N92-22350

SPACE SICKNESS PREDICTORS SUGGEST FLUID SHIFT INVOLVEMENT AND POSSIBLE COUNTERMEASURES

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ABSTRACT

Preflight data from 64 first-time Shuttle crewmembers were examined retrospectively to predict space sickness severity (NONE, MILD, MODERATE, or SEVERE) by discriminant analysis. From nine input variables relating to fluid, electrolyte, and cardiovascular status, eight variables were chosen by discriminant analysis that correctly predicted space sickness severity with 59% success by one method of cross-validation on the original sample and 67% by another method. The eight variables in order of their importance for predicting space sickness severity are sitting systolic blood pressure, serum uric acid, calculated blood volume, serum phosphate, urine osmolality, environmental temperature at the launch site, red cell count, and serum chloride. These results suggest the presence of predisposing physiologic factors to space sickness that implicate a fluid shift etiology. Addition of a tenth input variable, hours spent in the Weightless Environment Training Facility (WETF), improved the prediction of space sickness severity to 66% success by the first method of cross-validation on the original sample and to 71% by the second method. The data suggest that WETF training may reduce space sickness severity. Astronauts while in WETF training are not oriented by gravity but remain physiologically susceptible to it, causing cephalad shifts of fluid when they are head down. As a result, they may physiologically adapt to the fluid shifts by reducing their blood volume, which also occurs in weightlessness. If fluid shifts contribute to space sickness, preadaptation of the circulation by preflight blood volume reduction may counteract fluid shifts in weightlessness and help to alleviate space sickness.

INTRODUCTION

Space sickness is an operationally significant problem that occurs to varying degrees of severity in about two-thirds of Shuttle astronauts (Davis et al., 1988). Besides being a nuisance, mission performance can be negatively impacted when astronauts are severely space sick, and safety is an important issue. An emergency Shuttle landing early in a mission could be endangered if the pilot and commander were spacesick (Vanderploeg et al., 1985). The risk of fatality from vomiting in a spacesuit is presently minimized by an operational policy prohibiting extravehicular activity (EVA) during the first three mission days when space sickness is most likely to occur. Space sickness typically begins about an hour after orbital insertion, reaches a peak within 24 to 48 hours, and usually resolves between 30 to 48 hours, although it can persist for 72 hours. The time course is variable, however, with occasional delayed-onset space sickness occurring after two days in space (Thornton et al., 1987). NASA has expended great effort in attempting to understand, predict, and treat space sickness to relieve crew discomfort, increase mission productivity, and enhance safety.

Space sickness did not occur in the early days of spaceflight; apparently the larger cabins in Apollo and later spacecraft permitted enough mobility to exceed vestibular susceptibility thresholds for the induction of space sickness. However, susceptibility to vestibular stimulation is not likely to be the sole etiologic factor in space sickness, because preflight tests of astronauts' motion sickness susceptibilities do not correlate significantly with space sickness and are not useful for prediction (Homick et al, 1987). Although the dominant paradigm at this time regards the space sickness problem as a form of motion sickness resulting from novel neurovestibular stimulation in the unique environment of weightlessness (Crampton, 1990), it may be more fruitful to consider space sickness as a binary process. While the dominant paradigm is probably correct in that an essential component of space sickness involves some unaccustomed neurovestibular stimulation, a second important factor may be a decreased threshold of susceptibility to nauseogenic stimuli in general, brought on by physiologic responses to weightlessness. Among the insults upon homeostasis in the early hours and days of a mission which might lower an astronaut's tolerance to provocative vestibular stimuli are some of the effects of fluid shifts.

There is believed to be a dramatic headward fluid redistribution with substantial physiologic responses immediately upon exposure to weightlessness (Greenleaf, 1984). This simple picture is complicated somewhat by the fact that fluid shifts probably begin while astronauts wait in the semi-supine position before launch (Lathers, 1989). Regardless, space sickness follows closely upon the time course of both these fluid shifts and the major physiological perturbations they produce. Fluid shifts caused by head-down tilt in bedrest studies sometimes are associated with

dizziness and nausea upon head movement, spontaneous nystagmus, and vestibular illusions of tilting and falling (Kakurin et al, 1975). Fluid shifts caused by water immersion have been reported to increase vestibular susceptibility to caloric stimulation so much that sometimes the caloric stimulation had to be stopped (Mitarai et al, 1981).

Several potential mechanisms exist by which fluid shifts may contribute to space sickness, whether or not the fluid shifts begin on the launch pad (Simanonok et al., in review). We have previously shown that nine preflight variables relating to fluid, electrolyte, and cardiovascular status can be used to predict space sickness incidence with about 80% success and space sickness severity with 55% success using two methods of "pseudo" cross-validation on the original sample of 64 subjects (Simanonok et al., in review). In the present study, the same nine predictor variables have been used, with the addition of the astronauts' training time in the Weightless Environment Training Facility (WETF) as a potential predictor of space sickness. This variable was added because Youmans et al. (1987) have reported an inverse relationship between WETF training and space sickness severity.

The WETF is a tank of water measuring 33 by 78 feet and 25 feet deep. It is used to simulate weightlessness for astronauts preparing for EVA; not all astronauts get WETF training. Astronauts who train in the WETF wear full space suits adjusted for neutral buoyancy in the water. Suit pressure is regulated to approximately 4.2 PSI above the water pressure at any given depth, so there is no externally applied hydrostatic gradient on their bodies as occurs in most water immersion studies. However, they are still in a gravity field and they may sometimes assume head-down positions, which would cause headward fluid shifts to occur. It is possible that repeated exposure to fluid shifts in WETF training confers some preflight physiologic adaptation to the astronauts which lessens their physiologic responses to fluid shifts in weightlessness, therefore helping to protect against space sickness if fluid shifts are involved in space sickness etiology. An alternative or adjunct hypothesis is that unusual positional orientations that the astronauts assume relative to the spacecraft mockups in WETF training help to visually adapt them to similar orientations they will experience in weightlessness. Visual adaptation might reduce the impact of the "sensory conflict" conceptions of the dominant paradigm (Crampton, 1990) that may also be an important component of space sickness.

METHODS

Preflight clinical data for 64 first-time Shuttle crewmembers were used in this study. Not all measures were available at the same times preflight, and some measures were made several times preflight. The first available data for each crewmember were used in this order: launch minus 30 days, launch minus 10 days, and launch minus 3 or 2 days. Variables not measured for a given astronaut on any of those occasions were obtained from their annual physicals. Each astronaut's space sickness severity was determined by a NASA flight surgeon according to the ordinal scale shown in Table 1. Space sickness incidence was defined as any occurrence of space sickness from MILD through SEVERE and called SICK, as opposed to the NONE category. However, the prediction of space sickness incidence was not improved by addition of WETF training over the 80% success obtained by the nine fluid shift variables alone (Simanonok et al., in review), so those results are not reported here. Space sickness severity was defined as the degree of space sickness from NONE through SEVERE. Predicted preflight blood volumes for each astronaut were calculated on the basis of sex, height and weight by the method of Feldschuh and Enson (1977). Free air maximum and minimum temperatures for three days before each Shuttle launch plus launch day at the Shuttle Landing Facility at Kennedy Space Center were obtained from the Landing Support Office at the Johnson Space Center. Means of the minimum four-day temperatures were used in the following analyses as the prediction variable representing environmental temperature at the launch site. The WETF training data we used are a subset of those previously analyzed and reported by Youmans et al. (1987) because we did not have available the other prediction variables for some of the astronauts in their larger WETF sample.

TABLE 1

SPACE SICKNESS SCORING CRITERIA
From Davis et al. (1988)

NONE (0)
NO SIGNS OR SYMPTOMS REPORTED WITH THE EXCEPTION OF MILD TRANSIENT HEADACHE OR MILD DECREASED APPETITE.

MILD (1)
ONE TO SEVERAL SYMPTOMS OF A MILD NATURE; MAY BE TRANSIENT AND ONLY BROUGHT ON AS THE RESULT OF HEAD MOVEMENTS; NO OPERATIONAL IMPACT; MAY INCLUDE SINGLE EPISODE OF RETCHING OR VOMITING; ALL SYMPTOMS RESOLVED IN 36-48 HOURS.

MODERATE (2)
SEVERAL SYMPTOMS OF A RELATIVELY PERSISTENT NATURE THAT MAY WAX AND WANE; LOSS OF APPETITE; GENERAL MALAISE, LETHARGY AND EPIGASTRIC DISCOMFORT MAY BE MOST DOMINANT SYMPTOMS; INCLUDES NO MORE THAN TWO EPISODES OF VOMITING; MINIMAL OPERATIONAL IMPACT, ALL SYMPTOMS RESOLVED IN 72 HOURS.

SEVERE (3)
SEVERAL SYMPTOMS OF A RELATIVELY PERSISTENT NATURE THAT MAY WAX AND WANE; IN ADDITION TO LOSS OF APPETITE AND STOMACH DISCOMFORT, MALAISE AND/OR LETHARGY ARE PRONOUNCED; STRONG DESIRE NOT TO MOVE HEAD; INCLUDES MORE THAN TWO EPISODES OF VOMITING; SIGNIFICANT PERFORMANCE DECREMENT MAY BE APPARENT; SYMPTOMS MAY PERSIST BEYOND 72 HOURS.

Statistical analyses were performed with BMDP (BMDP Statistical Software, Inc., Los Angeles, CA) on either a Digital Equipment Corporation (Westminster, MA) VAX 780 or VAX 3400. Prediction of space sickness severity was performed in this study by discriminant analysis. Chi-square analyses were done to provide a comparison of the prediction success expected due to chance alone

and to estimate the significance level of WETF training on reducing space sickness severity as compared to that which would be expected to occur by chance. Spearman correlation coefficients were done to describe the strengths of relationships among the prediction variables and between the prediction variables and the criterion. Mann-Whitney rank-sum tests were used to test for differences between variables in each of the space sickness groups with their counterparts in the NONE group, and between the two groupings of astronauts that either did or did not receive WETF training. Statistical significance was accepted at $p<0.05$.

Data Analysis

The discriminant analysis program calculated an analysis of variance in a series of steps, selecting one variable at each step with the greatest F value. A classification function was then derived which reduced the prediction variables into a single weighted composite with appropriate weighting coefficients for separation of the cases into the groups that they belonged. A similar application of discriminant analyses with a more extensive description of rationale and procedures can be found in Reschke et al. (1984). Our previous analyses were performed with nine preflght variables describing some aspects of fluid, electrolyte, and cardiovascular status (Simanonok et al., in review). In that work we initially compared the efficacy of the same nine variables in predicting several different groupings of space sickness incidence and severity, so the same nine variables were used in all cases; i.e., they were "forced" into the discriminant analyses rather than being chosen by the program. In this work we removed the force instruction and allowed the program to choose the variables which best predicted the criterion variable, space sickness score. Variable selection was limited by setting the minimum F-to-enter at 1.5, which provided an approximate F-value in terms of contributing to the predictions at the end of variable selection that was statistically significant at $p<0.05$.

Two estimates were calculated of the ability of the nine fluid shift variables to predict space sickness severity on an ideal hypothetical cross-validation sample composed of new cases. One type of cross-validation on the original sample termed a "jackknife" cross-validation was calculated, in which each case was removed from the analysis one at a time and new weighting coefficients on the classification functions (keeping the same variables) were computed with the remaining 63 cases. The new classification function was then used to classify each case as it was removed. Second, a subsample cross-validation was performed. Arbitrarily, 40 cases were selected by stratified random sampling and used to create classification functions to predict the remaining 24 cases. In this second method of cross-validation the variables originally chosen as predictors were forced into discriminant analyses to allow an evaluation of their success in predicting space sickness by this cross-validation method.

RESULTS

The nine fluid shift variables used as input in discriminant analyses are shown in relation to space sickness scores in Fig. 1. A similar plot of the relationship between WETF training time and space sickness severity is shown in Figure 2. Figure 3 depicts the WETF data in a different form, showing the number of astronauts in each space sickness category that did and did not have WETF training, regardless of the number of hours spent. Intercorrelations of the nine original predictor variables, WETF training time, and space sickness severity are shown in Table 2.

Prediction of space sickness severity using nine fluid shift variables as input is shown in Table 4. The program chose eight variables as predictors and used them to create classification functions which could classify the 64 astronauts into the correct space sickness category with 69% success. The eight variables were chosen in this order: sitting systolic blood pressure, serum uric acid, calculated blood volume, serum phosphate, urine osmolality, environmental temperature at the launch site, red cell count, and serum chloride. The jackknife cross-validation success of 59% prediction shows some shrinkage from the classification matrix, a typical phenomenon for cross-validation studies. The results of jackknife cross-validation may best reflect the true probability of correctly predicting new cases of space sickness on the basis of the 64 subjects used in this study. The subsample cross-validation success rate of 67% is more likely to be artifactually high due to chance, because only data from 40 subjects were used to predict space sickness severity in the remaining 24 subjects.

Addition of WETF training time as a tenth variable in another set of discriminant analyses improved the prediction of space sickness severity, shown in Table 5. The program again chose eight of the ten variables as significant predictors of space sickness, this time forming classification functions that separated the 64 astronauts into their correct space sickness category with 77% success. The eight variables were chosen in this order: WETF training time, sitting systolic blood pressure, serum uric acid, calculated blood volume, serum phosphate, urine osmolality, environmental temperature at the launch site, and red cell count; serum chloride fell out from the earlier prediction. The jackknife cross-validation success was improved to 66%, and the subsample cross-validation to 71%.

For comparison, the percent success in predicting space sickness severity that would result from chance alone is 32%, as shown in Table 3. This table was computed by chi-square analysis, but the expected values in some cells are less than 1, violating the necessary assumptions for probabilistic comparisons with the above predictions of space sickness severity with and without WETF training. Combining the MODERATE and SEVERE groups to increase the expected values enabled valid chi-square comparisons for the classification and jackknife matrixes but not the subsample matrixes; for both those sets of predictions with and without WETF training, the predictions are significantly better than chance at $p < 0.00005$.

When WETF training time was used as the sole input variable for discriminant analysis to predict space sickness severity, the prediction successes obtained by the classification functions and by jackknife cross-validation were both 42%. The subsample cross-validation showed 33% success, the same expected due to chance.

Finally, the 64 astronauts were split into two groups according to whether they had WETF training (n = 36) or not (n = 28). Mann-Whitney tests between these two groups were performed on the nine fluid shift variables and 46 other clinical and anthropometric variables, some derived by calculation, available for this sample of astronauts. Of interest are these differences (mean ± SEM) found in serum chloride, WETF = 104.25 ± 0.41 mEq/L, no WETF = 105.86 ± 0.42 mEq/L (p = 0.0153); plasma osmolality, WETF = 289.53 ± 0.62 mOsm/kg, no WETF = 292.21 ± 0.63 mOsm/kg (p = 0.0052); urine specific gravity, WETF = 1.0192 ± 0.0011, no WETF = 1.0162 ± 0.0012; and forced vital capacity indexed to body weight, WETF = 0.0660 ± 0.0018 L/kg (n = 35), no WETF = 0.0604 ± 0.0019 L/kg (n = 27), (p = .0400). These were the only variables found to differ between WETF trained and untrained astronauts at p<0.05.

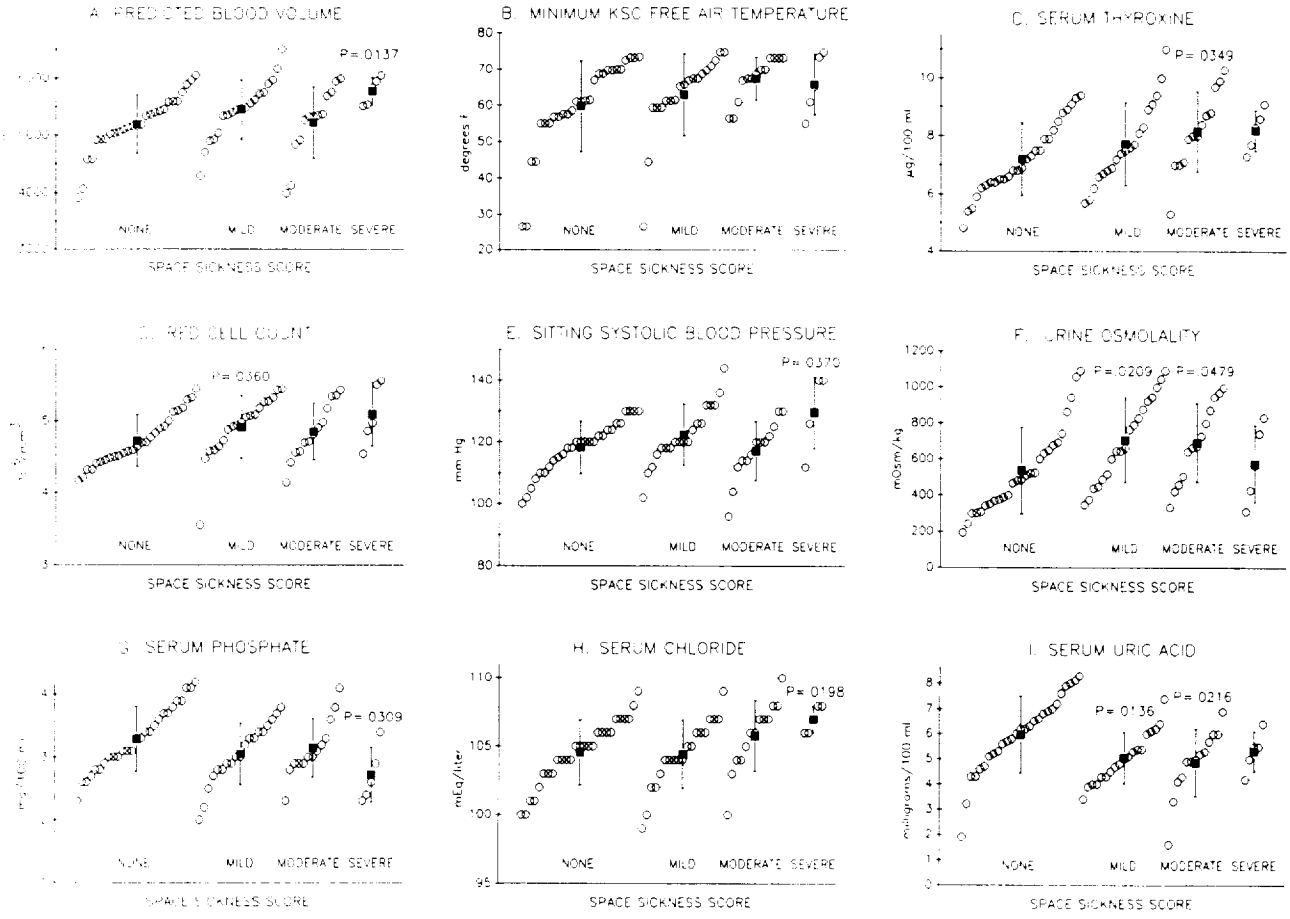

FIG. 1. NINE PREFLIGHT VARIABLES USED TO PREDICT SPACE SICKNESS.

Individual points are plotted in ascending order within each space sickness group at arbitrary but equidistant points along the x-axis for evaluation of the raw data. Black squares are means (± S.D.) for each group plotted at the median position in the range of points. P values are from Mann-Whitney significance tests of the three sick groups separately tested against the NONE group.

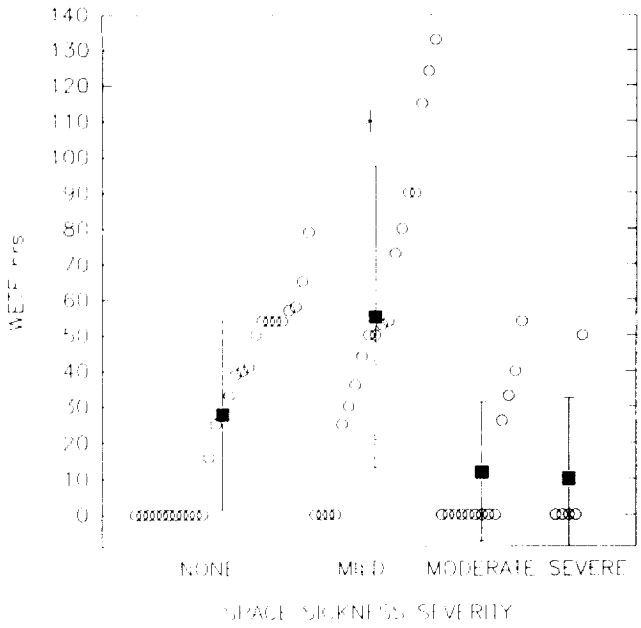

FIG. 2. HOURS IN WETF TRAINING VERSUS SPACE SICKNESS SEVERITY.

* The MILD group had significantly more training hours than all of the other groups by a Mann-Whitney test at $p<0.05$. Black squares are means ($\pm$ S.D.).

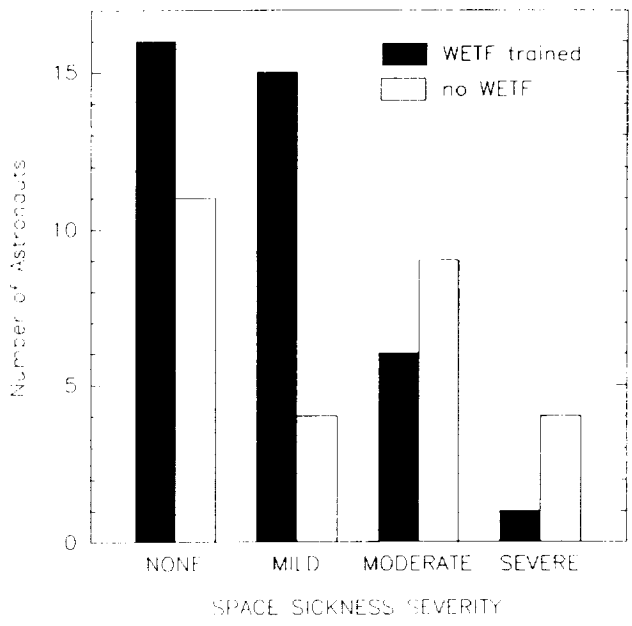

FIG. 3. PRESENCE AND ABSENCE OF WETF TRAINING RELATIVE TO SPACE SICKNESS SEVERITY.

When the MODERATE and SEVERE groups were combined to enable a valid chi-square test, the differences in space sickness severity due to WETF training were significantly different from chance at $p = 0.0067$.

TABLE 2. SPEARMAN CORRELATIONS AMONG THE ORIGINAL NINE PREDICTION VARIABLES RELATED TO FLUID, ELECTROLYTE, OR CARDIOVASCULAR STATUS; INCLUDED ARE WETF TRAINING HOURS AND SPACE SICKNESS SCORES.

	SCORE	URICAC	THT4	CL	RBC	MINT	PO4	UROS	BV	SITSYS
URICAC	-.32*	1								
THT4	.32*	-.17	1							
CL	.27*	-.08	.29*	1						
RBC	.26*	.25*	.18	-.02	1					
MINT	.25*	-.07	.06	.14	-.20	1				
PO4	-.25*	-.05	.03	-.21	-.12	.10	1			
UROS	.24	.00	.17	.01	.21	.12	-.13	1		
BV	.23	.14	.20	-.05	.28*	.16	-.11	.27*	1	
SITSYS	.14	.17	-.09	-.14	.33*	-.11	-.10	.17	.11	1
WETF	-.17	.04	-.06	-.28*	.01	-.17	.05	.11	-.07	-.02

* = $p < 0.05$. All pairs are $n = 64$. SCORE = space sickness score; URICAC = serum uric acid; THT4 = serum thyroxine; CL = serum chloride; RBC = red cell count; MINT = minimum free air temperature at the launch site; PO4 = serum phosphate; UROS = urine osmolality; BV = predicted blood volume; SITSYS = sitting systolic blood pressure; WETF = hours of WETF training.

TABLE 3. PREDICTION SUCCESS FOR SPACE SICKNESS SEVERITY THAT WOULD BE EXPECTED SOLELY DUE TO CHANCE (determined by chi-square).

		PREDICTED			
CHANCE	PERCENT CORRECT	NONE	MILD	MODERATE	SEVERE
NONE	47%	12.7	7.2	5.9	1.3
MILD	26%	8.9	5.0	4.2	0.9
MODERATE	21%	6.1	3.5	2.8	0.6
SEVERE	4%	2.3	1.3	1.1	0.2
TOTAL	32%	30	17	14	3

TABLE 4

PREDICTION OF SPACE SICKNESS SEVERITY USING NINE VARIABLES RELATED TO FLUID, ELECTROLYTE, AND CARDIOVASCULAR STATUS SHOWN IN FIGURE 1

I. MEANS AND STANDARD DEVIATIONS OF VARIABLES USED

GROUP =	NONE	MILD	MODERATE	SEVERE
VARIABLE				
BV	5191	5449	5223	5770
ml	509	524	620	242
MINT	59.8	63.0	67.5	65.9
deg. F	12.6	11.3	6.0	8.4
THT4*	7.20	7.73	8.16	8.20
µg/dL	1.25	1.43	1.38	.71
RBC	4.72	4.91	4.85	5.09
10^{12}/L	.36	.44	.39	.44
SITSYS	118	122	117	130
mmHg	8	10	10	12
UROS	536	706	692	574
mOsm/kg	241	234	218	215
PO4	3.29	3.05	3.15	2.72
mg/dL	.52	.49	.47	.44
CL	105	104	106	107
mEq/L	2	3	3	1
URICAC	5.97	5.06	4.86	5.32
mg/dL	1.53	1.02	1.35	.80
n	27	19	13	5

* THT4 was provided as input but not chosen by the discriminant analysis program

II. CLASSIFICATION FUNCTIONS

GROUP =	NONE	MILD	MODERATE	SEVERE
VARIABLE				
BV	0.02517	0.02621	0.02502	0.02804
MINT	0.96085	1.05467	1.10696	1.10827
RBC	29.40623	32.22703	33.21688	33.39625
SITSYS	1.97799	2.03264	1.97129	2.15279
UROS	-0.01940	-0.01654	-0.01594	-0.02076
PO4	31.37756	29.48028	29.95746	28.24583
CL	21.55503	21.49715	21.71196	22.00787
URICAC	-2.07219	-3.45289	-3.40062	-3.82808
CONSTANT	-1448.37415	-1462.26501	-1481.95349	-1544.08777

III. CLASSIFICATION MATRIX

		PREDICTED			
ACTUAL	PERCENT CORRECT	NONE	MILD	MODERATE	SEVERE
NONE	85%	23	3	1	0
MILD	68%	4	13	2	0
MODERATE	39%	1	7	5	0
SEVERE	60%	0	1	1	3
TOTAL	69%	28	24	9	3

IV. JACKKNIFE CROSS-VALIDATION MATRIX

		PREDICTED			
ACTUAL	PERCENT CORRECT	NONE	MILD	MODERATE	SEVERE
NONE	81%	22	3	2	0
MILD	58%	5	11	3	0
MODERATE	23%	2	8	3	0
SEVERE	40%	0	2	1	2
TOTAL	59%	29	24	9	2

V. SUBSAMPLE CROSS VALIDATION ON 24 CASES NOT USED IN CALCULATION OF THE CLASSIFICATION FUNCTION

		PREDICTED			
ACTUAL	PERCENT CORRECT	NONE	MILD	MODERATE	SEVERE
NONE	100%	10	0	0	0
MILD	57%	2	4	0	1
MODERATE	20%	0	4	1	0
SEVERE	50%	0	1	0	1
TOTAL	67%	12	9	1	2

TABLE 5

PREDICTION OF SPACE SICKNESS SEVERITY USING NINE VARIABLES RELATED TO FLUID, ELECTROLYTE, AND CARDIOVASCULAR STATUS SHOWN IN FIGURE 1, WITH WETF TRAINING TIME ADDED

I. MEANS AND STANDARD DEVIATIONS OF VARIABLES USED

GROUP =	NONE	MILD	MODERATE	SEVERE
VARIABLE				
BV	5191	5449	5223	5770
ml	509	524	620	242
MINT	59.8	63.0	67.5	65.9
deg. F	12.6	11.3	6.0	8.4
THT4*	7.20	7.73	8.16	8.20
µg/dL	1.25	1.43	1.38	.71
RBC	4.72	4.91	4.85	5.09
10^{12}/L	.36	.44	.39	.44
SITSYS	118	122	117	130
mmHg	8	10	10	12
UROS	536	706	692	574
mOsm/kg	241	234	218	215
PO4	3.29	3.05	3.15	2.72
mg/dL	.52	.49	.47	.44
CL*	105	104	106	107
mEq/L	2	3	3	1
URICAC	5.97	5.06	4.86	5.32
mg/dL	1.53	1.02	1.35	.80
WETF	27.67	55.10	11.77	10.00
hrs	26.41	42.16	19.32	22.36
n	27	19	13	5

* THT4 and CL were provided as input but not chosen by the discriminant analysis program

II. CLASSIFICATION FUNCTIONS

GROUP =	NONE	MILD	MODERATE	SEVERE
VARIABLE				
BV	0.01556	1.11410	1.15981	1.16245
MINT	1.01556	1.11410	1.15981	1.16245
RBC	33.38202	36.10495	37.26220	37.48561
SITSYS	1.32721	1.39953	1.30835	1.48284
UROS	-0.00915	-0.00660	-0.00547	-0.01019
PO4	8.93290	7.10558	7.34489	5.32631
URICAC	-4.14167	-5.60553	-5.44387	-5.91047
WETF	0.08596	0.11994	0.07066	0.07598
CONSTANT	-222.64264	-246.32925	-237.16216	-265.42923

III. CLASSIFICATION MATRIX

		PREDICTED			
ACTUAL	PERCENT CORRECT	NONE	MILD	MODERATE	SEVERE
NONE	89%	24	2	1	0
MILD	63%	5	12	2	0
MODERATE	77%	1	2	10	0
SEVERE	60%	0	1	1	3
TOTAL	77%	30	17	14	3

IV. JACKKNIFE CROSS-VALIDATION MATRIX

		PREDICTED			
ACTUAL	PERCENT CORRECT	NONE	MILD	MODERATE	SEVERE
NONE	81%	22	2	3	0
MILD	58%	5	11	2	1
MODERATE	54%	3	3	7	0
SEVERE	40%	0	1	2	2
TOTAL	66%	30	17	14	3

V. SUBSAMPLE CROSS VALIDATION ON 24 CASES NOT USED IN CALCULATION OF THE CLASSIFICATION FUNCTION

		PREDICTED			
ACTUAL	PERCENT CORRECT	NONE	MILD	MODERATE	SEVERE
NONE	100%	10	0	0	0
MILD	57%	2	4	0	1
MODERATE	40%	0	2	2	1
SEVERE	50%	0	1	0	1
TOTAL	71%	12	7	2	3

DISCUSSION

The validity of any prediction is limited by the reliability of the predictors and of the criterion variable, in this case space sickness score (Calkins et al., 1987). The possibility of errors in the predictor variables and the criterion should be recognized. Space sickness scores were evaluated by various flight surgeons over five years, based on medical debriefs from 64 individuals with varying subjective symptoms, many of whom were medicated in attempts to reduce the severity of their space sickness. It is possible that anti-motion sickness medication (primarily scopolamine-dextroamphetamine) may have reduced symptom severity in enough astronauts to bias the space sickness scores. However, because space sickness usually recurs in the same astronauts in subsequent flights (although there is a tendency for symptoms to lessen on a second flight), it is generally believed that space sickness scores are sufficiently reliable to be predictable (Calkins et al., 1987).

The reliability of the predictors probably varies from one to the next. Because the clinical variables were measured at different times before flight, few of them probably exactly matched the astronauts' physiologic status on launch day, with the possible exception of height, which was measured to the nearest inch, or half-inch in a few cases. Preflight blood volumes were only calculated, not measured. The free air temperature at the launch site is only a rough approximation of the actual environmental temperatures to which astronauts may have been exposed. Considering the potential sources of error in the data, it should not be surprising that even the best correlations of the predictor variables with space sickness are as low as they are. Conversely, detecting statistically significant relationships in the midst of noisy data implies the presence of fairly strong relationships.

Previous analyses (Simanonok et al., in review), if they hold up on further cross-validation, achieved NASA's technical goal of the development of a risk profile for predicting space sickness incidence with 80% confidence (Lackner, 1982). That rate of success in predicting space sickness severity, however, may await an understanding of the underlying mechanisms causing space sickness and improvements in the reliability of predictor and criterion scores, as has been proposed (Calkins et al., 1987).

Because the nine fluid shift variables describe aspects of preflight fluid, electrolyte, and cardiovascular status, applying them to predict space sickness with levels of success substantially better than chance is supportive of a fluid shift role in space sickness etiology. We cannot conclude if these predictor variables are markers for other factors or are somehow themselves determinants of space sickness, but some of them seem to present clearer relationships than others to a potential role of fluid shifts in space sickness, relationships which can be integrated into a mechanistic hypothesis for a fluid shift etiology of space sickness developed previously (Simanonok et al., in review). To summarize, the magnitude of an individual's response to fluid shifts probably depends on the magnitude of the fluid shift itself and on the individual's heart size relative to their blood volume. People with elevated blood volumes may suffer a greater central volume expansion in weightlessness, and vice versa. One response to central volume expansion on earth and in space is the release of atrial natriuretic peptides (ANP) from the heart (Epstein et al., 1987; Gharib et al., 1986; Leach et al., 1988). Mountain sickness may in some respects resemble space sickness because it is associated with central volume expansion and elevated plasma ANP (Bärtsch et al, 1991). And infusion of ANP at high doses into human subjects can cause nausea without any provocative motion stimulus at all (Weidmann et al., 1986). Therefore it is plausible that space sickness could result in part from a lowering of the threshold for nausea induction by ANP released in weightlessness in a dose-dependent fashion relative to individual responses to fluid shifts.

It is consistent with this fluid shift hypothesis of space sickness etiology that factors which modify the blood volume upward or downward might affect the volume of the fluid shift in weightlessness and subsequent physiologic responses. A variety of factors may modify the blood volume, some of which emerged previously among the nine predictor variables for space sickness (Simanonok et al, in review). In water immersion studies and head-down tilt as well as in weightlessness there is observed a contraction of the blood volume. It may be that with intermittent exposure to head-down tilt in WETF training, astronaut's blood volumes are reduced somewhat so that their subsequent fluid shifts in weightlessness are lessened in magnitude, hence their physiologic responses to fluid shifts are damped. WETF training may therefore be effective in ameliorating space sickness severity by partially preadapting the circulation to fluid shifts through a reduction of blood volume.

Alternatively or in addition, WETF training may be protective against space sickness because of the visual adaptation that it might provide. In WETF training, astronauts can assume almost any orientation with the spacecraft mockups. This could help to accustom them to the visual orientations of the spacecraft that they experience in space, thereby reducing their sensitivity to the "sensory conflict" that presently forms the dominant paradigm of space sickness etiology (Crampton, 1990).

The present data cannot be used to conclusively determine which of these two potential mechanisms of WETF training, preadaptation of the blood volume to fluid shifts or visual adaptation to weightless surroundings, plays the single or dominant role in ameliorating space sickness severity. However, the fact that the WETF trained group of astronauts had significantly lower serum chlorides and plasma osmolalities, and higher urine specific gravities and forced vital capacity indexes is consistent with probable effects of WETF training on fluid balance. There was also a low but significant inverse correlation between WETF training time and serum chloride concentration (Table 2). Lower serum chlorides and plasma osmolalities in WETF trained astronauts could indicate a state of partial recovery from fluid shifts, in which fluid and electrolyte losses caused by fluid shifts in WETF training were partially restored by drinking but electrolyte restoration lagged. Higher urine specific gravities in WETF trained astronauts would suggest renal states of fluid retention, increased electrolyte excretion, or thirst inhibition, any of

which might result from fluid shifts in WETF training depending on the timing of the training and the sampling. Forced vital capacity is greater in human subjects when standing compared to supine (Dikshit and Patrick, 1986) and after bed rest of 11 or 12 days (Beckett et al., 1986). This suggests that a decreased central blood volume allows greater lung capacities due to postural fluid shifts, after adaptation to fluid shifts in bedrest, and after adaptation to fluid shifts in WETF trained individuals.

Although mechanisms remain speculative, the data suggest that WETF training may be a partially effective method to reduce the severity of space sickness for astronauts. If WETF training is effective in ameliorating space sickness through visual adaptation, its role could be expanded so that all astronauts, or perhaps those who are predicted most likely to become space sick, get WETF training. If WETF training is shown to be beneficial as a countermeasure to space sickness by reducing the preflight blood volume and thereby diminishing the physiologic effects of fluid shifts in weightlessness, other more direct interventions to preadapt the circulation to fluid shifts may be even more effective.

ACKNOWLEDGEMENTS

The authors gratefully acknowledge Marion Li and Betty Guidry for their help in assembling the data used in this analysis, Marcie Stricklin and Dick Calkins for statistical consultations, Gene Hafele for providing meteorological data at the Kennedy Space Center for each Shuttle flight, and Dr. Sam Pool for his help in initiating the original study and providing computer support.

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