for the squirrel monkeys. The squirrel monkeys were active a greater percentage of the time (median = 100%) than the rhesus monkeys (median = 77%), Mann-Whitney $U = 5$, $p < 0.02$. Of the 10 rhesus monkeys, 6 were less active than all of the squirrel monkeys and 5 of the 10 squirrel monkeys had no periods of inactivity (i.e., were active 100% of the time).

DISCUSSION

Although it has been shown that rhesus monkeys have a complete emetic reflex (6,8,11,12,14,17,19), there appears to be no published evidence documenting their responses to motion stimuli. The results of this study indicate that they apparently are not susceptible to motion sickness during either continuous or intermittent vertical-axis rotation, stimuli that elicit motion sickness in squirrel monkeys (2,5), chimpanzees (13), and humans (7,10). Although the influence of age on susceptibility to motion sickness has not been rigorously investigated, studies with rats, squirrel monkeys, and humans (2) suggest that susceptibility to motion sickness may decrease with advancing age. This information indicates young, or sub-adult animals may be the most susceptible of the species. If this is correct, the rhesus monkeys tested in this experiment should have biased results toward detecting motion sickness in the rhesus monkey. The fact that none of the rhesus vomited in this study substantiates anecdotal reports and is consistent with unpublished comments that they are refractory to motion sickness.

However, several factors indicate that caution should be exercised in concluding that rhesus monkeys are immune to motion sickness. Motion sickness is known to be elicited most effectively by qualitatively different stimuli in various susceptible species (2). One example is the differential susceptibility of the squirrel monkey and the cat to vertical-axis rotation and vertical-linear acceleration. While the squirrel monkey is highly susceptible to rotation but not to vertical bouncing, the reverse is true for the cat. Such differential susceptibility of species to selected motion profiles reveals how difficult it is to demonstrate complete immunity to motion sickness. This fact indicates that additional testing with stimuli of different types (i.e., linear acceleration, parallel swing, etc.) should be conducted before concluding that rhesus monkeys cannot be made motion sick.

Evaluation of observational data also suggests that caution should be exercised before concluding that rhesus monkeys are not susceptible to motion sickness. When the animals in this study were tested using continuous rotation at 150°/s, it appeared that the activity levels of the two species were quite different, with the squirrel monkeys being more active during rotation. The lower level of activity of some rhesus monkeys could perhaps be interpreted as a "behavioral strategy" to minimize vestibular stimulation during rotation. Two characteristic behavioral patterns occurred in the rhesus monkeys: (a) Rhesus monkeys that were active during rotation periodically terminated movements and adopted positions which stabilized their heads and/or bodies. Such positions included leaning against the wall, placing the jaw or head against the wall, or lying prone on the floor of the cage. (b) Rhesus monkeys that were characteristically inactive during rotation commonly adopted a prone position on the floor of the cage, often with their heads very close to the axis of rotation. In addition, informal observations of the squirrel and rhesus monkeys indicated that their spontaneous movements were distinctly different. The squirrel monkeys made many high-frequency, jerky movements, with numerous small pitching movements of the head, while the rhesus monkeys tended to sit upright and made relatively slower head and body movements in the yaw plane with fewer, and slower pitch movements. Thus, inherent behavioral differences between these two species could lead to qualitative differences in actual stimulation resulting from a single imposed stimulus condition (e.g., rotation).

These observations suggest that rhesus monkeys might behave in a manner that minimizes vestibular stimulation produced by continuous vertical-axis rotation and thereby avoid becoming motion sick. Therefore, to ensure that the animals were subjected to angular accelerations even if they were inactive, the Sudden-Stop Condition was used. However, during the Sudden-Stop Condition vomiting latencies increased for the squirrel monkeys indicating that, at least for squirrel monkeys, this stimulus was less provocative than continuous rotation. Thus, the Sudden-Stop Condition may not have been a more provocative stimulus than continuous rotation, and therefore, may not have been a stringent test of susceptibility for the rhesus monkeys.

The test conditions used in this experiment do not provide a comprehensive evaluation of the susceptibility of rhesus monkeys to motion sickness. Further testing with a wider range of motion stimuli should be considered. If other tests continue to indicate rhesus monkeys are immune to motion sickness, then comparative investigations of neural, physiological, and hormonal differences between rhesus monkeys and other primates susceptible to motion sickness may be a useful approach to increase our understanding of the mechanisms underlying the etiology of motion sickness.

REFERENCES

1. Adey WR. Central nervous, cardiovascular, and visuomotor studies relating to spatial orientation in a 30-day primate flight. In: Second symposium on the role of the vestibular organs in space exploration, NASA SP-115, 1966:293.
2. Daunton NG. Animal models in motion sickness research. In: Crampton GH, ed. Motion and space sickness. Boca Raton: CRC Press, 1990:87–104.
3. Daunton NG, Fox RA: Motion sickness elicited by passive rotation in squirrel monkeys: modification by consistent and inconsistent visual stimulation. In: Igarashi M, Black O, eds. Vestibular and visual control on posture and locomotor Equilibrium. Basel: S. Karger, 1985:164–9.
4. Daunton NG, Fox RA, Crampton GH. Susceptibility of cat and squirrel monkey to motion sickness induced by visual stimulation: correlation with susceptibility to vestibular stimulation. Motion sickness: mechanisms, prediction, prevention and treatment. NATO AGARD Conference Proceedings, 1984; 31(No. 372), 31(1)–31(5).
5. Fox RA, Daunton NG, Coleman J. Susceptibility of the squirrel monkey to several different motion conditions. Neuroscience Abstract 1982; 8:698.
6. Franz CG. Effects of mixed neutron-gamma total-body irradiation of physical activity performance of rhesus monkeys. Radiat. Res. 1985; 101:434–41.
7. Graybiel A, Lackner JR. A sudden-stop vestibulovisual test for rapid assessment of motion sickness manifestations. Aviat. Space Environ. Med. 1980; 51:21–3.
8. Heywood R, James RW, Sortwell RJ. Toxicology studies of linear alkylbenzene sulphonate (LAS) in rhesus monkeys. I. Simultaneous oral and subcutaneous administration for 28 days. Toxicology 1978; 11:245–50.
9. Johnson WH, Stubbs RA, Kelk GF, Franks WR. Stimulus required to produce motion sickness. J. Aviat. Med. 1951; 22:365.
10. Lackner JR, Graybiel A. Some influences of vision on susceptibility to motion sickness. Aviat. Space Environ. Med. 1979; 50(11):1122–5.
11. Legeza VI, Shagoian MG, Kamynina MF, Markovskaia IV, Martirosov KS. Mechanism of the species characteristics of the sensitivity of monkeys and dogs to the emetic action of various pharmacological agents. Biull. Eksp. Biol. Med. 1982; 93(6):64–6.
12. Liu CT, Helm JD, Beisel WR. Cardiovascular and vomiting responses to a lethal intravenous dose of staphyloenterotoxin A in rhesus monkeys. J. Med. Primatol. 1976; 5:353–9.
13. Meek JC, Graybiel A, Beischer DE, Riopelle AJ. Observations of canal sickness and adaptation in chimpanzees and squirrel monkeys in a "slow rotation room." Aerosp. Med. 1962; 33:571–8.
14. Middleton GR, Young RW. Emesis in monkeys following exposure to ionizing radiation. Aviat. Space Environ. Med. 1975; 46:170–2.
15. Reason JT, Brand JJ. Motion sickness. New York: Academic Press, 1975.
16. Suri KB, Crampton GH, Daunton NG. Motion sickness in cats: a symptom rating scale used in laboratory and flight tests. Aviat. Space Environ. Med. 1979; 50:614–8.
17. Suzuki H, Yoshida T, Ozaki H, Miki H, Shiobara Y. 6-week intravenous toxicity test of cefpiramide in rhesus monkeys. Jpn. J. Antibiot. 1983; 36:1411–34.
18. Wilpizeski CR, Lowry LD, Contrucci RB, Green SJ, Goldman WS. Effects of head and body restraint on experimental motion-induced sickness in squirrel monkeys. Aviat. Space Environ. Med. 1985; 56:1070–3.
19. Yochmowitz M, Patric R, Jaeger R, Barnes D. Protracted radiation-stressed primate performance. Aviat. Space Environ. Med. 1977; 48:598–606.