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Reliability of Autonomic Responses and Malaise Across Multiple Motion Sickness Stimulation Tests

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Summary

There is general agreement that a high degree of variability exists between subjects in their autonomic nervous system responses to motion sickness stimulation. Additionally, a paucity of data exists that examines the variability within an individual across repeated motion sickness tests. Investigators have also examined the relationship of autonomic responses to motion sickness development. These investigations have used analyses at discrete points in time to describe this relationship. This approach fails to address the time course of autonomic responses and malaise development throughout the motion sickness test. Our objectives were to examine the reliability of autonomic responses and malaise using the final minute of the motion sickness test across five testing occasions, to examine the reliability of the change in autonomic responses and the change in malaise across five testing occasions, and to examine the relationship between changes in autonomic responses and changes in malaise level across the entire motion sickness test. Our results indicate that, based on the final minute of testing, the autonomic responses of heart rate, blood volume pulse, and respiration rate are moderately stable across multiple tests. Changes in heart rate, blood volume pulse, respiration rate, and malaise throughout the test duration were less stable across the tests. We attribute this instability to variations in individual susceptibility and the error associated with estimating a measure of autonomic gain.

Introduction

Changes in autonomic responses during exposure to motion sickness stimulation have been the topic of numerous reports (refs. 2, 5, and 15). There is general agreement that changes in autonomic responses are descriptive of exposure to motion sickness stimulation and physiological responses to motion sickness are idiosyncratic between subjects (refs. 2 and 3). In contrast, evidence that changes in autonomic responses during motion sickness testing are reproducible within a subject is sparse. In general psychophysiological studies of response characteristics, researchers have reported reproducibility of individual patterns of cardiovascular and electrodermal responses to various experimental stressors (ref. 10). Cowings (ref. 2) concluded that individual autonomic responses to motion sickness testing are also highly reproducible. This conclusion was based on the stability of the magnitude of autonomic responses across two days of motion sickness testing. We suggest that a more sensitive criteria to determine the reproducibility of changes in autonomic responses during motion sickness stimulation would be to assess the reliability of responses across five motion sickness testing occasions.

Motion sickness symptom development that accompanies changes in autonomic responses has also been the topic of numerous investigations. Although there are few consistencies in the procedures by which investigators have chosen to assess the relationship between physiological responses and motion sickness symptoms, clearly motion sickness malaise is related to autonomic responses during motion sickness stimulation. However, these investigations fail to address relevant information about the onset and the time course of the relationship between symptom development and physiological changes throughout the entire motion sickness test. Some investigators have differentiated groups based on their symptoms and examined the differences in autonomic responses between these groups (refs. 9, 15, and 17). Other investigators have compared physiological responses at one point in time or at discrete time intervals during developing sickness levels (refs. 2, 5, and 9).

Our objectives of this investigation were as follows. First, to examine the reliability of four autonomic responses (blood volume pulse (BVP), heart rate (HR), respiration rate (RR), and skin conductance(SC)), malaise level, and susceptibility level (minutes of rotation tolerated) across five motion sickness test occasions. These analyses were conducted both for the final minute of the motion sickness test and for the entire duration of the motion sickness test. Our second objective was to examine the relationship between each of four autonomic responses and malaise over the entire duration of the motion sickness test. A third objective was to determine if there were differences between males and females in the reliability of their autonomic responses across the five motion sickness test occasions.

Material and Methods

Subjects

Twenty- six males (average age 21.19 years, ranging in age from 18-35 years) and seven females (average age 22.42 years, ranging in age from 18-38 years) participated in the study. All subjects were given a complete physical examination and were certified as medically qualified as they were good health and had normal vestibular function. Subjects were recruited from public announcements, were paid, and were assured a minimum of 2 hr pay per visit. Informed consent was obtained after the possible consequences of the study were explained.

Apparatus

A Stille-Werner rotating chair was used to provoke the symptoms of motion sickness using a standard test procedure (ref. 1). The rotating chair was located in a sound-proof booth in the laboratory. The chair is capable of both clockwise and counterclockwise rotation, with speeds ranging from 6 rpm to 30 rpm. Padded headrests mounted at 45 degrees from the vertical on the left, right, front, and back of the chair enabled subjects to execute head movements in these directions. Biomedical amplifiers were mounted on the rear and sides of the chair, and the physiological signals were sent through slip rings to strip chart recorders and a 14-channel FM analog tape recorder. Physiological data were digitized real time and were reduced and stored as 1-min averages for subsequent analyses using a DEC PDP 11/34 computer (ref. 1).

The physiological responses measured were: a) heart rate derived from electrocardiography using precordial placement of silver/silver chloride disposable electrodes, with heart rate computed beat-to-beat and processed with a Gould Biotachometer; b) respiration rate, derived through a nose clip thermistor, with respiration rate computed breath-to-breath using a Gould Biotachometer; c) blood volume pulse, derived from a photoplythesmograph transducer placed on the right index finger, with changes in the peak-to-peak amplitude of the waveform measured in arbitrary units; and d) skin conductance derived from pregelled disposable electrodes placed on the index and middle fingers of the left hand.

Procedure

Rotating chair test– All subjects were given six clockwise rotating chair tests approximately one week apart. The subjects were tested at approximately the same time of day. For the third and fifth tests, the direction of rotation was reversed to eliminate effects due to naturally occurring habituation to clockwise rotation. Following a resting baseline of 10 min, chair rotation was initiated at 6 rpm (0.628 rad/s) and incremented by 2 rpm (0.209 rad/s) every 5 min. The rotational velocity during each 5-min interval was held constant. The maximum velocity was 30 rpm (3.124 rad/s). During each 5-min period, subjects executed 150 head movements in the four quadrants. Instructions for making head movements at 2-s intervals were delivered to subjects by tape-recorded instruction. The direction of head movements was randomized. Following each 5-min interval of rotation there was a 30-sec pause (no head movements, but continued rotation) in which a standard diagnostic scale was administered (ref. 7). Prior to the start of the test, each subject was instructed to attend to his or her symptoms and to report the symptoms during the 30-sec pause. Subjects were asked to report any symptoms that occurred during the preceding five min. Tests were terminated at 30 rpm or at severe malaise (ref. 7), whichever came first.

Diagnostic scale– The diagnostic scale used to assess motion sickness symptoms was a standardized scale used to grade each subjects level of malaise (ref. 7). This instrument is based on self-report and experimenter observation of subjective body temperature, dizziness, headache, drowsiness, sweating, pallor, salivation, and nausea. A single composite score is calculated using a weighted scoring system .

Data analysis– For 22 subjects, BVP, RR, HR, SC, and malaise were used in the analyses. For 11 individuals, skin conductance measures were either not recorded or contained artifacts and their data was excluded. For these subjects, BVP, RR, HR, and malaise were used in the analyses. Data obtained during the first rotating chair test was not analyzed, because autonomic responding and symptom reports might be influenced by sources of error not present in subsequent days of testing. The first rotating chair test served to familiarize subjects with the procedure.

To examine the change in each autonomic response and malaise level over the entire duration of the motion sickness test, we performed linear regression analysis, with time as the independent variable (ref. 13). For 22 subjects, BVP, RR, HR, SC, and malaise were dependent variables. For the 11 individuals without skin conductance measures, BVP, RR, HR, and malaise were dependent variables. A separate analysis for each of five rotating chair tests on each physiological response and malaise for each individual was performed.

Baseline data, i.e. resting autonomic activity levels without rotation, of all subjects, was collected for ten minutes prior to each test. We used the average baseline physiological response from minutes 6 through 10 as the first data point in each subjects analyses. We used five minute averages of physiological responses in the linear regression analyses. These averages were used because symptom scores (malaise levels) were recorded at discrete time intervals at the end of each five minute rotation interval. Averaging these physiological responses across each five minute interval allowed us to make comparisons between both physiological responses and malaise levels in later analyses. Because subjects varied in the number of minutes of rotation tolerated during testing, the number of data points following initiation of rotation varied for each subject. The number of data points ranged from 3 to 14; 26% of the subjects had either 3 or 4 points, 44% had either 5 or 6 data points and 30% had 7 or 8 or more data apoints. This difference in the number of data points used to estimate slopes was for the most part random across

subjects and occasions and should not have provided any systematic bias.

From the regression analyses, we obtained the slope (B_1) for each individual for each autonomic response and for malaise across time. The slope (rate of change) for each dependent variable was used as a measure of gain and retained for further analyses. From these slopes, we determined the value of the variance components across the five motion sickness tests with a random effects analysis of variance (components of variance model) (ref. 12). The statistical model related the variance in the observed measure to variance between and variance within subjects. This basic 2 parameter model is described in more detail by Winer (ref. 17). We also determined the values of the variance components for the amount of time that each subject tolerated the motion sickness tests. Using the obtained variances, interclass correlations were calculated to asses the within subject reliability of the response slopes and minutes of rotation tolerated (refs. 8 and 12). To estimate reliabilities based on multiple test occasions (average scores), we applied the Spearman-Brown prophecy formula (ref. 8).

Based on the results of this assessment, averages of the slopes of each autonomic variable and malaise for each subject over all five motion sickness tests were obtained. Pearson Product-moment correlation coefficients were computed to determine the relationship between the average slope of each autonomic response and the average slope of malaise. In addition, Pearson Product-moment correlation coefficients were computed to determine the relationship between the average slope of each autonomic response and the average number of minutes of rotation tolerated over the five test occasions.

In addition to calculating interclass correlations for the slopes of the physiological responses, the slopes of malaise, and the number of minutes of rotation tolerated, we estimated interclass correlations for the final minute of each physiological response and the final malaise level across the five motion sickness tests. The results of the components of variance model for the final minute of were compared to those calculated across the entire testing session. To test for possible differences in reliabilities between males and females, these calculations were repeated for each group.

Results

Entire Test Duration

Random effects analysis of variance (ANOVA), based on the slopes for each response, the slopes for malaise, and minutes of rotation tolerated were conducted to derive variance components. These values are shown in table 1. For skin conductance, the amount of within subject variability was higher than the amount of between subject variance. This produced negative estimates of variance, and we chose not to include it in further analyses of slope estimates.

In table 1, the components of variance are estimates of the variation from two sources: between-subjects and within-subjects. The term σ_b is a measure of the variance between subjects. The more the different subjects vary in the rate of change of each variable, the greater this term will be. On the other hand, if all subjects have the same rate of change, $\sigma_{b=0}$. The term σ_w is a measure of the variation associated with the slope values within a subject. In this study, this value represents the variability of the rate of change across the five test occasions. The value of this term will increase as the variability within subjects (or across multiple test occasions) increases.

Table 1. Variance components for each autonomic response slope, malaise, and minutes of rotation

Variable (change in)	$\sigma^2 b$	$\sigma^2 w$
Heart rate	4.873	2.522
Blood volume pulse	23.086	37.310
Respiration rate	0.554	1.609
Malaise level	1.240	0.992
Minutes of rotation	52.830	45.729

$\sigma^2 b$ = between subject variance.
$\sigma^2 w$ = within subject variance.

The interclass correlations, derived from the variance components in table 1, are presented in table 2 (when number of tests equals 1). Interclass correlations pertain to the relative degree of consistency among sets of intraclass scores. The interclass correlation and reliability estimates in table 2 are each based on the number of test occasions. As more test occasions are included in the estimate, the reliability increases. For example, the reliabilty of change in heart rate, from two tests is 0.7944. If we base our estimatte of change on the mean of three test occasions, the rate of change of heart rate tends to approach an acceptable scientific standard (reliability $\geq$ 85). Malaise level and minutes of rotation tolerated estimates approach acceptable standards only when five test occasions are considered. Neither slopes of blood volume pulse nor respiration rate reach acceptable reliability levels.

Because the rate of change across the motion sickness test was not reliable on only one test occasion, but became more statistically reliable as the number of tests increased, we averaged the slopes of the five motion sickness tests. From these averages, we calculated Pearson Product-moment correlation coefficients for the average slope of each autonomic response and the average slope of malaise level and minutes of rotation tolerated. These values are presented in table 3. Changes in malaise level are positively related to changes in heart rate (as heart rate increases, the level of malaise also increases). Changes in malaise level are negatively related to changes in blood volume pulse and positively related to changes in respiration rate. Although these correlations are somewhat weak, they are in the predicted directions. As respiration rate increases, malaise levels also increase. As blood volume pulse decreases, malaise levels increase. Changes in heart rate, blood volume pulse, and respiration rate are all moderately related to the minutes of rotation tolerated. As heart rate change increases across the duration of the motion sickness test, the amount of time tolerated in the test decreases. Similarly, as respiration rate change increases across a motion sickness test, the amount of time a subject tolerates the motion sickness test decreases. As blood volume pulse change increases (blood volume pulse is decreasing), the minutes of time tolerated decrease.

Final Minute of Motion Sickness Test

Shown in table 4 are the variance components derived from random effects analysis of variance (ANOVA), based on the final minute of each autonomic response an the final malaise level.

The interclass correlations and estimates of reliabilities, derived from the variance components in table 4, are pre sented in table 5. As can be seen in table 5 correlation estimates of the final minute of heart rate, blood volume pulse, and respiration rate were reliable after two test occasions. The final malaise level estimates approach re able limits only when three test occasions are considere

Table 2. Interclass correlation and estimated reliability of the slopes across multiple motion sickness tests

Dependent variable	Number of tests				
(Change in)	1[a]	2	3	4	5
Heart rate	0.6590	0.7944	0.8528	0.8854	0.9062
Blood volume pulse	0.3823	0.5531	0.6499	0.7122	0.7558
Respiration rate	0.2562	0.4090	0.5081	0.5794	0.6327
Malaise level	0.5557	0.7144	0.7895	0.8353	0.8621
Minutes of rotation	0.5360	0.6979	0.7761	0.8220	0.8524

[a]Intraclass correlation estimate when test equals 1.

Table 3. Correlation coefficients for changes in autonomic responses, changes in malaise, and minutes of rotation

Autonomic response	Malaise change	Minutes of rotation tolerated
Heart rate change	0.625[a]	–0.610[b]
Respiration rate change	0.233	–0.441[b]
Blood volume pulse change	–0.286	0.360[a]

[a]$p < 0.05$
[b]$p < 0.01$

Table 4. Variance components for each autonomic response and malaise for the final minute of testing

Variable	σ^2b	σ^2w
Heart rate	157.33	43.86
Blood volume pulse	1113.74	347.90
Respiration rate	24.24	9.110
Malaise level	6.170	3.315

σ^2b = between subject variance.
σ^2w = within subject variance.

Table 5. Interclass correlation and estimated reliabilities of the final minute of autonomic responses and malaise level

	Number of tests				
Dependent variable	1	2	3	4	5
Heart rate	0.7819	0.8777	0.9162	0.9350	0.9459
Blood volume pulse	0.7619	0.8644	0.9059	0.9275	0.9411
Respiration rate	0.7270	0.8419	0.8887	0.9141	0.9301
Malaise level	0.6505	0.7882	0.8482	0.8814	0.9028

Our final analyses was to examine the differences between males and females in the reliability of autonomic responses across five motion sickness tests. Males and females did not differ from each other, nor did the reliabilities differ from both groups combined. There were no differences in the reliabilities for the change in each autonomic response (BVP, RR, HR, and SC) and malaise across the tests, the number of minutes of rotation tolerated, or the final minute of testing for each autonomic response, or the final malaise level.

Discussion

Cowings (ref. 2) found that the amplitude of autonomic responses across two days of testing was stable for each autonomic response (heart rate, blood volume pulse, respiration rate, and skin conductance) for approximately 60% of subjects tested. Despite the disparity in statistical approaches, our findings not only replicate her conclusions, but extend them to include five motion sickness tests. Our results, based on the autonomic response at the final minute of an individuals motion sickness test during Coriolis stimulation, indicate that autonomic responses to motion sickness testing exhibit consistency over time, thereby reflecting a relatively stable characteristic of individuals.

The findings that a high degree of individual variability exists in the change of each autonomic response (slope) across the duration of the motion sickness test when comparing across multiple days of motion sickness testing is new. Our findings indicate that the rate of change of autonomic responding across one motion sickness test is not a reliable descriptor of an individual's autonomic response pattern; only when an individual is tested across five occasions and an average is determined does the response pattern become reliable.

In any type of testing, multiple sources of error, which undermine the reliability of the measurement, are present. One potential source of variance, is a characteristic of the test itself; or measurement error. For example, potential sources of measurement error during a motion sickness test include loose electrodes and failures in measuring equipment. The problem of reliability of measurements is inherent in all science, because whenever man (being infallible) attempts to measure anything there is always the possibility of errors of measurement. The large within subject variability in skin conductance may be attributed to measurement error. A second source of error may occur in the estimations of the slopes of each ANS response and malaise. These estimations are derived from a small number of observations, in some cases, as few as three. These estimates may increase in reliability if our slope estimates are calculated from a larger number of data points. To increase the number of data points, malaise levels must be measured continuously instead of at discrete time intervals of five minutes. This could easily be done with a

continuous monitoring symptom device, such as a keypad attached to arm of the rotating chair, that could be used to enter symptoms as they occur during a test.

A third potential source of variability in the response slopes is the relationship these slopes have with susceptibility levels. Our results indicate that heart rate and respiration rate increase at a higher rate when minutes of rotation tolerated are shorter; when the number of minutes of rotation tolerated are longer, heart rate and respiration rate increase at a slower rate. The opposite occurs for blood volume pulse; as blood volume pulse decreases faster, minutes of rotation tolerated are shorter. Thus, individual differences in autonomic responding across multiple days of testing may be, in part, related to daily fluctuations in susceptibility. Unfortunately, explaining why daily fluctuations in susceptibility occur is quite another issue. One major source of variability inherent to human research is in the general physiological state of the subject on different days, or natural biological variation. Clearly, if a test is repeated, results will vary and this variability should be looked on as a property of an individual which will influence the scores of repeated observations, regardless of how accurately the test is made.

Our findings that reliable estimates of changes in autonomic responses are related to changes in malaise clearly demonstrates that autonomic responses are related to malaise. The autonomic response most closely related to malaise was changes in heart rate throughout the motion sickness test. As heart rate increased, malaise levels correspondingly increased. Cowings (ref. 3) reported significant correlations between initial symptom scores and changes in heart rate from the first to fifth minute of rotation. In another study, Cowings found significant increases in heart rate across increasing malaise levels (ref. 3). We also demonstrated that decreases in blood volume pulse were associated with increases in malaise levels. Previous research has also shown vasoconstriction associated with increasing levels of malaise (ref. 3). In our study, respiration rate also increased in accordance with malaise. This has also been supported by previous findings (ref. 3).

Given that our findings demonstrate stable autonomic responses across multiple testing of a single motion sickness stimulus, perhaps we can also determine if autonomic responses maintain stability across different motion sickness stimuli. It is not known whether autonomic responses to motion sickness stimuli are influenced by the quality of the stimulus, although research using mental and physical stimuli has demonstrated that autonomic responses are influenced by both stimuli and the individuals characteristics (ref. 4). Preliminary evidence by motion sickness researchers suggests that individuals show stable autonomic response hierarchies across types of motion sickness provocation; Coriolis stimulation, vertical acceleration, and combined optokinetic and Coriolis stimulation (refs. 2 and 11). In contrast, indirect evidence that habituation is highly specific to the stimulus condition and exhibits poor transfer to other environments suggests that physiological responses are stimulus specific (refs. 6 and 14). We suggest that the contribution of both individual autonomic response differences and stimulus specific influences on responding across different motion sickness stimuli should be examined in future research.

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13. ABSTRACT ***(Maximum 200 words)***

There is general agreement that a high degree of variability exists between subjects in their autonomic nervous system responses to motion sickness stimulation. Additionally, a paucity of data exists that examines the variability within an individual across repeated motion sickness tests. Investigators have also examined the relationship of autonomic responses to motion sickness development. These investigations have used analyses at discrete points in time to describe this relationship. This approach fails to address the time course of autonomic responses and malaise development throughout the motion sickness test. Our objectives were to examine the reliability of autonomic responses and malaise using the final minute of the motion sickness test across five testing occasions, to examine the reliability of the change in autonomic responses and the change in malaise across five testing occasions, and to examine the relationship between changes in autonomic responses and changes in malaise level across the entire motion sickness test. Our results indicate that, based on the final minute of testing, the autonomic responses of heart rate, blood volume pulse, and respiration rate are moderately stable across multiple tests. Changes in heart rate, blood volume pulse, respiration rate, and malaise throughout the test duration were less stable across the tests. We attribute this instability to variations in individual susceptibility and the error associated with estimating a measure of autonomic gain.

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