THE INFLUENCE OF AGE ON SUSCEPTIBILITY TO MOTION SICKNESS IN MONKEYS

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Abstract — A longitudinal study on the effects of age on the susceptibility to motion sickness in the squirrel monkey was carried out over a 10-year period (1982 to 1991). The typical life span of squirrel monkeys is 15 years. Ten mature male squirrel monkeys of the Bolivian subspecies were found to be susceptible to motion sickness induced by a combination of vertical oscillation at 0.5 Hz and rotation in the horizontal plane at 25 rotations per minute (RPM) in a visually unrestricted environment. Signs of motion sickness were quantified according to a rating scale based on Graybiel’s diagnostic criteria. Latency to vomiting/retching and severity of sickness obtained from year 1 (baseline), 3, 5, 7 and 10 were subjected to repeated-measures design analysis. There were no significant differences in the susceptibility level (as measured by latency to vomiting/retching and cumulative sickness scores) in the monkeys throughout the 10-year period. The habituation to 7 consecutive daily exposures remained the same throughout the same period. We conclude that, in the squirrel monkeys from maturity to near the end of their life span, there is no change in susceptibility to motion sickness with aging.

Keywords — motion sickness; susceptibility; age: squirrel monkey.

Introduction

Age has long been suggested as a factor that will affect susceptibility to motion sickness (1,2,3,4), although no controlled study has been published. Most of the evidence has been based on anecdotal reports and questionnaire surveys. In humans, it is widely held that children under 2 years of age (1) and elderly persons show less susceptibility than those of intermediate age, with maximum susceptibility in pubertal childhood. For example, over the age of 25 years, susceptibility to sea sickness is half of what it is at 17 to 19 years (5). On the other hand, Noble (6) reported that susceptibility to swing sickness actually increases after the age of 40; in 23 men over the age of 40 the incidence of vomiting was 74% whereas in men under 40 the incidence of vomiting was 53% (from 30 to 39 years) and 60% (from 18 to 29 years).

Based on veterinarians’ observations, puppies and kittens tend to lose their susceptibility by the end of the first year of life. However, Best and colleagues (7) reported that 2-week-old puppies appeared to be quite unconcerned by swinging motion whereas 85% of mature dogs will exhibit varying degrees of motion sickness, and many adult dogs and cats are in fact susceptible (8,9). In primates, older monkeys were reported to have longer latencies to vomiting in response to rotation than young ones, if the age range is large (10). As in human studies, most information on animals has been based on anecdotal reports, surveys, or cross-sectional studies; and the influence of age on susceptibility is, in fact, unclear. In this study, we investigated the susceptibility to motion sickness in a group of squirrel monkeys through a 10-year period.

The findings of this study were presented at the 63rd Annual Scientific Meeting of the Aerospace Medical Association, May 10–14, 1992, Miami Beach, Florida.

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Methods

Subjects

A group of thirteen male squirrel monkeys (Saimiri sciureus) of the Bolivian subspecies was utilized in this study. These monkeys were bred for research purposes from a primate colony. Care and handling of the animals were in accordance with recommendations specified in the Guide to the Care and Use of Experimental Animals, provided by the Canadian Council on Animal Care (10a). All were fed with a commercially-prepared high-protein monkey diet, supplemented with fresh fruit. Water was available at all times. Based on body measurement, body weight, dentition, sexual maturity, and information from the supplier, the monkeys were estimated to be 3 to 5 years of age upon arrival at our laboratory. The estimated life span in captivity under favourable conditions is approximately 15 years (11). All of the monkeys were experimentally naive. The integrity of their vestibular function was examined, by visual and electronystagmographic observations of spontaneous and induced nystagmus (12). None of the monkeys showed any signs of spontaneous or positional nystagmus, and they exhibited normal rotation-induced nystagmus.

Motion Stimulus

The motion stimulus profile of simultaneous angular rotation in the horizontal plane of 25 RPM with a constant 0.5 Hz vertical sinusoidal excursion of 15 cm was found to be effective in inducing motion sickness (13,14). The major component of the apparatus consists of a Contraves model 803 drive assembly for rotation about the earth vertical axis (Z axis), and a second motor mounted on the drive assembly, controlling a pre-loaded ball bearing screw to drive the animal platform in a vertical sinusoidal oscillation. A transparent well-ventilated lucite chamber 30.5 x 30.5 x 35.6 cm housing the squirrel monkey was bolted onto the platform.

Procedure

The monkeys were subjected to the motion profile described above. Like most diurnal mammals, squirrel monkeys are known to be most active in the early to mid-morning. All testing took place in the morning between 0700 and 1000 to avoid possible circadian variations. About 20 minutes prior to motion stimulation, the monkeys were fed approximately 20 grams of banana, to standardize stomach loading. For each trial, the monkey was placed in the ventilated lucite chamber positioned at the axis of rotation. The monkey was unrestrained but confined to the immediate vicinity (<15 cm) from the axis of rotation by the test chamber. During the test, the behavioural responses of the monkeys to the motion stimulation were visually monitored and recorded in detail. The susceptibility to motion sickness was evaluated according to a rating scale modified from Graybiel’s diagnostic criteria for grading acute motion sickness in humans (15).

Table 1 illustrates the criteria used for grading the severity of acute motion sickness in the

<table>
<thead>
<tr>
<th>Pathognomonic Major</th>
<th>Minor</th>
<th>Minimal</th>
<th>Qualifying symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>16 points</td>
<td>8 points</td>
<td>4 points</td>
<td>2 points</td>
</tr>
</tbody>
</table>

Vomiting or retching Frequent vigorous chewing Salivation occasional chewing Reduced activity and alertness (drowsiness), occasional licking of lips Reduced activity and inquisitiveness, unusual postures

*Based on Graybiel’s diagnostic criteria for acute motion sickness in humans. Maximum sickness scores: 31 points.
squirrel monkey allowing a maximum sickness score of 31 points. For the initial screening for susceptibility, the experimental endpoint was at the end of 60 min of stimulation regardless of whether retching and/or vomiting had occurred. The duration of subsequent tests were extended to 120 min, to control the length of exposure to the stimulus and to avoid the possibility that the monkeys might learn to vomit in order to escape the stimulation. Latency to vomiting and/or retching and the cumulative sickness scores were recorded. In year 1, for baseline susceptibility level, this rating scale was employed throughout a series of 5 trials (one trial every 10 days) for each animal; three of the monkeys that did not vomit or retch in all five trials were considered non-susceptible. Ten susceptible monkeys qualified for the study; the other three monkeys did not vomit within 60 min and remained resistant when the duration of motion was extended to 120 min. In years 1, 3, 5, 7, and 10, after at least two weeks of intertrial period without testing, the effects of repeated exposures to the motion profile was investigated by exposing the monkeys to the same motion profile for 7 consecutive days. The endpoint of these tests was extended to 120 min regardless of whether or not vomiting/retching took place, and the latency to the first bout of vomiting/retching was used as the quantitative measure.

Throughout the years, the efficacy of a variety of experimental drugs was also tested on the ten susceptible squirrel monkeys using identical motion stimulus, profile, and a duration of 120 minutes as in the present study, with results published elsewhere (14). All ten susceptible monkeys were given all tests in the pharmacological study so that they all shared the same experience. At the end of the series of tests of each drug treatment, and after at least a 4-week intertrial interval without treatment, the monkeys were subjected to a single trial in years 3, 5, 7, and 10 using the original baseline motion profile. Responses from years 3, 5, 7, and 10 were assessed and compared with the mean sickness baseline score from year 1. The effects of habituation to the 7 consecutive days of testing, as in year 1 were also investigated in years 3, 5, 7, and 10. The three non-susceptible monkeys were also tested once in years 3, 5, 7, and 10.

**Results**

**Signs of Motion Sickness**

Susceptible monkeys exhibited varying levels of sickness starting with prodromal signs such as licking of lips, varying degrees of salivation, occasional and vigorous chewing movements, and in the final stages, retching and/or vomiting. Unusual posture is defined as contorted posture not normally observed in the monkeys, and such posture was scored as part of the sickness symptoms only if it was maintained for 15 minutes or longer. These postures included crouching or bracing against one corner with the lower limbs stretching across the chamber. Most often the monkeys assumed the crouching position with the head turned completely down and placed between the hind legs, with the hands grasping the head and the tail curled over the shoulder. Urination and defecation were frequently observed when the animal was placed in the lucite chamber even before motion was to begin; these signs were not rated as part of the motion sickness syndrome. The three non-susceptible monkeys did not exhibit any of the signs of motion sickness as described above during any of the testings throughout the 10 year period.

**Age Effect**

Baseline cumulative sickness score and latency to retching and/or vomiting of the ten monkeys are shown in Tables 2 and 3. Analysis of variance using repeated measure performed on the 5 baseline tests, with each test separated by 10 days, provided no evidence of habituation of the emetic response. Consequently the baseline tests were pooled. Among the ten monkeys, the mean baseline cumulative sickness score ranged from 20.6 to 24.2 and the mean latency to vomiting ranged from 17.1 to 42.3 min. Comparison of the cu-
cumulative sickness score and latency to vomiting collected from the same test in years 3, 5, 7, and 10 with the mean of the 5 baseline values are presented in Figure 1. Analysis of variance using repeated measures design was employed for the analysis, followed by multiple comparison tests (Fisher PLSD, Scheffe F-test). The analysis revealed no significant changes in the cumulative sickness scores \((F = 1.03; df = 4, 36; p < 0.2)\) nor in the latency to vomiting \((F = 0.89; df = 4, 36; p < 0.2)\) in all the monkeys throughout the 10 year period.

**Age and Habituation**

The latency to vomiting in the 7 consecutive daily trials performed in years 1, 3, 5, 7, and 10 was plotted in Figure 2. The daily exposure to the specific motion stimulus led to a substantial habituation by the fourth day as shown by the significant increase in the latency to first bout of vomiting/retching (paired t-test, \(p < 0.001\)). The squirrel monkeys never became completely refractory to motion induced emesis over the period of 7 days but a longer latency to the first bout of vomiting was observed. The mean latency to vomiting was 72.4 min in day 7 as compared to a mean of 31 min in day 1. They also exhibited a decrease in the number of vomiting responses during the 2-hour test period from about 4 to 5 responses on the first day to 1 response on the 7th day. The animals exhibited essentially the same pattern of response variation on the subsequent approximate biennial testing.

**Other Symptoms of Motion Sickness**

Another symptom complex centering around drowsiness and a crouching or defensive body posture has been proposed as concomitant or a manifestation of motion sickness that might occur before or after emesis, or in the absence of emesis (13). This behavioural response with irresistible drowsiness was known as Sopite Syndrome (16). The Sopite Syndrome before emesis was observed in our susceptible monkeys. When data from the different periods (years 1, 3, 5, 7, and 10) were pooled together, there was a correlation between the

### Table 2. Base-line (no drug) Sickness Scores

<table>
<thead>
<tr>
<th>Animal #</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
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<tbody>
<tr>
<td>Trial 1</td>
<td>24</td>
<td>18</td>
<td>26</td>
<td>26</td>
<td>19</td>
<td>21</td>
<td>24</td>
<td>28</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Trial 2</td>
<td>24</td>
<td>26</td>
<td>26</td>
<td>18</td>
<td>26</td>
<td>21</td>
<td>23</td>
<td>8</td>
<td>20</td>
<td>28</td>
</tr>
<tr>
<td>Trial 3</td>
<td>21</td>
<td>24</td>
<td>26</td>
<td>24</td>
<td>24</td>
<td>20</td>
<td>21</td>
<td>26</td>
<td>22</td>
<td>22</td>
</tr>
<tr>
<td>Trial 4</td>
<td>24</td>
<td>18</td>
<td>26</td>
<td>27</td>
<td>19</td>
<td>18</td>
<td>18</td>
<td>25</td>
<td>24</td>
<td>20</td>
</tr>
<tr>
<td>Trial 5</td>
<td>26</td>
<td>21</td>
<td>18</td>
<td>26</td>
<td>25</td>
<td>24</td>
<td>18</td>
<td>22</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>23.8</td>
<td>21.4</td>
<td>23.6</td>
<td>22.8</td>
<td>24.2</td>
<td>20.6</td>
<td>21.6</td>
<td>21.4</td>
<td>22.4</td>
<td>23.4</td>
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<tr>
<td>SO</td>
<td>1.8</td>
<td>1.6</td>
<td>1.4</td>
<td>1.8</td>
<td>1.2</td>
<td>1.3</td>
<td>3.3</td>
<td>1.7</td>
<td>1.4</td>
<td></td>
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</tbody>
</table>

Each trial is separated by an intertrial period of 10 days without treatment.

### Table 3. Base-line Latency to Vomiting/Retching in Minutes

<table>
<thead>
<tr>
<th>Animal #</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial 1</td>
<td>38.0</td>
<td>18.0</td>
<td>40.0</td>
<td>31.0</td>
<td>20.4</td>
<td>43.0</td>
<td>24.9</td>
<td>29.0</td>
<td>33.8</td>
<td>49.5</td>
</tr>
<tr>
<td>Trial 2</td>
<td>20.4</td>
<td>18.3</td>
<td>47.8</td>
<td>30.3</td>
<td>29.0</td>
<td>39.3</td>
<td>33.4</td>
<td>30.0</td>
<td>30.2</td>
<td>40.4</td>
</tr>
<tr>
<td>Trial 3</td>
<td>24.4</td>
<td>13.0</td>
<td>36.5</td>
<td>41.3</td>
<td>24.8</td>
<td>25.3</td>
<td>24.3</td>
<td>30.9</td>
<td>22.8</td>
<td>42.8</td>
</tr>
<tr>
<td>Trial 4</td>
<td>25.3</td>
<td>23.0</td>
<td>32.7</td>
<td>40.5</td>
<td>28.3</td>
<td>23.1</td>
<td>26.7</td>
<td>36.0</td>
<td>25.2</td>
<td>40.0</td>
</tr>
<tr>
<td>Trial 5</td>
<td>30.3</td>
<td>13.3</td>
<td>39.0</td>
<td>38.3</td>
<td>31.0</td>
<td>30.3</td>
<td>20.8</td>
<td>35.7</td>
<td>30.0</td>
<td>38.8</td>
</tr>
<tr>
<td>Mean</td>
<td>27.7</td>
<td>17.1</td>
<td>39.2</td>
<td>36.3</td>
<td>26.7</td>
<td>32.2</td>
<td>26.0</td>
<td>32.3</td>
<td>28.4</td>
<td>42.3</td>
</tr>
<tr>
<td>SD</td>
<td>6.7</td>
<td>4.1</td>
<td>5.5</td>
<td>5.2</td>
<td>4.1</td>
<td>8.6</td>
<td>4.6</td>
<td>3.2</td>
<td>4.2</td>
<td></td>
</tr>
</tbody>
</table>

Each trial is separated by an intertrial period of 10 days without treatment.
Figure 1. Comparison of the mean latency to first bout of vomiting (left axis) and mean cumulative sickness scores (right axis) from years 3, 5, 7, and 10 with the mean of the 5 baseline scores from year 1. Statistics revealed no significant changes in either parameters throughout the 10-year period.

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latency to the Sopite Syndrome and the latency to the first bout of vomiting. The sooner the monkey adopted the crouching posture and exhibited irresistible drowsiness (perhaps as a mean to minimize the aversive vestibular and optokinetic stimuli), the longer the latency to the first bout of vomiting (Pearson product moment correlation $r = 0.98$, $p < 0.001$). Further studies are required to investigate the significance of this correlation as the various sequence of the Sopite Syndrome was interwoven with other aspects of motion sickness.

Discussion

Under the conditions of the motion stimulation used in this study, our data on the ten susceptible squirrel monkeys demonstrate that
Figure 2. The mean latency to first bout of vomiting in the 7 consecutive daily trials performed in years 1, 3, 5, 7, and 10. Substantial habituation to the motion stimulus was evident by the fourth day ($p < 0.001$). The monkeys exhibited essentially the same pattern of response variation on the subsequent biyearly testing.

from the time of maturity to nearing the end of their life span, there was no correlation between age and motion sickness susceptibility, and that the habituation to daily testing was also unchanged throughout the test period. A definite statement cannot be made about the age effect on the susceptibility level of the non-susceptible monkeys (due to the limited number of subjects). However, none of these three monkeys showed any signs or symptoms of motion sickness in later years using the same motion profile.

Few controlled animal studies on the influence of age on susceptibility have been done. Using angular rotation about the vertical axis as motion stimulus, Elfar (10) concluded that, in a sample of young monkeys of Bolivian subspecies (estimated to be 2 years old), tested periodically over a two year period, there were no reliable differences in latencies to vomiting. A concurrent cross-sectional study to compare susceptibility between the original 2 years old group and an older group (whose precise age was unknown), revealed that the
mean latencies to vomiting of the older group was much longer. Cautious interpretation of these data is necessary. The older group of monkeys included Bolivian and Guianan subspecies, and interspecies differences are known to contribute to variations in susceptibility (13). Furthermore, within the older group of monkeys, there was a significant decrease of latencies to vomiting over three separate tests during the 2 year period. Therefore, within the older group it appears that susceptibility to motion sickness was increasing with advancing age. Based on these data, definite conclusions on the relationship between age and susceptibility cannot be deduced.

Mitchell and colleagues (17) demonstrated that when rats were subjected to rotation, they engaged in the consumption of kaolin, a nonnutritive, hydrated aluminum silicate with a clay-like taste. In an attempt to determine the underlying mechanism between age and susceptibility to rotation, McCaffrey and Graham (18) reported that the degree of rotation-induced kaolin consumption in older rats (20 months of age) was significantly less than that of the younger rats (2 and 11 months of age).
Rodents are not suitable for studies of motion sickness as they are incapable of vomiting. It is not clear whether motion-induced consumption of kaolin reflects a state which has the same underlying mechanisms as motion sickness in humans, although the behavioural changes do reflect the disruptive effects of motion on the rats. The rotational stimuli of 78 rpm for two hours employed in this study seemed to be excessive when the recommended effective stimulus for horizontal rotation is 10 to 25 RPM (19).

Current proposed explanations for the relationship between motion sickness and age regard the differences in susceptibility as the result of a life-long process of habituation to various forms of effective motion; that is, experiential factors are thought to contribute to the supposed decrease in susceptibility with age. Other explanations include degenerative changes in the neuronal elements of the inner ear, or general and unspecified changes in the central nervous system with increased age. Although age-related changes in the peripheral vestibular organs, including loss of hair cells, vestibular nerve fibres and Scarpa's ganglion cells in subjects older than 55 years, have been documented (20,21,22); Peterka and colleagues (23) found that in subjects ranging from 7 to 81 years, there was no significant age-related decline of vestibular ocular reflex function (VOR) paralleling the anatomical deterioration.

Our data on habituation to daily testing was similar to one of the three patterns that was described by Brizzee and Dunlap (24) who employed an identical motion profile. In their study, one group of monkeys habituated in about 5 days and were refractory for the last few days of the test series. After a rest period of 1 month these animals responded with essentially the same pattern as before. Our data demonstrated that the monkeys habituate after three daily two-hour testing, and respond in this way similarly at subsequent biyearly intervals. However, in our study they never reached the point of total refractoriness to the motion stimulus but the latency to vomiting increased more than two-fold by day 7. The susceptibility of the squirrel monkeys to the motion profile in this study appears to be consistent throughout the 10 years. In dogs, Noble reported that they retain their susceptibility to swing sickness when tested regularly over a period beyond three years (25). In cats, Crampton and Lucot (26) reported that weekly and daily testing led to a substantial habituation, with the daily regimen showing a more pronounced graphic but not statistically different effect. On the other hand, biweekly testing of the cats failed to show any habituation.

In the first comprehensive review of motion sickness, Tyler and Bard (1) in 1949 cited 7 articles to support their statement that children under 2 years of age and elderly persons show less susceptibility to seasickness than those of intermediate age. All subsequent reviews and chapters on the subject were referenced to this statement. All of the studies cited were based on personal observations and collective experience of physicians who had been in the service of passenger steamers for from two to ten years. In fact, three of the seven articles reported that infants are relatively immune (27,28,29). These reports also reported that children under 12 seldom suffer motion sickness severely and that they are rapidly adaptable. However, there were no reports on elderly subjects (27,28,29). Three other articles reported that both infants and aged persons suffer least in seasickness (30,31,32). It is of interest to note that as prophylaxis to seasickness, one of the recommendations is that aged persons should not take prolonged voyages which is contradictory, if elderly people are supposed to be relatively immune (28). Two of the seven articles also reported that certain people, even among seafaring persons, never acquire immunity (29, 33). Elderly people going on a voyage for the first time have been reported to be susceptible, and some sailors who have been to sea all their lives (including the historical case of the great Lord Nelson) are always seasick on returning to sea. There has been no clear quantitative evidence to suggest that age has a considerable influence on susceptibility, although it seems likely that infants are immune.

Although an inverse relationship between age and susceptibility has been described in text books for the past 40 years, supporting data is utterly lacking. One of the more recent
comprehensive questionnaire surveys of seasickness, on 20,029 passengers pooled over different voyages and vessels, revealed that variations in vomiting incidence with age appeared only to affect the lowest age group that was under 15 years of age (34). Illness rating, however, showed a continuous but slight decrease with increasing age, although the actual size of the difference was not clear. The observed effect could be attributed to self-selection due to previous experience, since novice travellers who experience seasickness tend not to return as passengers.

Based on the present findings in the squirrel monkeys, the influence of age on susceptibility to motion sickness in humans needs to be explored in well-controlled experimental investigations.

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