bio-dynamics incorporated

human factors | physiological monitoring | bionics

one main street, cambridge, massachusetts
An Evaluation of the Role of Training in the Suppression of the Motion Sickness Syndrome

A Review of Research and Anecdotal Sources

prepared for

Aerospace Medicine Directorate
Office of Manned Space Flight
National Aeronautics and Space Administration

under Contract No. NASw-553

11 January 1963

Bio-Dynamics, Inc.
One Main Street
Cambridge, Massachusetts
Forward

This Report presents a summary and analysis of what is known about the effectiveness of training in suppression of motion sickness. The material was gathered and studied during a ten week period, by a staff of engineers and psychologists under the direction of Arthur Taub, M.D., Senior Medical Scientist of Bio-Dynamics, Inc. and Stanley Molner, Manager of Biomedical Engineering. The staff's effort was greatly assisted by Edward McLaughlin, Ph.D. of the Aerospace Medicine Directorate.

Information and guidance contributed by the following persons, and in many cases, by their associates, constituted an invaluable resource.

Tenley Albright, M.D.  Boston, Mass.
Charles A. Berry, M.D.  Manned Spacecraft Center - NASA
Richard Button  New York City
Ashton Graybiel, Capt. USN, M. C.  US Naval School of Aviation Medicine
Ross A. McFarland, Ph.D.  Harvard School of Public Health
E. A. Spiegel, M.D.  Temple University
Jack Steele, Maj. USAF, M. C.  6570th Aerospace Medical Research Laboratory
Stanley C. White, M.D.  Manned Spacecraft Center - NASA
Summary

The literature relating to vestibular physiology and motion sickness has been reviewed to determine what is known about suppression of the motion sickness syndrome by means of training. Experimental studies of habituation to motion and the experience of figure skaters, acrobats, pilots and others confirm what is suggested by the structure and organization of the vestibular system: that most persons can learn to resist motion sickness. Individual differences in ability to acquire such habits are great, however, and there is as yet not sufficient information concerning the etiology of the syndrome and the mechanisms of its suppression to permit specification of a training regimen for an individual.

While manned space flight experience to date has been that "space sickness" of vestibular origin is not a threat to mission success, the prolonged flights of future programs, the selection of non-pilots as Astronaut candidates, and the employment of rotating space vehicles may present the need for development of vestibular training procedures. In view of the apparent specificity of habituation, such training procedures must expose the trainee to motion within an environment closely simulating the situation in which the disturbances for which he is being trained will occur. The reversibility of
habituation adds the requirement that vestibular training be continued through all stages of preparation for flight, and possibly in flight as well.

Use of interoceptive conditioning techniques -- making the trainee aware of the earliest signs of motion sickness, thereby, perhaps, facilitating and generalizing his control of suppression mechanisms -- may be an efficient training method.

It is recommended that this and other approaches to training be pursued experimentally to evaluate their respective merits, and to compare the effectiveness (including side effects) of training with the protection afforded by drugs.
Contents

Forward

Summary

Part I

A. Introduction

B. Physiological and Anatomical Considerations of the Vestibular System

1. Structure and Organization of the System
2. Vestibular Stimulation
3. Effects of Stimulation
   a. Tests of Vestibular Function
   b. Autonomic Effects
4. Summary

C. The Motion Sickness Syndrome

1. The Syndrome
2. The Situations
3. The Motions
4. Facilitating and Inhibiting Factors
5. Susceptibility
   a. Incidence
   b. Correlates and Tests
   c. A Biochemical Hypothesis
6. Etiology
7. Theoretical Considerations
D. Space Sickness with Respect to the Vestibular System

1. Speculations
2. Space Flight Experience
   a. Disorientation
   b. Changes in the Vestibular System
   c. Effect upon Threshold

E. Measures used to Control Motion Sickness

1. Pharmacological
2. Training
   a. Habituation in Figure Skaters and Others
   b. The Effect of Flying Experience
   c. Preparation of the Astronauts
   d. Exercises for Vestibular Training

F. Habituation and Conditioning

G. Conditioning Resistance to Motion Sickness

1. Psychogenic Factors
   a. Emotional Stress
   b. Neurosis
   c. Suggestion, Conditioning and Motivation

2. Neurological and Psychological Factors
   a. Effect of Unstructured Training and Practice
   b. Conditioning
   c. Interoceptive Conditioning
   d. Other Psychological Factors
3. A Model of Training

4. A Method of Training
   a. Prerequisites for a Training Protocol
   b. The Training Situation
   c. Potential Side Effects of Training

H. Conclusions

I. Recommendations

Part II

A. Introduction

B. Physiology of the Vestibular System

C. Vestibular Disturbances in the Space Environment

D. Mechanical Aspects of the Vestibular Apparatus

Bibliography
Illustrations

Part I

Figure 1. Training Model Diagrams (1, 2, 3)
Figure 2. Training Model Diagrams (4, 5, 6)

Part II

Figure 3. Sensory Epithelium of Crista Ampullaris
Figure 4. Innervation of the Crista Ampullaris
Figure 5. Afferent and Efferent Fibres of the Vestibular Nuclei
A. Introduction

Experience in manned space flight has demonstrated that "space sickness" arising from vestibular disturbances is of no practical consequence to experienced pilots operating non-rotating vehicles on missions of four days or less. Whether a syndrome akin to motion sickness will occur in the longer flights of the 1965-1970 Gemini and Apollo missions, and its successor programs cannot be predicted with any assurance at the present time. Should evidence of the syndrome be observed in early extended flights, however, questions of major importance to the future manned space flight program will have to be answered. One question will be: Can a pre-flight and on-board training program adequately prepare crew personnel to suppress the syndrome?

This study was undertaken to determine how well that question can be answered today.

There is little rigorously derived information available concerning the effectiveness of training in suppressing motion sickness symptoms.
Investigations have generally been concerned with problems of motion sickness incidence, effects of this disturbance upon behavior, and the effectiveness of drugs in preventing or suppressing these effects. We do not know of any United States experimenter who has studied motion sickness itself specifically as a training problem; despite the numerous investigations of the phenomena of "natural" adaptation* to various motions, only a few Russian workers have sought to determine the relative effectiveness of alternative training procedures in increasing individuals' resistance to the undesirable effects of motion. Anecdotal material is only suggestive of the capabilities and limitations of training.

This review, therefore, began with a re-examination of the basic anatomy and physiology of the systems involved in order to establish the neurophysiological bases of training. Survey and analysis of conditioning theory and anecdotal evidence lead to the

*The several disciplines from which material was drawn for this review assign respectively specific, but collectively confusing definitions to the terms, "adaptation", "habituation", "acclimitization", "learning", "transfer", etc. In the following text these terms are used interchangeably.
outline of a training regimen. Part I of this report presents the major results of the review. Part II contains a discussion of some of the more intimate details of the systems involved - details which may not be immediately relevant to the question of whether an individual can be trained, but which contribute to an understanding of the motion sickness syndrome.
B. Physiological and Anatomical Considerations of the Vestibular System

Essential to the consideration of the efficacy of training in the suppression of undesirable symptoms and signs generated by the vestibular system is an understanding of the information it is capable of transmitting to the central nervous system - whether 'reaching consciousness' or not - the method of central nervous computation and comparison with data of other sensory systems, ways in which the vestibular system may control itself, and how it may be affected by environmental variations, whether internal or external. In addition, it is desirable to review the detailed structure of the vestibular system taken as a whole to determine the most likely places where training may be expected to intervene in the operation of the system. An overview and discussion of some points essential to the considerations of training is presented in summary form in this section, and treated in somewhat more detail in Part II.

1. Structure and Organization of the System

The membranous labyrinth is encased in the bony labyrinth, and is surrounded by perilymph. Within it is the endolymph, whose
composition differs markedly from cerebrospinal fluid. The **semicircular canals** of the labyrinth lie in three planes that are at approximately right angles to each other. The horizontal or external canals lie in a plane at an inclination of $30^\circ$ to the frontal plane of the body, and the vertical canals on each side make an angle of about $45^\circ$ with the sagittal plane. The plane of each of the anterior canals is parallel to that of the posterior or inferior vertical canal of the opposite side. At one end of each canal, near its junction with the utricle, is the **ampulla**, in which is contained the **crista ampullaris** supplied with hair cells projecting into a gelatinous mass termed the **cupula**. In some forms the cupula closes the opening of the semicircular canal, but in others does not, permitting fluid flow. The **utricle** and **saccule** are in communication with the fluid in the semicircular canals and with that in the **cochlea** (via the **ductus reuniens**). The maculae of the utricle and of the saccule are oriented in an approximate horizontal and vertical position respectively, and otoliths - concretions of calcium carbonate, lie above them.
Present concepts of vestibular physiology consider the total system to be organized into right and left halves with separate but complementary functions. For each of these halves is provided a set of peripheral sense organs, a group of nuclei in the brain stem, and certain higher centers. Three principles are useful in "explaining" vestibular function.

1. At rest the entire vestibular system is considered to be in a state of tonic activity.

2. If the tonic activity of one portion of the vestibular system be reduced, that of the other half is predominant, producing symptoms and signs, for example, nystagmus.

3. Coding of the vestibular signal is based upon the increase and decrease in frequency of a resting neuronal discharge. Modifying factors are introduced with varying internal and external environmental situations.

The vestibular division of the eighth cranial nerve, innervating the vestibular receptive epithelia, has six main branches of origin, one each from the posterior, superior, and lateral ampullae, and the utricle, and two from the saccule; the horizontal, and anterior ampullae, the utricle and the vertical portion of the saccular macula receiving fibers
from the proximal eighth root, and the horizontal portion of the
saccular macula receiving fibers from the distal eighth root. Primary
cell bodies of these fibers are found in Scarpa's ganglion. It is claimed
that secondary nerve cell bodies are also to be found in the vestibular
root, as in the auditory. (SS) Recent investigations have also shown the
presence of efferent fibers in the vestibular nerve, and while their
loci of origin has been defined to some extent, their function is as yet
unclear. (SG)

2. Vestibular Stimulation

The cristae ampullares of the semicircular canals are thought to
respond primarily to angular acceleration, and to some extent to linear
acceleration. The cupula behaves as a spring-loaded overcritically
damped torsion pendulum. Cupular movement results from pressure
changes equivalent to 0.05 mm. of water. Although fluid may flow
through the utricle, the other semicircular canals form a shunt with
a relatively high resistance to flow so that fluid displacement is es-
sentially in the plane of the canal stimulation, if appropriate orientation
is maintained. Movements of the endolymph stop in about 3 seconds,
but the cupula requires a longer period to return to the resting position. (IO)
Dynamic analyses of the response of the semicircular canals have not yet provided a description of the behavior of these angular accelerometers under complex motion stimulation. (13c)

It is probably safe to conclude that the present consensus concerning the utricle is that it is the chief organ responding to linear accelerations. The function of the saccule is obscure despite its heavy innervation. It can be destroyed bilaterally without disturbing vestibular reflexes. It is claimed that vibrational stimuli are effective in stimulation of the saccule, fibers conducting impulses in response to vibrational stimuli being derived from the anterior 2/3 of the saccular macula. (158)

The lagena, and the macula neglecta, two structures also present in the labyrinth, in some forms, have not as yet revealed their respective functions.

While the non-acoustic labyrinth responds primarily to acceleration stimuli, acoustic, caloric and electrical stimulation can produce responses. It is open to question, of course, whether such caloric and electrical stimulation is actually administered to the labyrinth alone.
3. **Effects of Stimulation**

a. Tests of Vestibular Function

1) Semicircular Canals

In the standard Barany test of vestibular function, the patient normally orients his head so that the horizontal canals are in the plane of rotation. The direction of rotation as well as the head orientation determines the direction of the post-rotational nystagmus. When he leaves the chair the normal subject tends to fall and "past-point" in a direction opposite to the fast component of the nystagmus. The blindfolded subject experiences the illusion of rotation in the direction of the post-rotational nystagmus.

In recent years a refinement of rotational testing termed cupulometry has been used in experimental investigation and testing of semicircular canal functions. The plot of duration of post-rotational effect (either sensation or nystagmus) versus velocity of rotation usually yields a linear semi-log plot which appears to reflect, "the constants, not only of the cupulo-endolymph system, but of the entire vestibular nervous system". The use of cupulometry in investigating functional difference between flyers and non-flyers, and persons susceptible to motion sickness and those who are not will be discussed subsequently.
The occulogyral illusion has been used to examine vestibular function. Rotary acceleration in a darkened environment produces the illusion of movement of a spot of light which is actually fixed relative to the individual. (12) A technique has been devised to permit a complete analysis of the response to a single stimulus to minimize the effects of habituation. (32) Although the occulogyral illusion can be present without visible nystagmus, results of the illusion test conform to the torsion-pendulum model of response which nystagmus and sensation data yield. (43)

As stated earlier, the vestibular system responds to thermal stimulation; the caloric test of function is widely used. Upon irrigation of the external auditory meatus with cold water, (30°C) the head vertical, the slow phase of nystagmus, conjugate deviation of the eyes, past pointing, and falling tendency is toward the side of stimulation, and the rapid phase of nystagmus is directed to the opposite site, the reactions reversing when hot water (44°C) is used. (150) Cawthorne et al state that the caloric tests as done by their procedure "are remarkably stable, and are not altered by habituation, (during the tests) as may occur... in the case of the rotational tests." (32)
2) Otoliths

Functional defects of the otolith organs can be demonstrated on the tipping table or horizontal swing only when marked bilateral lesions have occurred. (1) The occulogravic illusion provides an indication of otolith function in normal individuals. The illusion is an apparent movement or displacement of a visual stimulus, originating from the resultant of an applied acceleration and the gravity field. During forward acceleration in flying, there is an objective illusion that a target is displaced upward, and during deceleration downward. The illusion may be subjective as well. Although Quex indicated the presence of a otolithic system "blind spot" the illusion is perceived in any position of the head, even inverted. (17, 46)

b. Autonomic Effects

1) A prominent symptom of stimulation of the entire body in moving vehicles is drowsiness. Some slowing of the electroencephalogram occurs during exposure to movement. No distinct electroencephalographic abnormalities could be detected in personnel subject to motion sickness. (83, 101)

2) Peripheral vasodilatation, accompanied by a feeling of warmth, and dependent upon splanchnic dilatation, occurs as a result of rotation. (149)
3) Some controversy exists concerning the direction of blood pressure changes in human subjects exposed to rotation, but there is unequivocal evidence that decerebrate animals respond to rotation by hypotension. In human subjects, a brief rise in blood pressure, attributed to proprioceptive influx, may precede the usually obtained hypotension. No electrocardiographic abnormalities beyond slight bradycardia have been observed.

4) Regionally decreased cerebral blood flow has been observed in experimental animals as a response to rotation. This effect depends upon the integrity of the medial vestibular nucleus, and not on the vagi or cervical sympathetic innervation. It appears thus to be passive, not changing with section of vasoconstrictor or vasodilator fibers to brain.

5) Gastrointestinal effects of vestibular stimulation have also been somewhat controversial. Contemporary descriptions minimize gastric antiperistalsis, and stress gastric relaxation, duodenal antiperistalsis and psylospasm, and abdominal wall contraction, preceding vomiting. Significant displacement of viscera has not been observed.
6) Cold sweating, as distinct from thermoregulatory sweating, occurs, but careful experimental studies of quantity and time relationships to stimulation are not available. Facial pallor (peripheral vasoconstriction) and "change of color" often described have also not been quantitatively studied, as far as our literature survey has revealed.

7) Respiratory changes of several varieties involving rate and depth of breathing, and brief respiratory arrests have been observed during violent pitching movements.

8) In this respect, all "vomiting" must not be considered related to vestibular stimulation, despite being associated with motion. Marked changes in direction of G-force can expel vomitus. (113)

9) Miosis of pupils, followed by mydriasis and hippus, has been observed during rotation, and the retinal vasculature has blanched. Measurements of ophthalmic arterial pressure as a response to vestibular stimulation have been helpful in validation of cupulometric procedures and show some evidence of "habituation" in a small series. (149)

10) Salivation has been shown to occur to caloric stimulation, perhaps as a result of stimulation of the chorda tympani. (43)
11) Oliguria may follow dehydration of vomiting, or may be associated with release of antidiuretic factors.

12) The major catastrophic event in susceptible individuals following vestibular stimulation is vomiting. \( \textbf{(22, 35)} \) Present theory describes two half-centers as responsible. The first, the chemoreceptive trigger zone (area postrema), is essential for drug induced vomiting, whether directly applied or intravenously injected. Drugs producing emesis do not act uniformly on the chemoreceptive trigger zone, digitoxin, for example not provoking emesis when applied to the surface of the brain stem, while apomorphine characteristically produces a brisk emesis under the same conditions. Both compounds are active when intravenously administered.

The second half-center, the emetic center (located in lateral medullary reticular formation) is essential for the production of vomiting, and, if present, will allow vomiting to occur upon gastric stimulation with copper sulfate, in the absence of the chemoreceptive trigger zone. The mechanism of vomiting to vestibular stimulation remains the key problem in the investigation of vestibular symptoms. It has been shown that vomiting in situations of vestibular stimulation designed to produce motion sickness
in animals is prevented with ablation of the chemoreceptive trigger zone, as well as by removal of both nodulus and uvula. (170,101)
Pernicious vomiting has been described as a result of brain tumor and following neurological surgery. Visceral congestion following splanchnic dilatation may be a factor but this has largely been uninvestigated neurophysiologically, and experiments with abdominal binders have been unsuccessful in the prevention of vomiting in the clinical motion sickness situation. (142)

13) Evidence has been presented of changes in cerebrospinal fluid pressure of 70-85 mm. of water in response to linear acceleration. This may produce vomiting by pressure in the fourth ventricle, but further investigation seems warranted.

14) Chemical changes include alkalosis leading to clinical tetany in individuals who hyperventilate in response to a motion stimulus, or alkalosis and ketosis may develop as a response to vomiting. No significant changes in CO₂ content, O₂ content, O₂ capacity, or O₂ saturation of arterial blood were noted, with stimuli sufficiently intense to provoke motion sickness in dogs. A slight decrease in plasma potassium has been described, but no changes of
significance have been noted in acetylcholine or acetylcholinesterase content of the blood in response to stimulation or in susceptible individuals. Measurement of calcium, phosphorus, sodium, potassium, and blood sugar levels before and after motion of 13 subjects revealed only a rise in blood sugar and drop in blood phosphorus independent of vomiting. Cells in the vestibular ganglion and in the lateral vestibular nucleus (Dieter's nucleus) have shown chemical modification as a result of vestibular stimulation.

4. Summary of Physiological and Anatomical Considerations

Translation and rotatory stimuli are separated out by the vestibular apparatus and coded in a complex way. The properties of the transducer probably are subject to variation physiologically via efferents, and anatomically via chemical changes in the nerve cells composing the vestibular pathway. The first cell station in the vestibular pathway, the vestibular nuclei provides for connections with oculomotor centers (interstitial nucleus of Cajal), reticular formation (perihypoglossal nuclei), spinal cord and cortical mechanisms (vestibulospinal tract, medial longitudinal fasciculus), and for complex interactions within the nuclei themselves (internuncials).

The precise mode of production of autonomic responses, the causal sequences of these responses, and facts about them other than the simple ones of their occurrence as a response to vestibular stimulation, and certain broad considerations of the pathways involved in their production, is not known, and thus their relationship to symptoms of motion sickness is somewhat conjectural.
C. The Motion Sickness Syndrome

Exhaustive reviews of the physiological basis for the motion sickness syndrome and therapeutic measures are available. The vast literature will not be reviewed here. Certain pertinent statements can be made, however, concerning the syndrome, its etiology and pathogenesis, which have relevance to the application of training techniques in the control of its symptoms.

1. The Syndrome

As generally thought of "motion sickness" comprises a symptom complex consisting of a variable combination of drowsiness, malaise, illusions of motion, feeling of warmth, peripheral vasoconstriction and facial pallor, nausea, vomiting, occasionally pernicious and sometimes projectile, decrease in proficiency of performance, dehydration, and prostration. Nystagmus is notably absent in sea sickness although fine ocular nystagmoid movements have been reported to occur.

2. The Situations

The situations in which the total syndrome or its parts have been described to occur in a severe fashion are many, including aircraft in evasive maneuvers, crash boats, flight to parachute drop areas, troops
crouching in landing craft, automobiles, elevators, trains, swings, and others. It is notably decreased or absent in modern commercial jet transport aircraft and in submerged atomic submarines at depth. Aspects of the "motion sickness" syndrome without body motion have occurred during observation of the Cinerama illusion, and notably to instructors on a helicopter simulator. (99)

Although it is probably safe to say that anyone can be made to suffer a partial motion sickness syndrome given the proper motion, it has been extremely difficult to determine (1) the precise characteristics of that motion, (2) to describe inhibitory and facilitatory situations for the syndrome, and (3) to advance an explanation for the obvious fact that motion of a particular sort may have a devastating effect on one individual, while leaving another undisturbed. Marked species differences exist, the cat being much less prone to develop motion sickness than the dog, although it vomits quite often as a result of its frequent dietary indiscretions. The rat is another animal somewhat resistant, while the spider monkey provides a good subject for motion sickness studies. (22)

3. The Motions

In so far as the characteristics of the motion have been concerned exhaustive studies have been undertaken to analyze ship motions, swing
motions, elevator motions with varied wave forms, and to
determine which of these was most productive of the "motion
sickness syndrome". These results have been reviewed often and
in extenso, and will not be repeated in this discussion except for
the following points. (1) The motion sickness syndrome is not
produced in general by rotation, at constant velocity, but may be
produced by linear and rotary acceleration, providing the correct
acceleration profile is chosen. (2) The most effective way to produce
the motion sickness syndrome using rotatory stimuli is the pro-
duction of a Coriolis acceleration by head movement, while a
constant velocity rotation is being imparted to the labyrinth, by
voluntary head movements, or forced by a mechanical device
holding the head, or, by movement of the entire enclosure of the
experimental subject. (3) It has been claimed that the pitching
and ascending motions of naval vessels are most effective in the
generation of the syndrome, and that roll and yaw, and horizontal
translation are not, though in fact in operational situations, a combination
of these effects particularly forward motion, roll and scend exist, a
corkscrew motion. (158)
4. Facilitating and Inhibiting Factors

Enclosed spaces, lack of visual fixation points, the erect position, change from driver-pilot to passenger-navigator position, odors, disgusting sights, suggestion and psychoneurosis have been advanced as facilitatory factors, but only the first four appear to have etiological significance. The supine position, visual fixation, the right side of a commercial aircraft (DC-3) (perhaps related to a preference for direction of roll), various revolting and fatty diets, and head fixation, have been suggested as mitigating maneuvers, but only the first two appear to be well established experimentally and clinically. Various medications have been administered for therapy and prevention. These will be discussed in a subsequent section of this report. Neck cuffs, binders of the abdomen, special suits, and the like have not been successful.

5. Susceptibility

a. Incidence

A vast body of hearsay evidence has accumulated concerning susceptibility, its age, sex, and racial incidence. Critical analysis of the data leads one to conclude tentatively that young adults are somewhat
more susceptible than older adults, and to age 40 that women are more susceptible than men. That infants are not susceptible or that any racial differences exist is questionable.

An effort to estimate the proportion of susceptibles in the total population, from the literature, would be useless in view of the variety of stimuli used in determining motion sickness incidence. Some conception of order of magnitude of susceptibility in individuals motivated for military piloting may be gained from reviewing the results of studies made during World War II. (15a) The aviation student received his first flying in the form of 10 hours of dual instruction (pilot and participant passenger duties). During the training the total incidence of motion sickness was 1 in each 40 flights. Eleven percent of the trainees were sick on at least one of their 10 flights. The incidence decreased with increasing number of flights flown, from 5.7% on the first flight to 1.1% on the tenth flight. Among those who were eliminated from the program 19.8% were airsick, while among those who graduated only 10.8% were airsick. Questionnaires of combat veterans revealed a total incidence of 5.4% in combat, with an incidence of 25.7% in training. Although the groups investigated were not comparable, it may be safe to assume as an order of magnitude individuals of about 5% in severe conditions, with an irreducible minimum of 1% for mild airflight maneuvers.
Knowledge of motion sickness at the present time makes it impossible to generalize with regard to incidence from one operational situation to another. There is evidence that experience in a piloting position, that jet pilot experience does not prevent seasickness, and that "physical" training although reported to produce a "low incidence of seasickness and airsickness" does not prevent seasickness. Our investigations of ice skaters reported elsewhere in this report indicate no protective effect (with regard to "dizziness") of rotation about one axis as compared with rotation about a different and unpracticed axis.

b. Correlates and Tests

An extensive literature has accumulated concerning predictive correlates of susceptibility to motion sickness. Few have been found to date - a history of previous motion sickness elicited by questionnaire being the best. Attempts have been made to study electroencephalographic changes, type of stomach, blood chemical composition, (including acetylcholine and acetylcholinesterase) galvanic skin response, abnormal response to parasympathetic or sympathetic stimulation, neurosis (as tested with the Minnesota Multiphasis Personality Inventory and other tests), cold pressor test, breath holding capacity with positive and negative
pressure, dermatographia, tilt table test, respiratory pattern, blood pressure, pulse rate, skin temperature, forehead sweating, salivation, and the like. The Barany chair test was early disregarded. (\textsuperscript{10}) Some evidence has accumulated in favor of a refined caloric test.

Ability to carry out an assigned task involving head movements in the slow rotation room at Pensacola is correlated with a tendency to resist the development of motion sickness induced by crash boat. (\textsuperscript{10}) It had previously been suggested by Spiegel, that his rotating chair with forced head movements could be used predictively. This appear to have been borne out by the work of Graybiel and his collaborators with the slow rotation room. (\textsuperscript{15}) Cupulogram techniques (nystagmus, sensation, oculogyral illusion) appear to be predictive in that chronically seasick individuals have steeper cupulograms than normals. (\textsuperscript{43, 81}) There was some evidence advanced in a small group that vasolability as measured by oscillation of central retinal arterial pressure as measured by ophthalmdynanamometry was predictive and correlated well with the cupulogram in chronically seasick patients. This remains to be confirmed in a larger series.
c. A Biochemical Hypothesis

There has been no convincing evidence to date of a biochemical basis for susceptibility to motion. This in itself should not discourage attempts to develop a test which would be useful as an additional screening procedure, and which may shed some light on the action of motion sickness preventatives. Recent research in pharamcogenetics has indicated that certain biochemical defects depend upon the presence of a homozygous state for a recessive gene. The pseudocholinesterase system is a case in point. Patients deficient in this esterase develop prolonged apnea when treated with succinylcholine, a muscle relaxant, during surgery. This evidence suggests that a search for an enzymatic deficiency may be rewarding in a situation in which a small segment of the population demonstrates an idiosyncrasy to a particular drug or situation.

The fact that great interspecies differences exist in the metabolism of the belladonna alkaloids, that these are among the most effective remedies for motion sickness, and that destruction of the chemorector trigger zone of the area postrema prevents motion sickness, all serve to suggest the presence of a higher concentration of an atropinesterase-like or a decreased concentration of an acetylcholinesterase-like derivative in some restricted region of the nervous systems of the susceptible. Comparative histochemical study of the area postrema in different species and analysis of individual differences in the blood enzymes of intact subjects are logical pathways for future research.
In summary then, although some useful techniques appear to be developing for selection of non-susceptibles, emphasis must be placed not only upon some hypothetical immunity but upon testing of the capacity to adapt to motion, which holds hope of being more successful in prediction both of the value of training, and the ability to recover from motion sickness during operation. In this respect cupulometry shows good possibilities. Attempts to derive other predictive parameters from models of the semi-circular canal cupula system should be pursued but not much can be said about them at the present time.

6. **Etiology**

It is fairly clear from our considerations of the circumstances attending motion sickness, and its wide range of incidence and susceptibility, that the establishment of a unitary cause is far from being achieved. Unquestionably the labyrinths are critically involved, as labyrinthectomy in experimental animals and man produces immunity operationally and experimentally. (92, 93) That the mechanism for the syndrome exists in experimental animals in the decerebrate case, testifies to the possibility of inducing it in situations which seem devoid of consciousness, which would tend to militate against the concept that "psychodynamic" factors are anything but ancillary.
The fact that the syndrome in experimental animals can be blocked with ablation of the nodulus plus uvula or the chemoreceptor trigger zone, when vomiting to gastric copper sulfate is still possible via the vomiting center, indicates an indispensible function of the vestibular portion of the cerebellum most likely for the activation of neural or hormonal mechanisms in the chemoreceptor trigger zone. The slow time scale of development of the syndrome suggests not so much neural temporal summation of a central excitatory state as increase of a slowly produced hormonal concentration.

The absence of nystagmus in sea sickness suggests to some a non-participation of the semicircular canals in the syndrome, as does the evidence that motion sickness is best produced by scend, pitch, and linear and coriolis acceleration. (35,154) Evidence for the function of the utricle in the syndrome is provided by the salutary effect of the recumbent posture, which, although probably not placing the otolithic system in its "blind spot" nonetheless, probably alters the complex vestibular neural signal. However, the production of nystagmus is a total effort of the labyrinth, the vestibular nuclei, reticular formation, mesencephalic occulomotor nuclei, cerebral cortical centers and others. (150). It should not be taken for granted that the semicircular
canals have been not stimulated simply because no nystagmus is observed. Small movements of the cupula may still be enough to cause motion sickness, even when the levels of rotation are insufficient to elicit an experience of rotation. Violent pitching has been estimated to produce angular velocities of $2^\circ/\text{sec}^2$, which may be below the level of awareness for the semicircular canals. But evidence from cupulometry indicates a semicircular canal involvement in the syndrome.

Controversy exists over the effect of blindfolding, experimental animals showing later development of motion sickness, and operational and human subject experience tending to indicate that enclosed spaces, crouching in gunwales, and blindfolding, provoke motion sickness most readily. The significance of the "walk upon the deck for fresh air" is obscure, except insofar as vomiting does appear to relieve nausea temporarily under certain circumstances.

That specific motions of the eyes in a nystagmoid fashion may provoke motion sickness, while relative fixation may mitigate it is suggested by the experience of automobile drivers or pilots of aircraft who are relatively less susceptible to motion sickness while driving or piloting
than while acting as passengers. (149) This conforms with the experience concerning visual fixation as one of the best physical maneuvers for the prevention of incipient motion sickness in the experience of the Pensacola investigators. (75)

That mental effort or concentration is in fact provocative of motion sickness under certain circumstances is indicated by the experience of navigators and navigator trainees, among whom the incidence of motion sickness is significantly greater than it is among pilots in the identical aircraft. The development of nausea and vomiting while observing the Cinerama illusion or while participating in a simulated helicopter flight, though not moving, and the experiments of Crampton, Witkin and others, suggest that visual factors themselves can be effective in generating the syndrome. In fact, it is quite probable that the visual factors that are involved are related to forced eye movements. (149)

Little evidence is available concerning the effect of altering proprioceptive input upon the incidence of motion sickness, although Sjoberg claimed to have decreased the incidence of swing sickness among dogs placed in a plaster body cast as compared with controls. Certainly evidence for proprioceptive convergence upon the cerebellar nuclei via the spino-vestibular tracts is present and it would seem reasonable that alterations in limb weight in the weightless state would change the proprioceptive input
to the vestibular nuclei either directly or via the cerebellum. The nature of this input is obscure, however, and in this regard no definitive statement can be made.

In summary then, it appears that particular patterns of linear and Coriolis acceleration experimentally, and a wide variety of motions clinically, excite the vestibular apparatus, to interact in an as yet unknown fashion with autonomic release mechanisms to produce the motion sickness syndrome. Visual factors, most likely eye movements, summate with the vestibular system effects, and sufficiently potent, produce autonomic release probably by a somewhat different mechanism not involving the vestibular nuclei. Other factors are not of significant importance.

The detailed genesis of the motion sickness syndrome may be interpreted in terms of the autonomical effects described earlier for vestibular stimulation. Malaise, drowsiness, and cold sweating may be related to splanchnic engorgement, hypotension, and decreased cerebral blood flow. Nausea may be related to visceral engorgement, but is most likely central in origin, as is retching, and is related in some obscure fashion to the function of the vomiting center-chemoreceptor trigger zone mechanism. It is essential to determine the precise sequence of the development of symptoms and signs in the motion sickness syndrome, and to establish causal sequences if any. This has not been done. Nor
have studies been undertaken in recent years to determine with modern instrumentation methods the configuration of stimuli required to elicit, not only nystagmus and illusory phenomena, but autonomic signs as well. This may prove to be of significant importance as the discussion of autonomic conditioning and training will emphasize.

7. **Theoretical Consideration of the Motion Sickness Syndrome**

Implicit in the discussion in this report is the concept that "motion sickness" as ordinarily experienced is the result of stimulation of a particular set or sets of vestibular receptors, and data processing nuclei whose sensitivity varies genetically and as a result of previous experience, in such fashion as to activate built-in autonomic connections. Essential nervous system activity associated with the development of these autonomic effects is located in brain stem centers, and is only slightly modulated by other central nervous system factors. Concomitant with but not essential to the development of the autonomic discharge is the appearance of sensory illusions relating to spatial orientation. While other factors in moving vehicles or in a stationary environment may produce autonomic release when suitably arranged, it is likely that the mechanisms responsible for such release differ in detail from the mechanisms responsible for autonomic release as a result of vestibular system stimulation. Thus procedures necessary for counteracting such release are highly variable.
In fact, as we have seen, various modes of stimulation of the vestibular system have little predictive value with respect to reaction to other modes of stimulation (and various therapeutic procedures directed to one disorder of the same level of the vestibular system have little relevance to another disorder at that same level). Agents suppressing vomiting on one basis often have little effect in suppressing it on another basis.

Attempts have been made to include motion sickness as a member of a larger class of disorders relating either to sensory confusion and disorientation or to the effort involved in conflict resolution in the sphere of spatial orientation. The approach which maintains the generation of motion sickness symptoms to be a result of conflict between vestibular, visual, and proprioceptive information, and explains the effects of labyrinthectomy as being related to the removal of one input channel, cannot explain the facilitating effect of blindfolding upon motion sickness, the ineffectiveness of decerebration, and the production of motion sickness when sensory information is apparently quite congruent. Certainly sensory conflict leads to momentary confusion and difficulty in operation of complex systems (as in "blind flying") but whether this confusion is in fact maintained for the long periods customarily necessary for the development of motion sickness is problematical.
Recently, a new approach demonstrates the inadequacies of theories of motion sickness which attach too much importance to particular properties of the environment and the sensory modalities monitoring it or to conflicts, inaccuracies, or ambiguities per se in the perception of this environment. It emphasizes, rather, an information-theoretical view and indicts the central nervous system's continual effort to achieve a rapport between all interpretations of the various sensory inputs. The term "vigilance" has been applied to this effort but the choice of term is perhaps unfortunate because an anthropomorphic image of the external aspects of vigilance is called to mind. The meaning of vigilance is apparently intended as one of computation rather than of data collection.

The central nervous system is envisioned as being totally isolated from the environment and relying entirely upon the information fed into it by the senses: visual, kinesthetic, vestibular, interoceptive, etc. In its attempts to establish an inertial reference frame which will reduce sensory conflicts to an acceptable level, the central nervous system applies weighting functions to and sets assumed operating points for the sensory modalities. Unaccustomed or unorthodox spatial or accelerative environments can make the CNS computations difficult - occasionally to the point of being self-defeating. In fact, so unfamiliar is the CNS with the aspect of having to
deal with even a single channel in conflict with all others that motion sickness may result from very mild disturbances or from ones apparently unrelated to motion. The CNS can even assign assumed operating points and weighting functions to the sensory modalities which are so incorrect as to produce symptoms in a totally stationary environment.

This approach to analysis of the problem does not generate any intrinsic solutions but does engender an attitude which should be maintained when considering realistic attempts at constructing training or selection procedures. It implies, for example, that in setting up a test for use in selection of candidates for a particular environment, either that environment should be simulated exactly or it should be capable of eventual alteration so that it simulates the test itself. Since neither of the latter alternatives is ideally attainable in selection or training of astronauts, one must be satisfied with compromises and must search diligently for correlations of results with feasible procedures.

In summary then, no general theory of motion sickness can be advanced at this time which will reasonably explain the experimental evidence in a heuristic fashion. Direct intervention into the symptom sequence awaits detailed analysis of this sequence and the determination of its vulnerable points of access.
D. "Space Sickness" with Respect to the Vestibular System

1. Speculations

Even before it became certain that man would be a space traveler, there was speculation that exposure to the weightless environment would produce severe, even incapacitating, disorientation leading to a form of motion sickness. The arguments which have been advanced in hypothesizing the existence and nature of this problem are generally based upon one or more of the following assumptions:

- that the complex of vestibular, kinesthetic, tactile and visual cues which result from given body movement on earth will be disastrously different when the same movement is made in space,

- that absence of normal gravitational acceleration will cause the mechanical components of the vestibular receptor to respond abnormally to head movement, and prolonged exposure to the weightless environment will result in changes in the structures of the inner ear, and in the circulatory system related to them,

- that this adaptation will lower the vestibular threshold (or de-condition) the individual so that the accelerations encountered in later portions of a mission will be severely disturbing,

- that the use of a rotating environment to counter the physiological effects will introduce additional problems of vestibular disturbance.
The following discussion summarizes the considerations which have lead to these speculations.

The values proposed for translational and rotational motions of non-rotating space vehicles during lift-off, tumbling, rendezvous, mid-course corrections, extraterrestrial landing and returns are not in themselves likely to induce motion sickness. In a weightless environment, however, even slight accelerations were once thought to be potentially hazardous. Simons summarizes the theories of Gauer and Haber and others in this regard: (146) "...they postulated that the Weber-Fechner Law may profoundly influence the sensorium in the weightless state. Thus, a given increment of acceleration acting as a vestibular stimulus would, during weightlessness, be expected to provide a much greater sensory response than under normal conditions." Attention has been directed to the otoliths as the probable source of such abnormal transduction, since, as Vinograd (163) summarizes the case, "there is no input from the semicircular canals without rotation, and lack of semicircular canal stimulation is a normal, everyday experience causing no symptoms."

Insertion into orbit, apparently analamous motions of an object in rendezvous, extension of visual search from the capsule interior to the approaching lunar surface are among the transient events in space missions
which could produce confusing patterns of vestibular, kinesthetic, proprioceptive and visual stimuli. The resulting spatial disorientation could trigger the symptoms of motion sickness.

That vision alone (or in the presence of contradictory sensory data) can provide satisfactory spatial orientation is demonstrated by flyers - who learn to selectively disregard cues conflicting with visual data - , labyrinthectomized persons, subjects in Kepplerian trajectory flights, subjects who adapt to wearing distorting lenses, and, of course, the experience of space pilots to date. Whether a person chooses the vehicle structure as his frame of reference, or his own body seems to be immaterial. (33) Failure of vehicle illumination might produce serious disorientation if the interior of the vehicle were large, for complete lack of a visual frame of reference has been shown by Johnson and others to facilitate sickness. (30) Indeed the better defined (or structured) the visual and haptic environment, the less likely will be the occurrence of disorientation. (31)

The transition from a normal visually-confirmed vestibular oriented frame of reference to a purely visual, or a purely postural frame of reference has been demonstrated by Graybiel and others to be a surprisingly
lengthy process. Studies at the Naval School of Aviation Medicine have shown that it may take sixty seconds or longer to shift from a visual to a postural frame of reference, but that with practice the perceptual error and the time required to make the shift is markedly reduced. (39) The sensation of tumbling following cessation of a centrifuge run and orientation problems of immersion study subjects are other examples of prolonged disorientation accompanying a major change in the acceleration vector. (67) Thus one would expect orientation problems to occur at those times in the mission when the crew must suddenly integrate sensory cues of a type which had previously been absent or minimal in order to orient themselves.

(It should be noted that the mere prolonged absence of a normal non-visual stimulus certainly should not lead to the disorientation and hallucination effects observed in experimental studies of sensory deprivation; crews on space missions will be "far from starved for sensory stimulation" (169).)

Among the damaging effects of prolonged weightlessness upon the vestibular system which have been suggested is the possibility of degeneration
of the utricular and saccular maculae as a result of a constant "pounding" of the otoliths against the sensitive epithelium. This "pounding" effect would be expected to become more prominent in situations where vigorous activity and many head motions are required, as in space stations, on the moon, or in prolonged orbits. Degenerative effects of this nature can be expected to have a slow time course, and would not be expected to manifest themselves behaviorally except in the most sensitive individuals and as a response to violent motion, but may be troublesome in re-entry and on return to earth.

It is not too far-fetched to expect that in the course of evolution the utricular macula has grown adjusted to the presence of the otolith not only as a mechanism of stimulation, but as an object whose weight is integrated with the function of the cell in the trophic sense. The removal of this hypothetical trophic influence may result in macular degeneration with some of the results seen in clinical neuro-otology (for example; a form of positional vertigo.)

Since little is known concerning the circulation of the labyrinth, but information is available concerning the relationship of the intimate labyrinthine circulation to the production of macular degeneration, and the "loose otolith" syndrome, it is essential to acquire data on the changes in labyrinthine
circulation during the weightless state so as to gain assurance that progressive ischemic or hyperemic degeneration of the labyrinthine end organ does not occur. It takes time for the labyrinthine epithelium to degenerate. How long is not known. Since some of its trophic function have been studied by tracer methods already, it may be appropriate to undertake studies which would indicate the time scale of degeneration expected to occur when circulation is lessened or increased.

Evidence is available to indicate that certain aspects of neural input have significance for the maintenance of neuronal integrity. Their precise nature has not been elucidated, but it would be well to consider the possibility that abnormal neural input induce a structural as well as functional alteration of central and peripheral neural structures.

The vestibular apparatus is subject to a variety of disorders, some genetic (producing animals with bizarre motions), some considered circulatory in origin as Meniere's disease (vertigo, tinnitus, deafness) probably involving the semicircular canals, utricle and saccule, and benign positional nystagmus of various types probably involving the utricular macula. (52) Other disorders include labyrinthitis, vestibular neuronitis, eighth nerve tumors, and involvements of vestibular and related pathways in the brain stem and cerebral cortex by tumor, circulatory deficit, and the like. (150) Though any of
these could conceivably arise, depending upon their causes, in a space vehicle and produce symptoms akin to those of vestibular stimulation, they are not, strictly speaking, within the purview of this report, which is primarily concerned with what may be called the undesirable effects of stimulation in a previously normal apparatus, or almost normal apparatus.

During the recent NASA-Martin Marietta lunar mission simulation study it was found that the most difficult tasks for the crew were lunar landing, lunar ascent and lunar orbit-rendezvous, and re-entry. These tasks were undertaken 3-1/2 to 7 days after simulated "lift off". The authors add that despite the difficulty of these tasks, they were performed by: the subjects (NASA pilots) with no evidence of performance degradation. Study of the etiology and suppression of space sickness must include exposure of personnel to the combination of stresses which are likely to occur, in the temporal sequence they will follow.

While valuable insight into ways in which crews can be prepared to perform their tasks in the latter phases of their mission with an adequate margin of safety may be obtained from use of ground-based simulators, the effects of prolonged weightlessness itself as a source of stress must
await definition until the Gemeni vehicles are available. These future space studies will provide the only valid basis for predicting the probability of sickness resulting from motions administered to individuals who have been subjected to the stress of demanding tasks for several days and whose physiological processes may have been altered by the environment.

The use of rotating vehicles providing an artificial gravity field would presumably eliminate many of the hypothetical problems discussed above. Rotational environments introduce a new set of problems, however, most of which have been described in some detail in reports of the U.S. Naval School of Aviation Medicine. The major findings of the Pensacola Laboratory are discussed in other sections of this review.

2. Space Flight Experience

The U.S. and U.S.S.R. animal experiments which preceded manned space flight established the fact that the experience of brief weightlessness with its attendant stresses produced no detrimental effects upon the vestibular system from causes unique to the space environment. While episodes of disorientation occurred, mice, rats, dogs, guinea pigs, pigeons and turtles gave evidence of establishing for themselves satisfactory inertial frames of reference. (87, 133)
Manned space flights have similarly demonstrated human ability to perform efficiently in space for periods as long as four days. The experience to date will be summarized in terms of the possible causes of "space sickness" which were identified earlier:

a. Disorientation

Glenn reports that, "Upon insertion, there seemed to be a barely noticeable sensation of tumbling forward when the capsule separated: it was only momentary, and I did not feel disoriented at any time." (246) Grissom experienced a brief tumbling sensation at launch-vehicle cutoff but no nausea, nystagmus or visual disturbances were observed. (14)

Titov - a younger and far less experienced pilot than the U.S. astronauts - was severely disturbed at this moment of insertion into orbit. "I felt as though I were turning a somersault, and then flying with my legs up. For the life of me I could not determine where I was. I was completely confused, unable to define where was the earth or the stars! It seemed as if the somersault had carried me completely around and that I was floating upside down, attached to nothing. The instrument panel was bobbing around somewhere alongside me...everything whirled around in a strange fog that defied all my attempts to separate order from the sudden chaos." (160)
Titov's disorientation difficulty then disappeared for a time. Then, in the fourth orbit "I felt changes in mood during abrupt movements of my head which produced unpleasant sensations resembling seasickness. I felt giddy and nausea." (152) "These moments caused additional distress when they repeated at more frequent intervals until the sensations were fixed... (6th-7th orbit). I noticed that when I observed something in rapid movement - a dial or a meter in the cabin, for example - the same dizziness and nausea increased." (160). This was accompanied by deterioration of the appetite. Falling asleep was a bit difficult." (159) It is important to note that in all Russian discussions of Titov's difficulties the statement is made that his discomforts did not affect his performance, although whether his reserve capacity for handling emergencies was affected is an open question. No satisfactory explanation for his difficulty has been made, save for the generally accepted statement that he was a poor choice for cosmonaut assignment. All attempts made to replicate his condition in space by violent head motions have been unsuccessful. Combinations of head movement, vehicle tumbling and novel perspectives of the earth have not induced symptoms of motion sickness.
Apparently only Titov has experienced difficulty in maintaining an adequate inertial frame of reference while in orbital flight. Carpenter states that "You can assign your own 'up' and put it anywhere - toward the ground, toward the horizon or on a line between two stars - and it is perfectly satisfactory." (24) Nikolayev and Popovich had no dis-orientation difficulty while floating about in their cabins, although in the early stages of their flights they took some "precautionary measures - fewer abrupt motions, and smoother, more gradual handling of the ship's equipment (than had been the case in Titov's flight)." (131)

b. Anatomical, Biomechanical and Physiological Changes in the Vestibular System

No alterations in the system have been observed during or subsequent to manned space flight.

c. Lowering of Threshold to Motion Disturbance

The deceleration, vibration and oscillations of re-entry and parachute landing have not produced motion sickness symptoms.

Summarizing, then, although acute phase "vestibular space sickness" does not seem to exist in the majority of astronauts, certain not unreasonable untoward possibilities present themselves for long term operations. The caution to be taken here is not simply that long term experiments have not been undertaken and so their effects are unknown, but that distinct pathological entities analogous to certain other known pathological entities (see Part II) can be imagined, all of which are quite disabling in their effects, and should be avoided if at all possible.
E. Measures Used to Control Motion Sickness

1. Pharmacological

Medications have been directed against emesis, against assumed pathogenetic mechanisms of altered labyrinthine structure, immunological and involving electrolyte balance, and toward depression of central and peripheral nervous system mechanisms. Agents active in Meniere's disease, hyperemesis gravidarum, and gastrointestinal disturbances have not generally been successful in motion sickness therapy. Belladonna derivatives (atropine, hyoscine) provide a standard against which other drugs may be tested, but whether their action is primarily central or peripheral has yet to be elucidated.

Certain of the antihistamines (dimenhydrinate, diphenhydramine) but not others have been found to be of great utility in controlled motion sickness therapy trials. Their efficacy is probably related to their antihistaminic potency, and it appears that anticholinergic peripheral symptoms (cycloplegia, dry mouth, and the like) must be present for a potent therapeutic effect. These drugs are extremely effective in the therapy of developed motion sickness, but are less effective in prevention than a newer antihistamine group of piperazine derivatives (cyclizine, meclizine) which have a longer duration of action when administered orally.
Phenothiazine derivatives have varied in effect, chlorpromazine being less effective than promethazine. Antispasmodics and sympatholytics have not been effective. Drugs of the thiobarbiturate group have had some success in controlled trials, as has had phenobarbital, but this is probably related to the general "sedating" effect of the medications.

A variety of other pharmacodynamic maneuvers, including administration of histamine in graded doses and acetazolamide have been tried. High potassium and low sodium diets, and various vitamins (for vasodilating purposes or by analogy to their effects in eliminating the vertigo of deficiency diseases such as pellagra (niacin)) have been used with limited success. Pyridoxine has looked promising, however, in controlled trials, and since it plays an important part in the metabolism of such central nervous system active compounds as glutamine, and gamma-amino butyric acid, may bear careful looking into.

In summary, the side effects of most drugs now in use preclude their routine administration in situations where alertness and some degree of comfort are prime considerations. Investigation into certain vitamin supplements (pyridoxine) as prophylactic medication would seem to be a useful, and apparently safe, procedure at this time. Certainly, no side effect is as severe as vomiting itself, and acute-phase medication
should be made available operationally.

2. **Training**
   
a. **Habituation in Figure Skaters and Others**

   In the course of the present study a number of persons were interviewed who have apparently learned to suppress undesirable response to certain high intensity motion and disorientation stimuli: figure skaters, acrobats, helicopter pilots, commercial fishermen, and structural steel workers. The motion situations they have mastered and their approaches to mastery reflect their respective activities, as well as the expected individual differences. All of the persons interviewed are quite normal to all outward appearance. They have good hearing, and are subject to the ordinary illusions of motion (of the Cinerama variety) and none is descended from a family of performers. An apparently important common characteristic is great self-confidence.

   Practice is to them of the utmost importance in avoiding the symptoms of motion sickness. A layoff of as little as two weeks will result in the performers becoming somewhat dizzy in a maneuver. The de-conditioning increases with time. Daily practice - or at least several sessions a week - seem to be necessary to maintain habituation.
In an experimental investigation of habituation in figure skaters, McCabe (11) found that expert skaters who spin at rates as high as 200-300 rpm display no nystagmus or gait disturbance after standard Barany (bi-directional) or caloric tests; "regardless of how the stimulus was applied." This is in apparent contradiction to the information given us by other skilled performers, who reported difficulty in performing spins in which direction or head position was different from that which they were accustomed.

1. His subjects (three experts) may have been consistently different from the skaters and acrobatic performer with whom we discussed the problem.

2. He did not request his subjects to perform any spin maneuvers in which they were not proficient. Had he done so he might have observed the same indications of disturbances which our sources report. (Assuming that high-speed spinning on ice is a more violent stimulus than caloric or Barany tests).

3. He recorded only the outward signs of motion disturbance - nystagmus and gait - after Barany and caloric stimulation. Thus his subjects might have felt dizzy, though they showed no nystagmus, and, conversely though our sources report a feeling of vertigo in a novel rotation situation, one might not observe nystagmus.
The apparent transfer, or generalization which he observes, he believes to be due to the fact that during any spin more than one set of canals is stimulated, and thus the individual becomes to some extent habituated to all rotational motions.

One of his most interesting series of data show the progressive habituation of student-skaters during their first five months of training. Their nystagmus response to horizontal rotation drops markedly during the course of training, and their response to vertical canal caloric stimulation begins to lower. He reports the same sort of de-conditioning results from layoff has been observed elsewhere. McCabe did not use cupulometry with his subjects so that one cannot compare the rate of change of their vestibular response mechanism with data from Ascham, DeWit and others.

Some of the fishermen who were interviewed in the present study stated strong odors or high temperature tend to facilitate sea sickness, but the skaters, acrobats, pilots and others rated these factors as inconsequential. The performers and pilots need only a minimal visual frame of reference, but when this minimal reference is lost or distorted, they experience the early symptoms of motion sickness. One skater
described the great difficulty encountered in spinning within a spotlight with the house lights off, and a motorcycle acrobat told of dizziness occurring whenever his vertical "roadway" is unevenly illuminated.

Emotional factors have long been considered to play an important role in motion sickness. Perhaps they do in the case of untrained persons, but in the case of the self-confident, highly motivated performer, fear, anxiety and other emotions are well controlled and, when they are consciously present these emotions do not affect the performer's habituation to motion.

We are inclined to draw a few tentative conclusions from the anecdotal evidence obtained thus far:

1. That appropriate training does in fact effect marked suppressions of the symptoms of motion sickness in highly motivated normal individuals.

2. That habituation is by no means permanent; continued practice (exposure to the motion stimuli) seems to be necessary to maintain habituation.

3. That habituation does not automatically transfer from one mode of stimulation to another.
4. That once habituation is achieved, such secondary environmental factors as odors, noises, and temperature, and emotional factors do not affect the habituation.

b. The Effect of Flying Experience

Aschan used cupulometry to address the question; does fighter aircraft flying, more or less permanently affect the vestibular apparatus of those concerned? The question was raised by experiments of Hallpike et al who found that differences in response to caloric stimulation seemed more related to flying experience than motion sickness susceptibility. One hundred Royal Swedish Air Force pilots on active duty were examined by cupulometry (with both sensation and oculogyral illusion response) and other methods over a 2-1/2 year period. The subjects were divided into three groups: those who were flying infrequently, and using low-performance aircraft; those who were on a more extensive, but still relatively limited flight status; and fighter pilots flying acrobatics daily.

The cupulograms clearly demonstrate the effect of current flying experience. The subjects who flew rarely had cupulogram indistinguishable from "normal" subjects. Those who flew more often produced cupulograms
having less slope (i.e., briefer post-rotational sensation) but about
the same threshold for motion perception as the first group. The
pilots on full fighter flight status had cupulograms of about the same
slope as the second (limited flying) group, but a markedly higher
threshold. Subjects tested while in "flying trim" who reverted to a
"desk job" during the course of the experiment manifested this
transfer of activities in their cupulograms: after a month or so of
lay off their cupulograms had returned to a more or less "normal",
unhabituated configuration. In general, it can be said that flying
high performance aircraft definitely increases a person's resistance
to rotary motion disturbance, but that the habituation is quite reversible.
A small number of commercial pilots tested showed no deviation from
normal. The absence of acrobatic maneuvers in their work was cited
as the cause of their 'normality'.

Aschan's findings are in agreement with DeWit's hypothesis that
persons who are immune to seasickness have cupulograms with low
slope, and high threshold. Mann and Canella have also found that
flyers (and sailors) not susceptible to motion sickness have cupulograms
showing these characteristics.
Dearnaley reported that flying instructors who were exposed to roll maneuvers experienced after-sensations of appreciably shorter duration than flight trainees. This was particularly noticeable when both classes of subjects were exposed to the roll while vision was blocked by an instrument hood. (42)

c. Preparation of the Astronauts

Both the U. S. and U. S. S. R. have selected fighter pilots as astronaut candidates although the Russians appear to have used in their earlier flights men less experienced in high performance aircraft than the men chosen for the Mercury program.

No particular emphasis was placed on tests of vestibular function in the screening program of U. S. Astronauts beyond a caloric test of nystagmus response. In designing the battery of tests it was recognized that control of tumbling in space flight might be necessary in an emergency; but, "Tumbling tests are so unpleasant and the nausea so prolonged as to warrant its exclusion." (76)

The effort to condition the U. S. Astronauts to resist vestibular disturbances seems to have followed two approaches: maintenance of a high level of proficiency in acrobatic flight maneuvers, and exposure to acceleration stresses in the centrifuge and disorientation devices (MASTIF and SRR). While Grissom writes, "I think MASTIF gave the seven of us
more confidence in our ability to pilot a spacecraft than any other test we took", the device was not used as a regularly scheduled practice device. (23a) It, along with the other vestibular challenging devices seems to have had a testing rather than a vigorous preparation role in the training program. Only one of the astronauts - Carpenter - has chosen a personal physical exercise program which includes appreciable vestibular disturbance, trampoline acrobatics.

The centrifuge and disorientation devices used for conditioning of Russian astronauts seem, from evidence in the open literature, to be quite analogous to those available in the U. S. One of their centrifuges which has been described, however, had a capability for vertical travel as well as bi-directional rotation. "The complex of exercises for the physical training of the cosmonaut...includes a large group of exercises directed toward strengthening the cardio-vascular and respiratory system, and the vestibular apparatus (rotation over complicated trajectories in special devices, etc.) and particularly toward adapting the neuromuscular apparatus to great stresses (exercises in special acceleration-producing devices, etc.)." (36) In addition, there are exercises designed to enhance his coordination of voluntary movement in the weightless environment. There are no details available as to the precise nature, or schedule of these exercises. "It was determined during (those portions of)
training which have considerable influence on the neuro-psychic sphere of a person that the emotional reaction of the cosmonauts was completely adequate. During centrifuge runs, in performing delayed parachute drops into water, and in complex acrobatic springboard exercises the cosmonauts did not display any emotion." (JC)

Titov was no stranger to disorientation when he encountered it during space flight. During his free fall parachute training he was caught in a "flat spin" producing a "violent corkscrew, the world a terrible blur, flashing around and around...the world began to turn grey, then darker, and I realized I was close to blacking out." Nevertheless he recovered, was awarded the classification of Parachute Instructor, and simultaneously presented his first official Soviet medal - Master of Sport. (O)

He describes his reaction to the "chamber of silence" - an anechoic room in which the cosmonauts were isolated for periods of up to 15 days:

"I did not like the chamber. The silence crashed against me with what seemed to be physical force. It was not just a matter of my being upset or fearful of the incredible lack of sound; I just did not like it. My dislike became intense, and on the third or fourth time in the chamber, I suddenly discovered something akin to low waver of nausea moving through me. I was startled, for never in my life had I become ill in this manner...
its discomfort it would not interfere with my work. I found that by sitting quietly in the seat and concentrating as hard as I could on some other subject I could not only ignore the stomach discomfort, but could even help in eliminating it greatly. Again and again I returned to the chamber, with two sessions a day for several days. By the third day I felt much more at ease in the room of silence, and the nausea was only a memory."

On his experience in a MASTIF-type device, he states "one thing I could say and with conviction - a feeling of nausea and body sickness for several hours afterward, then abated. Gradually I became accustomed to the sensation of the three-axis motion, and came to understand why the doctors were so convinced that I would cease to be bothered with the feeling of nausea."

Titov reported to the International Astronautical Congress in October 1962 that Nikolayev and Popovich were sent through a training program consisting primarily of physical exercises. (159) The emphasis of Russian training between the Titov flight and the two consecutive missions was upon more rigorous exposure of the cosmonauts to acceleration stress. It appears that no substantial difference was made in the training methods, simply much more was spent in time in subjecting the cosmonauts to centrifuge runs, tumbling, etc. It similarly does not appear that any
new screening techniques have been developed or will be used. The Russian speakers at the most recent IAF meeting indicated that the criteria of acceptability for vestibular sensitivity had been raised since Titov's experience. The implication is that he did not score particularly well in this respect during training but his other qualities were such that the program directors were willing to take a chance - which appears to have been unwise.

Thus far candidates for astronaut training have been selected from the test-pilot population - a group which, from the evidence of Aschan cited earlier, and others, is significantly less susceptible to vestibular stimulation (rotary) than the normal population. Because of the probability that future crews will include scientists who are not pilots, the question arises whether extensive experience in flying high performance aircraft is a necessary preparation for the disorientation challenges of space flight. Experiments have shown that non-flyers can become as well adapted as flyers to specific experimental motion or orientation challenge. Recent findings at the USAF School of Aviation Medicine, for example, have shown that experienced pilots are not peculiar in their ability to estimate a function of the postural vertical without visual cues; both pilot and non-pilot groups improve their performance with practice.
with approximately equal facility. (127) Yet the question remains as to whether non-pilots chosen for astronaut training must be given a direct analog of high-performance flight experience during their training, or whether "short cuts" will provide a "motion-resistance profile" equivalent to that of a test pilot.

A relevant issue is whether the fact that non-pilot crew members will not be in control of the vehicle will in itself render them more susceptible to motion sickness. (158)

d. Exercises for Vestibular Training

The Russians have placed considerable emphasis on exercises such as tumbling, swinging, jumping to condition the vestibular systems of their flyers and cosmonauts. Aerial gunners have been trained to fire from swings to improve their ability to fire accurately in aerial maneuvers.

Their "active training" exercises include gymnastics, acrobatic exercises, and groups of special motions such as head and body turns in a variety of positions, somersaults and equilibrium exercises. The latter consist in standing on one foot for a long period of time, thrusts, knee bends, figure skating, and use of the horizontal bars. In addition, "passive" training consisting of subjecting the trainee to motion which he does not control, is used. The major reliance is placed upon devices such as the Barany chair, 4-pole swings, multiple axis swings, centrifuges, elevators, etc. In combined exercises, the individual exerts voluntary control of a portion of his total movement pattern while he is being moved on a device.
There has been some value found in blindfolding the subject in all of the foregoing types of exercise. (16)

The most effective for air crew personnel appear to be the active class of exercise. The schedule of vestibular training should be daily or every other day exercises for 30 to 60 minutes. It is suggested that such training is of maximum effectiveness if it is done no less than 7 times per month. There is an indication that in individual cases the effect of the training is negative rather than positive, but explanations for this are not given. (8)

Molomut, reviewing the practices of Japanese aeromedicine in 1945, found that they had devoted great attention to the problems of motion sickness. Starting in the third grade all children participated in an exercise program designed, "particularly to train all school children in coordination after complicated rotational exercises. The effect of this training program was shown in an extremely low incidence of air and sea sickness, and was demonstrated clinically by a reduction in nystagmus time in such individuals after rotation." Molomut's report unfortunately gives no information on the nature or schedule of exercises, the method of testing, etc. (117)
Among the treatments used at a World War II AAF training base was an exercise program consisting of one hour of daily rotation and tumbling exercises for five weeks. "No particular improvement" was observed, although the number of other variables in this attack on air sickness seems to have been large enough to prohibit close analysis of the results. (2)

There is no evidence that general physical fitness serves to buffer the vestibular system against the disturbances generative of motion sickness.
F. Habituation and Conditioning

The anatomical basis of reflex on instinctive behavior is laid down in the synaptic connections of the central nervous system in a stable form. Reversing the functional location of receptors or effectors in lower animals uniformly leads to inappropriate responses which are not subject to modification by training. It is upon this stabilized neural structure that behavior is hierarchically established.

Instinctive behavior occurring without previous experience is characterized by innate releasing reactions. These reactions are coupled to sensory stimuli or to inner states of the central nervous system with sensory components. As we consider animals higher in the phylogenetic scale the control of behaviors formerly mediated by relatively peripheral reflexes comes under more central control where the functional organization of the nervous system is more plastic. A salamander whose eyes are rotated 180° forever responds up to down, and left to right, but a human wearing lenses which invert the visual field eventually learns a new set of appropriate motor responses.

The reflex responses of the autonomic nervous system, which proceed with little conscious awareness, appear as a part of our instinctual heritage and have long been considered to share the functional
rigidity of their evolution precursors. This assumption has lately been challenged by many conditioning experiments in the Pavlovian tradition, which have used autonomic effectors, the skeletal muscles, interoceptive stimuli, and exteroceptive stimuli in a wide variety of combinations with striking success. The powers of discrimination of the interoceptors are greater than have usually been supposed. Makrov for instance, placed three pronged electrodes on the gastric mucosa, 8 centimeters apart. Stimuli at intervals of less than 15 msec were reported as one sensation localized between the stimulus points. With an interval of 55 to 105 msec, two sensations resulted in reports of two successive stimulations in two successive loci.

The output of the autonomic nervous system is subject to control from either interoceptors or exteroceptors, or combinations of interoceptors and exteroceptors. The work of Pshonik illustrates this point well. Vascular responses to heating and cooling of the gastric mucosa and the skin and of the epigastric region were measured by plethysmography. Responses to interoception tended to blank out responses to exteroception. A blue light was turned on before each sequence of warming or cooling. When the
light was no longer followed by the same sequence of thermal stimuli, a "vascular neurosis" occurred with symptoms of vomiting, sensory disturbances, and headaches. The disruption of a stable autonomic reflex previously established by conditioning led to an uncoordinated response of the autonomic nervous system resembling motion sickness in some respects.

Attempts to control the autonomic response to the vestibular inputs have usually concentrated upon habituation rather than conditioning. The repeated presentation of the stimulus without any associated reinforcement usually leads to a diminution of the behavioral response and its electrophysiological correlates. This result is stimulus bound. A slight change in the stimulus is sufficient to restore its original arousing potential. (148)

Conditioned inhibition generalizes to a wider variety of stimuli. A stimulus presented repeatedly in association with a reinforcing stimulus comes to elicit behavior appropriate to the reinforceer and to inhibit other behaviors. This inhibition spreads to other similar stimuli and may persist indefinitely.
Certain features of motion sickness suggest that it is based upon conditioned responses. The drowsiness that preludes motion sickness resembles the sleeplike state of an animal in which generalized inhibition has been induced by prolonged exposure to a situation for which it has no adequate response. Conditioning is also suggested by the fact that movements of the visual field alone may be sufficient to produce motion sickness without stimulating the vestibular apparatus, but only in a subject in whom the vestibular apparatus is intact.

The minimum anatomical substrate necessary to mediate the conditioning of responses to vestibular stimulation seems to be available. Direct experimental evidence of conditionability has not been found, but the many persons who have ceased to be sick after repeated exposure to a particular kind of motion have accomplished a change in their behavior which we cannot now distinguish from conditioning.
G. Conditioning Resistance to Motion Sickness

The feasibility of training to lessen or defer the possible debilitating effects of motion sickness in space missions depends upon two main observations:

1. That subtle psychogenic factors will not interfere with a realistic training program. That is, that personality is not so large an issue in trainability that only special subjects -- who might otherwise be unsuitable for the role of Astronaut -- can be trained to mitigate their symptoms.

2. That training of such an unconscious response as motion sickness does not violate what is known of the neurological and psychological make-up of man. In particular, that men have indeed been trained to control at least some of their autonomically-mediated behavior.

Once these factors have been confirmed, it becomes pertinent to devise a method by which training can be carried out. One is then confronted with the several theories of learning and conditioning arising from controlled experiments with men and with other animals. The design of the training regimen depends, therefore, upon taking certain premises from these theories and treating the trainee in
accordance with them. If the training is successful, it may be because the premises were valid, or for other reasons. If the training fails, then new premises must be taken and an alternate training scheme devised.

1. **Psychogenic Factors**

Most often mentioned among the psychogenic factors which might increase a person's susceptibility to motion sickness are emotional distress, acute or chronic; suggestion and conditioning; and motivation. While some investigations have been carried out in attempts to establish the relevancy of these states, many of the experiments reported could not systematically examine an isolated factor. The studies of acute emotional distress -- anxiety, alarm and fear -- are usually complicated by an uncontrolled experimental environment while examinations of the relation of easily induced motion sickness to chronic neurotic inadequacy lack relevant norms.

a. **Emotional Stress**

What evidence there is suggests that most distressing emotional conditions have no discernible effect on the likelihood of motion sickness. Situations that couple the subjects' emotions with acute anxiety, such as air or sea combat, are not known to produce motion sickness more readily than less disturbing circumstances. (174)
Even the injection of adrenalin-like material, artificially inducing the physiological state associated with a high emotional pitch, does not predispose to motion sickness. (9) On the other hand, when electric shock as well as motion was administered to subjects, the incidence of motion sickness was increased over that of a control group. (14) It is of interest, in this case, that the subjects were shocked until they became motion sick.

That alarm and fear of the immediate environment plays little part in the production of motion sickness can be shown by noting that while a 25 cycle per minute oscillation is rarely alarming to a subject, it produces motion sickness in most people whereas motions of higher frequency are frightening but usually do not induce sickness. (175)

b. Neurosis

The relation of chronic neurotic inadequacy to motion sickness remains obscure, as mentioned above, in that a satisfactorily normal population is necessary for valid conclusions. Psychiatric examination of military personnel reassigned because of motion sickness -- persons released from flight training -- revealed a high incidence of neurotic symptoms. (21) The inference that a predilection to motion sickness is a neurotic illness could be drawn only if
personnel reassigned for other reasons were less often neurotic. In the absence of such control data it appears more reasonable to suppose that neurotics are more likely to fail in their duties or that those who fail are likely to be upset about it. The results of some personality questionnaires show a correlation with motion sickness, but when the predictive items of one such questionnaire were analyzed, almost all of them were about motion sickness or other experiences of nausea.

c. Suggestion, Conditioning and Motivation

The remaining factors, suggestions, conditioning and motivation are supported as important in motion sickness susceptibility largely by anecdotal data and by persons experienced in the assessment of motion sickness.\(^\text{[10]}\) The possible effect of suggestion, in fact, makes suspect some of the otherwise controlled experiments on psychogenic factors. That conditioning by a previous experience of sickness may occur seems reasonable and may well account for instances in which attempts to train subjects to resist the effects of motion resulted in just the opposite.\(^\text{[16]}\)

Motivation would seem to be the factor most strongly established by anecdotal sources. Whether it plays a significant role could be established by systematic experiment, but such an investigation
would, it appears, be largely academic in view of the fact that space travelers are likely to be highly motivated. It seems, then, that psychogenic factors will not prohibit attempts to train for the mitigation of motion sickness. While the distribution of neurotics in the population of course has some overlap with the distribution of motion sickness susceptibles, there is no specific evidence that personality is at all regularly correlated with susceptibility. What data there is suggests that the training must be done with care, avoiding the hazards of suggestion and conditioning, and that the high motivation of potential astronauts will be an asset.

2. **Neurological and Psychological Factors**

The role of neurological systems in the etiology of motion sickness has been reviewed earlier. The conclusions to be drawn from available knowledge are that the hypothesized mechanism of motion sickness is compatible with training, and that there exist fairly well established pathways by which appropriate training can affect the probable sequence of events so as to mitigate or delay the physiological disturbance and allay the untoward symptoms.

There is ample evidence -- both from controlled experiment and from anecdotal sources -- that unconscious functions can be affected by training. Some of the evidence is specific to motion
sickness while other attests to the conditionability of visceral and central nervous system responses. Still other available reports give helpful clues as to the way in which an autonomic conditioning situation should be structured.

a. The Effect of Unstructured Training and Practice

The anecdotal information coming principally from dancers, skaters and acrobats attracts attention in that it confirms the assumption that training is, indeed, feasible. For the purposes of these athletes, though, it is immaterial whether it is the sensory pathway or the response chain which is conditioned (or acclimated) to the motion. A reasonable inference is that where transfer of the training can be made so that the effects of disturbing motions other than those encountered in their practice sessions are repressed, then the learned interference is with the response; where the subjects reported no such transfer, however, it seems reasonable that the acquired suppression acts upon the sensations. If the usual response -- motion sickness -- is interfered with, it may be that the athlete has become able to evoke a set of mitigating responses that preclude motion sickness.

A more pertinent piece of information concerns the reduction in the number of persons apparently susceptible to motion sickness measured before and after flight training. (4) Also of topical
significance are the reports concerning the training of astronauts in the Soviet Union. There, the avowed purpose of the program is to inhibit unconditioned vestibular reflexes and reinforce regulations upon them. The dearth of quantitative data in these cases, however, leads to a search for verifiable instances of similar, but not necessarily identical, conditioning. These can be found in the accounts of "interoceptive conditioning".

b. Conditioning

Classical (Pavlovian) conditioning procedures have repeatedly verified that if an unconditioned stimulus (having a normally affective or response-eliciting characteristic) is repeatedly presented together with a previously neutral (non-affective, eliciting no special response) stimulus, the neutral stimulus will come to elicit the same response as the unconditioned stimulus. This phenomenon is most significant in conjunction with autonomic responses.

More recently, in conjunction with the peripheral nervous system and skeletal or striated muscle responses, "instrumental" or 'bperant' conditioning procedures have been most effective. It has been established that if a certain stimulus-response pair is repeatedly followed by a rewarding or reinforcing stimulus, the stimulus will come to elicit the response regularly, even though initially the response
may have occurred simultaneously with the stimulus only by chance. The rewarding stimulus can take the form of the lack of "penalizing" stimuli; conditioning by this means is called "avoidance conditioning". Skinner and others have shown that response behavior can be shaped by giving the reward only for a progressively more limited class of stimuli ("stimulus discrimination"). The reward presented on each trial can be a substitute for the primary reinforcement provided that the substitute, or secondary, reward eventually leads to a primary reward.

c. Interoceptive Conditioning

Interoceptive conditioning is narrowly defined as classical conditioning in which a stimulus is delivered directly to the mucosa of some specific viscus. A less precise definition, but a usable one, is that the behavior of an organ other than skeletal or striated muscle is involved in a conditioned response. Studies of interoceptive conditioning were begun in the Soviet Union in 1928, but the bulk of the work in this area has been done since 1940. It was not until the middle fifties that comparable results began to come from American laboratories.

The following examples will serve to show the variation and subtlety of interoceptive conditioning.

The duodenum of a dog was inflated with air in five seconds. On the fifth second an electric shock was applied to the animal's leg. Conditioned paw withdrawal in response to inflation appeared after
five trials. After 129 reinforced trials, the inflation, now no longer accompanied by shock, was joined by the sound of a buzzer. After eighteen such trials, the sound of the buzzer elicited paw withdrawal even though the sound was never associated with the administration of the electric shock. (169)

In another experiment, three patients with urinary bladder fistulas volunteered for experiments in which their bladders were distended by air or physiological solutions. The subjects were to signal the time and intensity of their desire to urinate. The bladder pressure was at first monitored by a manometer with a conspicuous dial, watched by the patient. Later, the manometer was detached, without the patient's knowledge, and the dial readings were varied by the experimenter. Conditioning to the sham readings was readily effected. The subject reported an intense urination urge -- and showed appropriate respiratory, vascular and psychogalvanic changes -- when the manometer readings were high even though the actual pressure was low. Contrariwise, low readings failed to produce the urge and its objective accompaniments even if the bladder pressure was considerably above that which normally produced them. (19)

An experiment was conducted in which the delay of an electric shock was made contingent upon the acceleration of heart rate
in human subjects. Although the interpretation of the changes in heart rate was confounded by respiratory motion, the number of accelerations rose across sessions for the subjects and fell for their yoked-controls who received equal amounts of non-contingent shock. (145)

Another attempt at conditioning cardiac function consisted in having as conditioned stimuli simply signals denoting inspiration and expiration. Extrasystoles are known to occur in healthy human subjects during common respiratory maneuvers. Under laboratory conditions it was shown that this kind of extrasystole can be conditioned. (33)

In a dramatic demonstration of the conditioning of "sensation", a conditioned discrimination training procedure was used to establish that there exist private stimulus concomitants of the EEG alpha burst. With monopolar recordings of the EEG, and the subject lying relaxed with his eyes closed, the experimenter sounded a bell sporadically about five times per minute. The bell was sounded on a random schedule, coinciding half the time with an alpha burst and half the time with the absence of alpha rhythms. The subject was instructed to guess "yes" or "no" depending upon "how he felt" at the time of the bell. The "yes" responses to the presence of alpha and the "no"
responses to its absence were reinforced by being called "correct" by the experimenter. In 50 to 500 trials, six subjects learned to make nearly 100 percent correct responses. Cardiac and respiratory activity, eye movement and muscle tension did not appear to be supplying cues. (97) In another investigation of the "sensation" accompanying the EEG, one subject learned to predict his own paroxysmal epileptiform activity. (154) How the subjects of these two experiments achieved a stimulus from what is considered a purely subjective effect is not suggested in the reports.

It is reported that a leading Russian worker in this field has published on a means of conditioning vasoconstriction in air crews. The method was presumably sufficiently perfected to permit its use with all fliers. The object of the training was to provide a prompt emergency measure in the event of pressure suit failure; a conditioned response would serve well.

Thus far, the examples given have served to show that sensations can be derived, once a subject is trained, from regions of the body which, for good, survival-oriented reasons, are usually "ignored". They have also shown that an external display can replace -- even falsely -- visceral sensations. They have further shown that external control over an activity which is usually mediated purely by
autonomic responses can be achieved with conditioning. These observations give credence to the idea that some measure of control over motion-induced symptoms can be achieved.

d. Other Psychological Factors

In order to rationalize a training procedure three more examples are given below. These, in the order which they are presented, demonstrate: that an aversive stimulus can be used to achieve a conditioning pattern similar to a pleasant one; that an appropriate warning signal will reduce the degree of autonomic response to a noxious stimulus; and that a "reward" need not be intrinsically valuable so long as it is independently more probable -- that is, that the reinforcement relation is reversible.

Brief electric shocks were delivered to monkeys at irregular time intervals but only while a light was on. At first, a single press of a lever was made sufficient to extinguish the light. Later, more lever presses were required. This method of training produced responses similar to a comparable scheme in which an animal was rewarded with food instead of being punished with shock. (3)

The galvanic skin response of rats to an electric shock was found to be smaller when a prior warning signal was given. If the signal was given too long before the onset of the shock, less
reduction in the autonomic response was noted. Likewise, if the warning barely preceded the shock, little reduction in response occurred. (114)

Using rats, experiments were conducted in which drinking was made contingent upon running an activity wheel. With the same animals, being permitted to run was later made contingent upon drinking. Which activity was the "reward" depended on whether that activity was the more probable under the conditions imposed. (137)

The two main observations mentioned at the start of this section have been reviewed. The data available with respect to each of them is encouraging. Because of the apparent irrelevance of psychogenic factors in motion sickness, it is possible that Astronauts may be trained to lessen the functional effects of motion while having any personality profile suitable for their work. The neurophysiology, the anecdotal data and the experimental evidence on conditioning all point to the possibility that a successful training protocol can be devised. The material to follow deals with the theoretical framework of such a protocol, with a particular experiment prerequisite to the training regimen and with a specific method of inducing resistance to motion sickness.
3. **A Model of Training**

Figure 1 (following page 81) shows, in the first diagram, a much oversimplified scheme of the motion sickness cycle. It depicts the various sensory inputs to a subject, a few typical signs and symptoms associated with motion sickness, and the cyclic nature of the disorder. In this diagram is made the distinction between the common sensory inputs, called exteroceptive, and the visceral and other "subjective" sensations, called interoceptive.

In the common sequence of severe motion sickness, leading to pernicious vomiting, the interoceptive stimuli tend to reinforce the imbalance already present and to drive the psychophysiological system farther from a homeostatic state.

The second diagram is of an early stage in the cycle, before the positive feedback has become established. It shows an interoceptive path by which a subject might have knowledge of his impending discomfort if only he were trained to become aware of the sensation. This early "warning", it is assumed, is present in the sequence but goes unheeded in untrained subjects. The model of training being set forth here depends, in part, upon structuring a training program so as to condition the trainee to use his earliest interoceptive stimuli as feedback, not to aggravate his symptoms but to mitigate them.
The third diagram shows the proposed means of conditioning the subject to an awareness of his early signs of motion sickness. Here, (one or more) early signs are detected by transducers which in turn activate a display sensible to one of the subject's exteroceptive pathways. The display will acquire the power of a secondary reinforcement by giving early warning of the imminence of motion sickness or of its successful avoidance. Since the display will now be paired invariably with the interoceptive stimuli, it can be expected that the subject will, in time, become conditioned so that what was "virtual feedback" becomes "intrinsic feedback" capable of modifying his behavior.

The first diagram of Figure 2 (following Figure 1) shows the presumed result of the instrumentation used for the conditioning. What had been merely a virtual interoceptive link has been established as intrinsic feedback, available for the subject's use as a stimulus to which mitigative behavior will be the response. That this effect can reasonably be expected is seen from a consideration of any training method in which, for example, the kinesthetic sensations are called upon. Whether one is teaching tennis, piano, or flying, one object of the
program is to make the student aware of sensations which he already has and to encourage him to interpret them as stimuli to which "correct" actions are the response.

The next diagram includes, schematically, the mitigating response which it is desired to elicit. That these responses do, in fact, exist is an assumption made credible chiefly by the instances in which persons have learned to control their motion sickness by fortuitous training. The rationale of this part of the proposed conditioning process is that when the subject has learned to interpret his interoceptive stimuli, making of them intrinsic feedback, he will then have a signal early enough to call upon a hypothesized mitigating response. In this way he will be able to interfere with the formation of the motion sickness cycle.

The anticipated consequence of the training is depicted in the third diagram. Here are shown the motion sickness producing stimuli, resulting in the early signs. These signs yield intrinsic feedback to the subject (drawn twice, for clarity) who summons a mitigating response. This response, in turn, becomes a stimulus which acts to reduce the effects of the disturbing motion. The intrinsic regulation, it is suggested, acts as negative feedback, allowing the
diminution or deferment of the symptoms of motion sickness. Thus, through a plausible training regimen, the subject can learn to adapt in a way that preserves physiological and psychological homeostasis.

The model of training presented here is consistent with what is known of interoceptive conditioning. Its validity depends upon the existence of the virtual feedback channels and on the conditionability of these channels to act intrinsically. It should be noted that the success of the scheme does not depend upon knowing the means by which the subject acquires his intrinsic feedback. Neither does it depend upon knowing the exact nature of the mitigating response which he chooses. Since at least some of the etiology of motion sickness itself is idiosyncratic, it is well that the means by which the training is effective also depend in its details upon the individual. The intrinsic feedback, for example, need not arise in the sign which is instrumented, so long as it is consistently concomitant with that sign. Similarly, it does not matter to the effectiveness of the method whether the intrinsic regulation achieved is related to the viscera or is a ritualistic gesture, so long as it works and does not interfere with the subject's normal activity. The object of the proposed method is to encourage quick and reliable
POSSIBLE RESULT OF INSTRUMENTATION

DETECTION III

VIRTUAL REGULATION

EARLY STAGE: POSSIBLE ADAPTIVE MECHANISM

CONTROL I

RESULT OF TRAINING

CONTROL II

bio-dynamics, inc.
Sight, Hearing & Other Exteroceptive Stimuli

Motion Sickness Producing Stimuli

Subject

interoceptive stimulus

nausea, vomiting, other late signs & symptoms.
dizziness
drowsiness
disturbed peripheral circulation
other early signs & symptoms

THE MOTION SICKNESS CYCLE

virtual interoception

Other Exteroceptive

Subject

Early signs & symptoms

Detection II

MS Producing

DISPLAY

extrinsic feedback

transducer

INSTRUMENTED EARLY STAGE

Detection I

Subject

Early sign(s)

bio-dynamics, inc.
acquisition of techniques which there is reason to believe are often learned fortuitously. The emphasis is operational; not how the subject is trained, but whether.

4. **A Method of Training**

In devising a training protocol to carry out the proposed conditioning procedures, it is well to consider the problem in more classical terms than those used above. A subject exposed to disturbing motion emits a broad variety of responses, some of which aggravate his illness and some of which may have reduced it had they come into play soon enough. In the unstructured situation, the positive reinforcement of the latter responses is so delayed that it is ineffective. If there existed immediate interoceptive or exteroceptive stimuli these may well acquire secondary reinforcing qualities, providing that they are distinctive and reliable. Essentially, what is proposed is to supply a prompt, distinctive and reliable display, changes in which will acquire reinforcing properties of their own. In this way it is thought that formerly ineffective (interoceptive) stimuli will in turn become secondary reinforcers by their invariant association with the artificial signal.

a. **Prerequisites For A Training Protocol**

It is important to avoid "failure" in the trials in which the extrinsic signal is coupled with the interoceptive stimuli; it is
during successful behavior in which the effectiveness of his response is exhibited to him that the subject learns the desired control. Every occasion on which the subject manages to control his responses is a success and these should be arranged to occur repeatedly.

Control over the display, of course, is not sufficient. The sign or signs used must be stably correlated with the symptoms of motion sickness so that suppression of the sign alone cannot occur. The selection of appropriate signs to instrument must take this and other factors into account. Among the other factors are the ease of obtaining a reliable measure, the temporal sequence (the earlier in the syndrome, the better, but this may be subject to individual variation), and the normal variability of the signs. Also, in view of the desirability, discussed below, of having the subject carry out his normal activity insofar as possible, the chosen sign should be capable of being instrumented in an unobtrusive way. On the other hand, data conditioning and processing equipment remote from the subject is not subject to the same limitation since it is to be dispensed with after the conditioning has taken place. It appears, in the light of these requirements, that it would be desirable to conduct a brief but systematic examination of signs which are potentially usable, not that there is any dearth of data on motion sickness, but that the
specific need for a sign usable in a conditioning situation has not been explicitly considered.

Table I (on the next page) sets forth a partial list of the signs which have been associated with motion sickness, along with the usual symptoms and the physiological system principally involved. The factors limiting the choice of a sign for conditioning make the following ten measurements appear to be the best candidates.

Central nervous system

1. Electroencephalograph

Peripheral circulation

2. Skin temperature
3. Pulse volume

Cardio-vascular

4. Auscultatory blood pressure
5. Pulse wave velocity
6. Deep body temperature
7. Heart rate
8. Oxygenation (ear-lobe oximetry)

Respiration

9. Trans-thoracic impedance

Psychophysiological

10. Galvanic skin potential
<table>
<thead>
<tr>
<th>System</th>
<th>Symptom</th>
<th>Sign(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central Nervous</td>
<td>drowsiness</td>
<td>EEG</td>
</tr>
<tr>
<td>Peripheral circulation</td>
<td>feeling of warmth</td>
<td>pallor</td>
</tr>
<tr>
<td></td>
<td></td>
<td>anomalous skin temperature</td>
</tr>
<tr>
<td></td>
<td></td>
<td>pulse volume</td>
</tr>
<tr>
<td></td>
<td></td>
<td>blood pressure</td>
</tr>
<tr>
<td>Cardio-vascular</td>
<td>headache</td>
<td>heart rate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>blood oxygenation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>blood pressure</td>
</tr>
<tr>
<td></td>
<td></td>
<td>cerebral blood flow</td>
</tr>
<tr>
<td>Gastro-intestinal</td>
<td>vomiting</td>
<td>gut pressure</td>
</tr>
<tr>
<td></td>
<td></td>
<td>peristalsis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>gastric pH</td>
</tr>
<tr>
<td></td>
<td></td>
<td>salivation</td>
</tr>
<tr>
<td>Ocular</td>
<td>dizziness</td>
<td>nystagmus</td>
</tr>
<tr>
<td></td>
<td></td>
<td>pupillary response</td>
</tr>
<tr>
<td></td>
<td></td>
<td>retinal artery flow</td>
</tr>
<tr>
<td></td>
<td></td>
<td>electro-oculograph response</td>
</tr>
<tr>
<td>Autonomic nervous</td>
<td>feeling of fear</td>
<td>galvanic skin response</td>
</tr>
<tr>
<td></td>
<td>feeling of alarm</td>
<td>heart rate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>respiration rate</td>
</tr>
<tr>
<td>Skeletal musculature</td>
<td>headache</td>
<td>myographic response</td>
</tr>
<tr>
<td></td>
<td>&quot;tenseness&quot;</td>
<td></td>
</tr>
</tbody>
</table>
The experiment designed to select an appropriate sign or signs and means of transduction will also yield valuable data concerning individual variability in the range of normal responses, the sequence of occurrence and the rate of change of signs.

The subjects in this experiment should not subsequently be used in the conditioning situation since it is possible that they become psychologically sensitized to the motion-producing equipment. Having been instrumented for one or more of the measurements listed above, each subject should then be introduced to movements sufficient to produce motion sickness. All degrees of motion sickness should be induced, stepwise if possible, from faint nausea to vomiting. The data thus acquired should be analyzed to determine which of the signs meet the necessary criteria: early occurrence and stable correlation with motion sickness. Of those that meet these requirements, the ones allowing the easiest and most reliable instrumentation will be used to provide extrinsic feedback.

The selection of an appropriate means of display to the subject also must be considered. Since the display is essentially a semantic device, not having any intrinsic connection either with motion or with sickness, its selection can be made on the basis of suitability and convenience. Several factors will bear upon its suitability:
The display must not be too "interesting", lest it distract the subject rather than play its proper part in conditioning. No display should be used which prohibits a subject from carrying out his normal activities, or which interferes with other displays.

The display should be capable of several discriminable states or intensities.

The display should be capable of being presented intermittently without affecting its discriminability.

A cursory survey of the sensory pathways seems to indicate than an audible display would suffice, providing it did not interfere with voice communication. To obtain the required variation in intensity without interfering, it is suggested that a tone of approximately constant (subjective) loudness be used, the frequency of which is proportional to the intensity of the chosen sign or combination of signs.

The proposed display has the required aspects; its pitch depends upon the intensity of the chosen sign and its frequency of presentation can be varied to suit a reinforcement schedule. In use, then, the subject will receive information about his performance each time a tone is presented. As the training proceeds,
the presentation of the tone will be caused to occur more and more rarely until the extrinsic feedback which they supply is no longer needed because the desired conditioning is established.

b. The Training Situation

Having selected a suitable sign or signs and having arranged an appropriate display such as the variable-frequency tone suggested, the subjects to be conditioned are initially exposed to motion sufficient to produce mild motion sickness. Care must be taken at this point to avoid severe motion sickness lest the apparatus itself become a conditioned stimulus for the very symptoms which are to be mitigated. Each subject is continued with the mild degree of stimulation until he is able to achieve a significant reduction in the intensity of the sign. He is then advanced to the next most sickening motion and again maintained at that level until he reduces the severity of the sign. Step by step, then, the nauseating motions are increased, waiting at each step until the subject reduces the sign to the criterion level. The reinforcement which the subject receives is the change in pitch which indicates a reduction in the sign.

During the period in which the severity of motion is being increased from the most mild to the most traumatic, the reinforcement tone has been periodically giving to the subject
information about his physiological response. The rate of presentation of the tone is maintained constant until the most severe motions are accommodated. When this occurs, the period between successive presentations of the tone is gradually increased until it is longer than the time it usually takes the whole motion sickness sequence to occur. It is then dispensed with and used only when it appears that reconditioning is required.

Thus, the progressive change in resistance to motion sickness is the measure of success of the method. Each exposure to motion serves as a control on the succeeding trial; if a subject goes from one level to the next, it is because of success at the lower level. Of course, it is recommended that as much instrumentation as is readily feasible be used to monitor the various physiological signs during the conditioning process.

If the procedure outlined above is found effective, it does not necessarily follow that the subjects have been conditioned by the display. If it is desired to demonstrate that the display is an essential part of the process, it will be necessary to expose a control group to the same motions without any extrinsic feedback but with the same transduced information available only to the experimenter.
c. Potential Side Effects of Training

Partly because the mitigating responses which may be developed by a subject who has undergone the proposed conditioning are unknown -- perhaps even to him -- there is the possibility that the very set of responses he develops to ward off motion sickness will prove undesirable in some other respects. It may not be sufficient to train a subject in an unfamiliar environment and test his job performance periodically since the responses he is developing may become too deeply ingrained before their undesirability is detected.

For example, they might interfere with the carrying out of an Astronaut's duties in space. To guard against this eventuality, it is suggested that his conditioning be done in a mock space capsule so that a continuous check on his performance can be made. Likewise, if a radio operator is to be a test subject for conditioning, it should be arranged that he can operate radios while he is being trained.

Another reason that a mock environment is suggested for the conditioning procedure has to do with the transfer of training. As with certain athletes, the object of the proposed training protocol is to allow interference with the symptoms of motion sickness. This training, if it succeeds, will probably continue to be effective
whenever sickening motions are experienced by the trainee unless steps are taken to relate the training program to a specific environment. To avoid the possibility that the set of conditioned responses ever become an unwanted characteristic, the training situation should be made constant and specific to the trainee's tasks. In this way, it is likely that he will be able to resist motion sickness in similar environments, but not in all.

A third reason that, for Astronauts, a simulated space vehicle is suggested for a training location is the minimizing of uncontrolled variables. To them, the inside of a capsule is a more familiar place than any laboratory rotating room or centrifuge.
H. Conclusion

1. Although the precise etiology of motion sickness and the mechanisms of its suppression are unknown, the anatomical and physiological bases for these processes can be described. From an operational point of view, the development and evaluation of vestibular training procedures need not wait upon detailed definition of these mechanisms. The immediate need is for methods of observing the early signs (physiological and behavioral) and symptoms of motion sickness, because training must be directed toward the elimination or interruption of the sequence of these syndrome precursors.

2. Most individuals do acquire a resistance to motion disturbance. Their habituation appears to be highly specific to the motions of themselves and for their environment which produced it; there is little, if any, automatic transfer or generalization of suppression from one motion situation to another. Habituation is reversible. Avoidance of exposure to the disturbing stimuli for a period of several weeks results in a marked de-conditioning.

Skaters and others who perform high speed maneuvers do not use any conscious "tricks" other than constant practice to acquire or maintain habituation.
3. Individuals having apparently equivalent vestibular functions (as observed in standard clinical tests) differ greatly in their ability to adapt to motion. There is no test known which will predict with certainty the parameters of an individual's 'susceptibility envelope', although cupulometry, personal history (motion sickness experience) questionnaire and response to coriolis acceleration provide suggestive evidence of susceptibility.

4. Methods which have been used to select and train Astronauts have served as adequate preparation for whatever vestibular disturbances might occur in the first four days of space flight. Symptoms which have been experienced produced no decrement in performance. If space sickness of vestibular origin occurs at all, it is more likely to be experienced in the latter portion of prolonged non-rotating vehicle flight, when unaccustomed acceleration forces are encountered.

High performance aircraft commanders on field flying status suppress motion disturbances far better than commercial airline pilots and non-flyers. Titov had considerable less acrobatic flying experience than the other Vostok and Mercury pilots. It seems safe to conclude that non-pilot Astronaut candidates will
have to be given special vestibular training to provide them with symptom suppression capability equivalent to that afforded by extensive pilot experience.

It is certain that some forms of training will have to be developed to prepare crews for the disturbances which have been observed during the first few hours on board rotating vehicles, and which reoccur upon leaving a rotating platform. Development of such procedures -- using the Slow Rotating Room -- will undoubtedly provide a basis for design of a training regimen for non-rotating vehicle crews, should the need for such training become evident as a result of future flight experience.

5. Data available from conditioning studies in which the conditioned stimulus or response involves organs and nerves not normally used in purposeful behavior, suggests that some measure of control over motion-induced symptoms can be achieved through a deliberate training protocol.

6. There is no experimental data on the relative effectiveness of alternative methods of training the vestibular system which would permit recommendation of a particular program of training. This review did not disclose any investigations of the efficiency (including side effects) of training versus use of drugs in suppressing motion sickness.
I. **Recommendations**

1. **Training Procedures to be Incorporated into Astronaut Training Program**

   There are no experimental data available at this time which would argue in favor of a particular type of vestibular training, although regular operation of high performance aircraft appears to afford beneficial proactice in suppression of motion sickness symptoms. Design of preflight and on-board training procedures to provide resistance to "space sickness" must await:

   a. Observation of the incidence of the syndrome in the space environment in order to determine its most probable causes and effects upon mission success, and,

   b. Terrestrial experimentation along the lines suggested below directed toward determining the sequence and interrelation of signs and symptoms of the motion sickness syndrome, and evaluating the efficiency of alternative approaches to conditioning individuals to interrupt or defer its progress, and comparing the effectiveness of these training approaches with drugs.

   Particularly in selection of non-pilot astronaut candidates, criteria of adequacy of vestibular function should include the rate of an individual's habituation to a novel motion. Any training procedure found
effective should be regularly used in preparation for flight -- and, if possible, in flight.

2. **Future Research**

The following general recommendations regarding future investigations are classified according to the apparent immediacy of their relevance to vestibular training. Many of these areas are now being studied or will be addressed in the near future.

a. **Experimental Findings Probably Needed for Design of Vestibular Training Program**

1) Investigation of the mechanism and sequence of the development of autonomic effects as a result of vestibular stimulation alone, and in the presence of other disturbing stimuli, should be pursued with modern methods of instrumentation and data analysis. A related experimental area is the determination of the effects of various levels of the syndrome on the ability of highly motivated persons to perform command-type tasks.

2) An attempt to directly condition subjects to resist motion sickness should be made, taking advantage of interoceptive conditioning procedures. At first, the subject population should consist of pilots who are not to become astronauts and of ground-based personnel. The conditioning situation should be
arranged so that a realistic working environment is maintained, "failures" occur rarely, and a continuous measure of conditioning is obtained. A control group should be paired with the subjects being conditioned.

3) Physiological and psychological measures should be used to attempt to distinguish between habituation and conditional reflex formation to determine their relative importance in the diminution of the effects of vestibular stimulation in the Slow Rotation Room.

4) Attempts to evaluate transfer of conditioning from the Slow Rotation Room to other stimulus devices (rotational and linear) should be undertaken, for example, by the study of the relationship of experience in the Slow Rotation Room to cupulometric responses.

5) Controlled studies of the effects of voluntary exercise in a stationary environment should be made.

6) A systematic investigation of the controller versus controlled (pilot-passenger) differences in response to motion stimuli should be undertaken.

7) The relationship of experience in the Slow Rotation Room to optokinetically produced nausea should be
investigated to evaluate the quantitative relationship between optic and vestibular stimulation as a factor in the production of motion sickness.

a. Longer Range Investigations

1) A careful roentgenological and anatomical study should be undertaken to determine whether significant individual differences in labyrinthine structure exist, and what the pertinent variables are. Further study of the biomechanics of the inner ear may provide insight into individual susceptibility to particular motion.

2) Some attempt should be made to develop techniques of remote neuro-otolological diagnosis for space experimentation.

3) Investigations into the biochemical aspects of motion sickness susceptibility should be made with attention given to pedigrees, using refined techniques of analysis for enzymes, particularly the cholinesterase type.
Bibliography


4. Anon., Adaptation to Flying Motion by Airsick Aviation Students, School of Aviation Medicine, Project 170, Report 4, 1943.


10. Anon., Manned Space Flight Program of NASA, Staff Report of Senate Committee on Aeronautical and Space Sciences, 4 September 1962.


58. Gerathewohl, S., Physiological and Psychological Tolerance for Survival to Weightlessness, USAF School of Aviation Medicine, Randolph AFB, Texas, Presented at the ARS Spring Meeting, Washington, D. C.

59. Gerathewohl, S. J., Personal Experiences During Short Periods of Weightlessness, Reported by sixteen subjects. Article #29, Epitome of Space Medicine, USAF.


77. Guedry, F. E., Jr., et al., Reduction of Nystagmus and Disorientation in Human Subjects., USN School of Aviation Medicine, Order R-47, NASA, Report 69, 19 June 1962.

78. Guedry, F. E., Jr., et al., Human Performance During Two Weeks in a Room Rotating at Three RPM, NASA Order No. R-47, U. S. Naval School of Aviation Medicine, 28 August 1962.

79. Guedry, F. E., Jr., et al., Reduction of Nystagmus and Disorientation in Human Subjects., NASA Order 47, U. S. Naval School of Aviation Medicine, 19 June 1962.


85. Hemingway, A., Results of 500 Swing Tests for Investigating Motion Sickness, AAF School of Aviation Medicine, Randolph AFB, Res. Project 31, Report No. 2, November 1942.

86. Hemingway, A., Cold Sweating in Motion Sickness, Am. J. Physiol., 141:72-175, 1944.


105. Kraus, R. N., Early Diagnosis of Hydrops of the Labyrinth., Review 1-61, School of Aviation Medicine, USAF Aerospace Medical Center (ATC), Brooks AFB, Texas, February 1961.


121. McCabe, B. F., Vestibular Suppression in Figure Skaters., Trans. Amer. Acad. Ophth. and Otol., 64:1960.


123. McNally, W. J. and Stuart, E. A., Physiology of the Labyrinth Reviewed in Relation to Seasickness and Other Forms of Motion Sickness., War Medicine, 2:683-771, 1942.


PART II

A. Introduction 100

B. Physiology of the Vestibular Systems 101

1. Receptors of the Non-Acoustic Labyrinth 101

2. Neurophysiology of the Vestibular System 105
   a. Vestibular Nerve 105
   b. Peripheral Neural Signal 106
   c. Projection of the Vestibular Nuclei and Associated Groups 107
   d. Interaction of Vestibular Information at Higher Levels 111

3. Effects of Labyrinthine Stimulation 112
   a. Semicircular Canals 112
   b. Otolith 117
   c. Postural Reflex Control 118
   d. Nystagmus 120

4. Modification of Vestibular Response 122
   a. Habituation 122
   b. Conditioning 123
   c. Habituation and Conditioning in Slow Rotation Room 124

C. Vestibular Disturbances in the Space Environment 129

1. Vertigo 129

2. Relevant Radiation Effects 135

D. Mechanical Aspects of the Vestibular System 137

Bibliography
Part II

A. Introduction

Part I of this Report presented experimental and anecdotal evidence which seems to be directly relevant to the question of whether the vestibular system can be conditioned to provide an individual with a high degree of resistance to motion sickness. The material in the following portion of the Report is not demonstrably related to this question; it is presented with a view toward providing additional background information to assist evaluation of the conclusions and recommendations presented earlier.
B. **Physiology of the Vestibular Systems**

1. **Receptors of The Non-Acoustic Labyrinth**

   Ref: 29, 49, 141, 156, 157, 168, 174, 175, 176, 177

   The sensitive hair-celled epithelia of the cristae and maculae of the non-acoustic labyrinth, are composed of two cell types, deployed such that those cells which connect with large nerve fibers (up to 6-9µ in diameter), (type I) are central, and those which connect with fine nerve fibers, (down to 1-2µ in diameter) are peripheral (type II). Type I cells, flask-shaped, have been shown by electron microscopy (figure 3) to be surrounded by a neural chalice, derived from a myelinated nerve fiber and devoid of "granulations" except at its distal tip. This chalice is impinged upon, in turn, by granulated end-feet whose origin is obscure, whether from recurrent collaterals, from collaterals from the finer fibers innervating the cristal periphery, or from true efferent fibers in the vestibular nerve rami. The smaller, peripheral, cylindrical cells, type II, receive many granulated end-feet probably collaterals from the larger fibers innervating the neural chalices of the type II cells.

   Both cell types possess cilia, the majority of which are of stereocilial configuration, though one process from each cell has a kinocilial structure. The hair-cells are surrounded by supporting cells, which in turn thrust small villous processes into the gelatinous
Figure 3

Highly schematic drawing of a section through the sensory epithelium of the crista ampullaris, showing the ultrastructural architecture of cells and nerve endings. HC I, hair cell of type I; HC II, hair cell of type II; SC, supporting cell; St, stereocilia; KC kinocilia; N, nucleus; GA, Golgi apparatus; IM, intracellular membrane system; VB, vesicular body; NC, nerve calyx; RM, reticular membrane; M, mitochondrium; NE, nerve endings; BM, basement membrane; MN, myelinated nerve; LG, lipid granule; MV, microvilli. From Wersall, 1956. Acta Otolaryng. Stockh., Suppl. 126, 1-85.
mass of which the cupula is composed. The nature of the granu-
lated endings is obscure, whether afferent or efferent. Recent
electron microscope investigation tends to support the concept
that granulated or vesiculated endings are pre-synaptic in function,
though exceptions to this concept have been found, as perhaps in
the case of the neural chalice of the type I unit.

"Hair cells of type I are looked upon as being highly differen-
tiated cells with a more specialized function than that of the type II
cells. Each of the thick nerve fibers innervates only a few nerve
chalices located within a small area, whereas the thin nerve fibers
often innervate a large number of cells within a considerable
area of epithelium. It is thus (sic) believed that the hair cell of
type II reacts to stronger stimuli spread over the entire sensory
epithelium, whereas the type I cell is more sensitive and represents
only the response within a very limited area of the epithelium." (53)

The cupula (Figure 4) has been shown to be composed of tubes,
into which the cristal hairs project. It has been suggested that a
generator potential is produced by electrostriction of the hairs in
the confined tubular spaces of the cupula acting on a viscous
glycoprotein matrix, whenever the cristae in the ampullae of the
semicircular canals are displaced by rotation.
Figure 4

Schematic drawing of one half of a crista ampullaris, showing innervation of its epithelium. Thick nerve fibres forming nerve calyces round type I hair cells at the summit of the crista; medium calibre fibres innervating type I hair cells on the slope of the crista; medium calibre and fine nerve fibres forming a nerve plexus innervating hair cells of type II. The sensory hairs pass from the hair cells into fine canals in the cupula, which is separated from the epithelium by a narrow subcupular space. From Wersall, 1956. *Acta Oto-laryngol. Stockh.* Suppl. 126, 1-85.
The maculae in the utricle and saccule are covered by a mucous or gelatinous substance which contains aragonite concretions (otoliths or otoconia) of calcium carbonate, whose specific gravity (2.93 - 2.95) is greater than that of the surrounding endolymph. It is claimed that the otoliths are of two or three grades of fineness arranged in a mosaic on the receptor surface, providing spatially separated graded inertial stimuli upon linear acceleration. The macula of the utricle is situated on its anterior and medial walls, the two portions being joined at an angle of 140°. The saccular maculae are situated obliquely forming an angle of about 30° with the vertical plane. With the head in the erect position, the utricular macula is in a horizontal position, with the otoliths lying upon the hair cells, while the saccular otoliths are inclined. The crista is about one-third the height of the ampulla (in mammals), and the utricle is shared by three semicircular canals, so that upon high rates of rotational acceleration, fluid flow may occur in the utricle and fluid transfer between canals may take place. This is thought to occur rarely.

The concept has been advanced that endolymphalic circulation arises in the stria vascularis and is absorbed in the connective tissue surrounding the saccus endolymphaticus. However, extirpation of the saccus endolymphaticus sympathetic stimulation and parasympathetic and sympathetic denervation of the inner ear produce surprisingly few results. A valvular mechanism for endolymph behavior in the region of the utricle has been described.
Investigation of the chemical composition of endolymph reveals two salient aspects: a much higher concentration of protein in endolymph and perilymph as compared with cerebrospinal fluid (about 120/130 mg. %), and reversal of the sodium/potassium ratio in endolymph as compared with cerebrospinal fluid (about 150/4 mEq. /L in cerebrospinal fluid as compared with 16/144 mEq. /L in endolymph). Small but significant differences in osmotic pressure and refractive index were also found to exist between the two fluids(32). The origin of perilymph and endolymph is obscure. Radioactive tracer studies reveal active secretion of an S35 label in the planum semilunatum of the ampullary epithelium, with a peak being reached 24 hours after administration.

Butyrylcholinesterase and acetylcholinesterase, characteristic both of afferent and efferent neural terminations (Pacinian corpuscle, muscle end-plate), are found in the basement membranes of the sensitive epithelia of the utricle and saccule.
2. **Neurophysiology of the Vestibular System**

   a. **The Vestibular Nerve**

   Ref: 29, 46, 49, 141, 174, 175, 176, 177

   The branches of origin of the vestibular division of the eighth cranial nerve were reviewed in Part I. Examination of the 12,000 - 20,000 vestibular root fibers in one mammal -- the guinea pig -- indicates that two-thirds of them are of 3-5μ dia. size, one quarters of them are smaller (1-2μ dia) and the remainder are larger (6-9μ). These differences in fiber size provide a basis for temporal dispersion of the neural signal.

   Recent investigations have revealed the presence of and provided some information concerning the loci of origin of the efferent fibers in the vestibular nerve (200 of the total 12,000 - 20,000 fibers). Petroff claimed a contralateral origin for a component of the efferent system, while Gacek demonstrated a contingent of fibers arising from the ipsilateral lateral vestibular nucleus. (135, 53) The main vestibular afferent group follows the utriculo-ampullar (proximal) branch of the vestibular nerve, after detaching from the efferent cochlear bundle at the saccular ganglion. Some fibers leave as efferents to the saccule and the posterior ampulla. Fibers were observed from their most distal point through Scarpa's ganglion, and were not
observed to be continuous with a cell body. Degeneration was followed into the basement membrane of the neuroepithelium. The fine fiber plexus found in this position, as previously described, was intact, however. Some efferent fibers, crossed and uncrossed, were thought to proceed from the fastigial nuclei of the cerebellum. (29) The precise efferent termination remains obscure.

b. The Peripheral Neural Signal

Ref: 62, 63, 64

A resting discharge is present in the vestibular nerve. It is increased by ampullopetal and decreased by ampullofugal deviation of the cupula in the case of the horizontal canals. These cupula deviations have reverse effect on the vertical canals. Controversy exists over the degree of adaptation of the peripheral vestibular semicircular canal receptor, and doubt remains as to whether adaptation to vestibular stimulation is primarily central.

The adaptation of gravireceptors is slow. The "minimal position" for the gravireceptive signal is found when the otolith rests upon the utricular macula. A "blind spot" has been postulated for the utricular macula based on reflex evidence, but perception of the oculogravic illusion in all orientations in space indicates that this is probably not the case. (63)

Ref: 24, 25, and figure 5

1) The superior vestibular nucleus projects to higher centers, and to the spinal cord and cerebellum. Its afferents arrive from the labyrinth and fastigial nucleus, and those from the labyrinth are centrally oriented in the nucleus.

2) The lateral vestibular nucleus is unique from the embryological standpoint, and possesses two distinct cell sizes, giant and small. All cells project to the vestibulospinal tract of the same side, and it has been suggested that the small cells control the fine-fibered "gamma-loop" reflex system.

Primary afferents are derived from the utricular macula, and project to the rostroventral portion of the nucleus, the same portion which projects the vestibulospinal tract to cervical regions. Cerebellar afferents project to the dorsocaudal portion of the nucleus, the region which projects the vestibulospinal tract to lumbar regions. Cerebellar cortical afferents project to the giant cells. Fastigial nuclear afferents (from the fastigial or "roof" nucleus of the cerebellum) project to the small cells.

3) The medial nucleus of the vestibular nuclear complex receives the only clear-cut downward projection from regions
Figure 5

Simplified diagrammatic representations of the principal afferent and efferent fibre connections of the four major vestibular nuclei. Internuncial cells, short internuclear connections, connections with the reticular formation, vestibular afferents from the flocculonodular lobe and some other quantitatively small fibre components are not included. In the diagrams the oculomotor nucleus represents the three nuclei of the nerves to the extrinsic ocular muscles. The other terminations of the ascending fibres in the medial longitudinal fasciculus are not indicated. The indications concerning crossed and uncrossed ascending and descending fibres in this bundle are derived from conflicting data in the literature and are not definitely established.

A. Principal connections of the lateral vestibular nucleus of Deiters. The inset below to the right represents a diagram of a sagittal section of the nucleus, showing the principles in the distribution of afferents from various sources. The broken line drawn across the nucleus subdivides it into rostroventral "forelimb" and dorsocaudal "hindlimb" regions, which receive primary vestibular fibres and spinovestibular fibres, respectively. Note that the border between the projections from the caudal and rostral parts of the fastigial nuclei cuts across the border between the somatotopic subdivisions. The modes of termination of the various groups of afferents are indicated. Note that cortical cerebellovestibular and spinal afferents end on giant cells, primary vestibular and fastigiovestibular fibres on small cells.

B. Principal connections of the superior vestibular nucleus. Inset below to the right shows a horizontal section through the nucleus in which the terminal areas of afferent fibres are indicated. Note the distribution of primary vestibular fibres chiefly to the central regions of the nucleus, of cerebellar fibres to the peripheral regions.

C. Principal connections of the medial vestibular nucleus. Inset below to the right shows a transverse section through the nucleus, in which the terminal regions of the various groups of afferents are schematically indicated.
D. Principal connections of the descending (inferior) vestibular nucleus, and the groups f and x. Inset below to the right shows a transverse section in which the terminal regions of the various groups of afferents to the descending nucleus are schematically indicated.
other than the cerebellus. This is a tract from the interstitial nucleus of Cajal in the mesencephalon. The medial vestibular nucleus in turn, projects to the spinal cord, cerebellum, and higher centers. In addition to the path from the interstitial nucleus of Cajal, afferents to the medial nucleus arrive from the crista and utricle, and from the fastigial nucleus of the cerebellum. The cerebellar cortex, however, does not project afferents to this nucleus. Efferents to the sensitive epithelium arise from this nucleus.

4) The descending vestibular nucleus projects to the spinal cord via the spinal portion of the medial longitudinal fasciculus. Fastigio-vestibular fibers traverse this nucleus to form the tractus parasolitarius and end in the perihypoglossal nuclei in the reticular formation. Their termination is close to the physiologically identified "vomiting center". The descending nucleus is characterized by its internuncial cells, providing the basis for computation and pattern recognition at a nuclear level.

5) Several small regions near the vestibular nuclei have been described. "Group f" does not receive primary vestibular afferents but does receive fastigial nuclear afferents and projects to the cerebellum. "Group x" receives spinal cord and
contralateral fastigial projections, and projects to the cerebellum.

The interstitial nucleus of the vestibular nerve does receive primary afferents, and projects to the spinal cord and the medial longitudinal fasciculus.

6) Reticular formation projections have not been defined with accuracy. Since vestibular stimulation produces ocular nystagmus even when the long tracts upward from vestibular system are sectioned, there may be alternate pathways via the reticular formation.

7) Cerebral cortical projections.

Ref: 24, 25

Variation of nystagmus by lesions in areas in the temporal lobe has been described (optokinetic nystagmus, directional preponderance) in clinical subjects. (30, 31, 44) In experimental animals, Speigel demonstrated a projection contralaterally to the posterior suprasylvian and etosylvian gyri (cat). (150) Gerebzoff demonstrated a projection to the posterior suprasylvian gyrus ipsilaterally. (59, 60, 61) Mickle and Ades demonstrated a projection contralaterally in a region rostral and lateral to the auditory area in the posterior bank of the anterior suprasylvian gyrus and the anterior bank of the anterior ectosylvian gyrus. (124, 125) The latter authors
believed the pathway to parallel, but not to coincide with, the auditory pathway, through Gernandt could record responses to vestibular stimulation from single units in the inferior colliculus (on the auditory pathway). (62) The projection to the colliculus was bilateral.

8) Cells in the vestibular ganglion and in the lateral vestibular nucleus (Dieters' nucleus) can be shown to be chemically modified by vestibular stimulation. Thirty to forty-five minutes after rotation of rabbits at various speeds and in alternating directions for two minutes "a considerable increase in the total amount of proteins in the ganglion cells can be observed. The original chemical composition is restored after 48 hours... A considerable production of nucleoproteins takes place in the cytoplasm of the ganglion cells... On repeated stimulation...the total amount of ribose nucleic acids and proteins is decreased in the rotated animals as compared with the controls". Transneuronal changes occur in the cells of the lateral vestibular nucleus following rotatory stimulation. These changes consist of an increase in the chromocentre areas of the nucleus of the cells after brief stimulation (2 minutes). With prolongation of the stimulus (16 minutes) an increase is found in the total nucleoprotein of the cells, although the increment is less than that of the ganglion cells. (81, 82)
d. Interaction of Vestibular Information at Higher Levels.

The spontaneous activity described in the vestibular nuclei remains after labyrinthectomy and eighth nerve section, suggesting either autogenous activity, or driving from other central nervous system regions. (24)

Recording of single units from the vestibular nuclei reveals a wide range of coding variations in the vestibular signal. One unit may respond to rotation in both directions with an increase in frequency, others may respond with an increase in frequency to rotation in one direction and with a decrease in frequency to rotation in the opposite direction, and still others may respond to rotation in opposite directions with a decrease in frequency.

Interaction between labyrinths directly rather than through the reticular formation has been maintained by some investigators, but this is not universally agreed upon.

Units responding to gravitation and to rotation are found at different levels in the cerebellar nuclear region, conforming with anatomical data. (1)

Units responding to activation of a single folium of the cerebellar cortex nevertheless respond to stimulation from all four
extremities and the trigeminal region, perhaps by previous
reverberation via the cerebellum, though this point has not been
proven. (24)

Recording in the ventral roots of the spinal cord
discloses a multiphasic response, bilaterally to unilateral
stimulation. (64) The multiphasic nature of the response persists
to the ventral roots of the thoracic region and no further. This
may be because the early phases of the response represent impulses
directly relayed from the lateral vestibular nucleus, while responses
arriving at the lumbar region may require cerebellar reverberation.
(24)

3. Effects of Labyrinthine Stimulation
   a. Semicircular canal
      1) Rotational Stimulation

The normal response to Barany chair tests was
reviewed briefly in Part I, and is well described in clinical texts.
Because the techniques of cupulometry is not as well known, and
because it appears to be a singularly useful tool in investigation of
motion sickness and its suppression, its theoretical basis deserves
further explanation (18, 32, 43, 118)
Steinhausen, Van Egmond and their colleagues formulated a mathematical expression for a model cupulo-endolymph system, taking as a basis for their treatment the differential equation of the torsion pendulum where there are no external forces,

\[
\dddot{\zeta} + \frac{\eta}{\phi} \dot{\zeta} + \frac{\Delta}{\phi} \zeta = 0
\]

(1)

where \( \phi = \) moment of inertia of the endolymph

\( \eta = \) moment of friction for unit angular velocity

\( \Delta = \) restoring force for unit angular deviation of the cupula

\( \zeta = \) the angular deviation of the endolymph in relation to the skull

\( \zeta = \) the angular velocity of the endolymph in relation to the skull

\( \dot{\zeta} = \) the angular acceleration of the endolymph in relation to the skull

The constants: \( \frac{\eta}{\Delta} = 10 \), and \( \frac{\phi}{\Delta} = 1 \) can be determined as follows: An approximate solution for impulsive stimulation, that is to say, a sudden stopping of rotation from constant velocity, \( \dot{\zeta} \), is:

\[
\zeta_0 = \gamma \frac{\phi}{\eta} \left[ e^{-\frac{\eta t}{\phi}} - e^{-\frac{\Delta t}{\phi}} \right]
\]

(2)

with limiting conditions \( t=0, \zeta = 0, \dot{\zeta} = \gamma \)

The return of the deflected cupula is determined by \( e^{\frac{\eta t}{\phi}} \), so that, assuming that the deviation of the cupula has
reached a minimal perceptible deflection (3 minutes) when the after-sensation has ceased, then the duration of the after-sensation, \( t_u \), is given by:

\[
\tau_u = \frac{\alpha}{\pi} \left( \frac{\omega \zeta}{\frac{1}{3} \zeta_{\text{m}}^2} \right) \approx \text{approx.}
\]

Thus, a plot of an individual's \( t_u \) vs. \( \log \zeta \) should be linear with \( \frac{\pi}{\alpha} \) the slope, and it generally is. This plot is termed a cupulogram, and either nystagmus or after-sensation are taken as variables for time measurement. It is believed to provide a measure of the cupular reaction time and a reflection of the mechanical characteristics of the cupulo-endolymph system. However, as pointed out in Part I, in the intact subject, such results "must clearly be the resultant of the constants, not only of the cupulo-endolymph system itself, but also of the entire vestibular nervous complex".

2) Caloric stimulation

While the caloric test was originally used as an all-or-none measure of labyrinthine function, it has been demonstrated that the effects of caloric stimulation are dependent not only upon the integrity of the labyrinth, but also upon an individual's "directional preponderance". This directional preponderance (or nystagmusbereitschaft) is a tendency toward increased nystagmus in one direction, and a diminished effect in the other. (31, 33, 50, 103)
This effect has been found to be related to partial unilateral lesions of the labyrinth or eighth nerve, resulting from Meniere's disease, eighth nerve tumors or lesions of the vestibular nuclei as in posterior inferior cerebellar arterial occlusion. Recent studies have indicated that directional preponderance is also dependent upon a lesion of the posterior portion of the temporal lobe, toward which the preponderance is directed. With lesions of the eighth nerve and/or labyrinth canal paresis is often associated with directional preponderance of nystagmus to the opposite side. The origin of this effect is obscure, but the suggestion has been made that it is due to the absence of tonic impulses originating in the otolith organs. Carmichael, Dix and Hallpike state that directional preponderance tends to occur with lesions in the brain stem below the level of entry of the eighth nerve, while canal paresis is less common, and found with lesions at or above this level. In Meniere's disease, eighth nerve tumors, and vestibular neuronitis, disorders of the caloric stimulus-response pattern occur in 90 - 100% of cases, and generally one or the other of the abnormalities is found in isolation, although mixed abnormalities may be present.

Caloric stimulation is not a pure stimulus to the non-acoustic labyrinth, as it involves also, cutaneous nerves of the
external ear and the external auditory meatus, tympanic plexus of cranial nerves, the cervical sympathetic fibers lying in bone close to the middle ear, and the chorda tympani. (149)

3) Electrical Stimulation

Binaural electrical stimulation at 0.5 - 2.0 milliamperes provokes rolling of the eyeballs toward the anode, and at 2 - 4 milliamperes a rotatory or combined rotatory and lateral nystagmus, with the rapid component toward the cathode. Reversal of direction of current reverses the nystagmus. Opening the circuit may or may not change the direction of nystagmus.

Monaural stimulation provokes nystagmus with the rapid phase toward the cathode, but the threshold may rise to 10 milliamperes. The effects of electrical stimulation persisted in decerebrate animals when the labyrinths were extirpated, but ceased with extirpation of the eighth nerve of the vestibular ganglion. (45, 150)

In addition to nystagmus, inclination of the head toward the anode, and falling in the direction of the anode occurs.

Electrical stimulation, like caloric stimulation probably involves cutaneous and cranial nerves, and other intracranial structures as well.

4) Acoustic Stimulation

The non-acoustic labyrinth probably responds to auditory frequencies following fenestration procedures. The cupula
has been found to respond to mechanical vibrations at 10 kc with a microphonic potential. (158)

b. Otolith

The limitations of tilt tables, horizontal swings and part-pointing tests in examining otolith junctions were pointed out in Part I. Functional defects can be noted only when marked bilateral lesions have occurred.

Barany demonstrated a patient in whom nystagmus and vertigo were produced only in the supine position and with the head to one side. The symptoms arose or a consequence of a position of the head in space, rather than or a result of motion. The vertigo was rotatory and subsided rapidly with maintenance of the critical head position. No hearing defect or disorders to caloric stimulation were present. It is thought that the basis of this disorder is a lesion of the internal ear, resulting from occlusion of a restricted portion of the labyrinthe circulation, with degeneration of the macular epithelium and the production of loose otoliths. The effect is termed benign paryxysmal positional nystagmus and vertigo.

Nylen described a variety of disorder which probably depended upon lesions of the central connections of the utricular system. In this disorder the direction of positional nystagmus changes
with the position of the head. This was termed the direction-changing variety of positional nystagmus. This disorder is a common accompaniment of deep lesions of the central nervous system within the posterior fossa, and it may be the only sign. (31)

Quix demonstrated the possibility of diagnosis of otolithic disorders by production of past-pointing and falling dependent upon the position of the head. Past-pointing in the frontal plane indicated lesions of the saccular system. In this test the deviation of movement was brought about by gestures of the patient in the plane perpendicular to the plane of deviation. (140)

c. Postural Reflex Control

Ref: 150

Attitudinal reflexes include local static reactions, general static reactions, segmental reactions, and the tonic neck and labyrinthine reflexes. The local static reactions stem primarily from gravitational stimuli. The general static reactions arise from the actual position of the head in space. Segmental reactions develop as result of afferents from one muscle acting upon fellow muscles of the same segment on the opposite side. Neck and labyrinthine reactions stem from receptors in the labyrinths and in the neck muscles.
The spinal animal possesses the basic pattern of the local and segmental static reflexes. The stretch reflex is elicitable though not strongly developed. The crossed extensor reflex may also be obtained; its presence indicating that segmental static reactions are also laid down at the spinal level. General spinal reactions are also seen, such as reaction pattern which tends to keep the animal from toppling over, and reflexes which are part of the pattern of movement involving forward locomotion.

In the lower decerebrate quadruped (the bulbospinal preparation) all types of static reactions are well developed. The stretch reflexes are present as well as the positive supporting reaction. This reaction starts from touch to the skin of the toe pad, (exteroceptive stimulus). This, however, is followed by a proprioceptive stimulus, which can be separated from the exteroceptive stimulus by anesthetizing the skin of the foot. The crossed extension reflex and an intersegmental static reaction also occur. For example, when a hind limb is caused to extend either through the positive supporting reaction or from a crossed extension reflex, the opposite forelimb also extends, thus demonstrating the influence of the lumbar segments upon the cervical. The same pattern also occurs in reverse. The extension of a forelimb is accompanied automatically by extension of the opposite hindlimb all of which is a pattern essential to quadrupedal standing. Autonomic leg reflexes and the labyrinthine reflexes are also present.
In order to differentiate neck from labyrinthine reflexes both labyrinths must be extirpated, so that only the influence of the neck muscles will be observed when the neck is turned. Rotation of the jaw to the right causes prompt increase in the extended posture of both limbs on the right side and the relaxation of the limbs on the other side. Dorsal flexion of the head of hopping animals causes extension of both forelimbs and relaxation of hind limbs. Ventral flexion of the head causes relaxation of both forelimbs and the hind-limbs. Section of the dorsal nerve roots in the anterior cervical region abolishes these reactions. These reactions are prominent in decerebrate cats and have been also demonstrated in labyrinthectomized monkeys following bilateral removal of the motor and premotor areas. When an animal is placed on its back in a horizontal supine position the extremities are maximally extended. Extension is minimal when the animal is prone with its mouth tilted 45 degrees to the horizontal plane.

d. Nystagmus

Ref: 150

Trigeminal and proprioceptive impulses from the eye muscles can be eliminated without the abolition of nystagmus. A unilateral lesion of the reticular formation may produce nystagmus even if both nerves have been cut. Extensive lesions of the reticular
formation do not inhibit nystagmus on vestibular stimulation. It has been suggested that the vestibular nuclei are the source not only of the slow component of nystagmus, as had been assumed but of the fast component as well. The reticular formation is important however, in this respect. (109, 110) Voluntary eye movements in the direction of the fast component of nystagmus hasten its development as a result of caloric stimulation. It has been maintained that the corticifugal path for voluntary horizontal eye movements proceeds to the eye muscle nuclei via the vestibular nuclei.

It had been thought for some time that optokinetic nystagmus was also dependent upon the integrity of the vestibular nuclei. An extensive study of temporal bones, eighth nerve, and brain stem of a case of advanced sensory neuropathy lent support to a concept derived from previous investigation with streptomycin-toxic subjects that optokinetic nystagmus persists despite massive lesions in the vestibular nuclei. It was felt that the regions in the brain essential for this action are to be found in the posterior portion of the temporal lobes (the supramarginal and angular gyri) of each hemisphere, the same regions which relate to directional preponderance of nystagmus. (30, 31, 44) Thus, this effect may be only indirectly related to any vestibular effects elicited by motion.
4. Experimental Modification of Vestibular Responses

Ref: 128

a. Habituation

Novel stimuli are associated with an orientation reflex behaviorally, and electroencephalographically with neocortical and hippocampal "arousal" over a wide area ("irradiation"). Repeated presentation of a stimulus results in restriction ("internal inhibition") of desynchronization to primary sensory neocortical regions, and also produces diminution of the amplitude of evoked responses at earlier stages in the primary sensory pathways ("consolidation"). The evoked responses in the primary pathways are probably under efferent control, and may be diminished in amplitude by distraction alone. Changing of the parameters of a stimulus configuration to which an animal is habituated, results in "dishabituation" with the appearance of appropriate increases in amplitude in electrophysiological records, and the return of the orienting reflex, which consists not only of electroencephalographic responses, but of autonomic, respiratory, and electromyographic ones as well. (An "habituated" response can also be "dishabituated" or increased in amplitude by barbiturate administration).
b. Conditioning

If a stimulus is reinforced, however, a series of electrical events occurs along with the establishment of a behavioral conditioned reflex. In the neocortex, desynchronization to the conditional stimulus now returns, or it occurs over a wider area, but as training proceeds is localized to more restricted areas. Cortical slow waves also appear in non-specific sensory areas, and frequency-specific slow waves may appear in specific sensory areas as well. In thalamic structures and in the hippocampus, slow waves appear during conditioning. Conditioning may occur on several levels, and hierarchies of conditioned reflexes may be raised. Sensory-sensory conditioning may occur, as may also conditioning involving inputs and outputs to the autonomic nervous system. Examples of this were presented in a discussion of training of autonomic responses.

The output of the vestibular system may be controlled by conditioning stimuli, and an animal may be induced to fall to one or another direction in response to varied tone frequencies by this means. Experiments involving frequent repetition of this effect result on occasion in sleep of the animal, despite reinforcement. (150) This occurs occasionally during conditioning of other somatic systems, and has been thought of by the Pavlovian school as a generalized "internal inhibition".
c. Habituation and Conditioning in the Slow Rotation Room

The phenomenon of habituation to vestibular stimulation has been observed under many experimental circumstances at the USN School of Aviation Medicine. One useful index of human habituation is the oculogyral illusion, described in Part I. As Graybiel et al. have pointed out, although the oculogyral illusion is not perfectly related to recorded vestibular nystagmus, it corresponds closely to it in (a) magnitude of growth during constant angular acceleration and (b) duration characteristics. (71) In a 64-hour run in the Slow Rotation Room, four subjects, chosen for a wide range of history of motion sickness susceptibility all demonstrated habituation (in the sense of a decrease in magnitude) to the oculogyral illusion. The most sensitive subject perceived the illusion throughout a first run at 5.4 r.p.m. The least sensitive subject perceived the illusion only during a run at 10 r.p.m., and then only during active head movements. (70) Post-rotation effects appeared to be inversely related to the degree of adaptation to the oculogyral illusion during the run. Illusions were perceived during the post-rotatory state which were opposite in direction to the direction in which the Room had been rotating during the time the adaptation occurred. This strongly implies a compensatory central effect in adaptation to an unusual vestibular stimulus (coriolis
acceleration). Nystagmus to head movements as well as illusions was revealed in this series of experiments. In a further series Guedry and Graybiel demonstrated compensatory nystagmus in six of seven subjects run for 64 hours at 5.4 r.p.m. more than one hour after the rotation had ceased. The nystagmus was opposite in direction to that induced during the Slow Rotation Room run by the identical head movements. (70)

An important aspect of these experiments was the observation that the reduction of nystagmus and illusions in the Slow Rotation Room was not eliminated by arousal, a situation which does not obtain when nystagmus produced by simple acceleration about a fixed vertical axis has disappeared. In that case nystagmus, but not-necessarily illusions of motion, are restored by arousal.

As has been pointed out, habituation and distraction result in a decrease of the magnitude of the neural signal at first, but not at all sensory subcortical stations. Certainly these mechanisms are distinct, in that distraction involves cortical arousal, whereas habituation is generally associated with the absence of such arousal. Furthermore, habituation is stimulus-configuration bound, slight variations in the stimulus producing cortical arousal, but a release from the depression of the magnitude of the neural signal of the first
central station. From this discussion, one may conclude that there are at least two situations which produce electroencephalographic "arousal": the first, a completely novel stimulus, and the second, a small variation in a stimulus to which the subject has previously been habituated.

It has been stated that one mechanism for the reduction of nystagmus with repetition of a rotating stimulus is "reduction of arousal". (76) In this respect it is important to distinguish reduction of arousal as a direct result of repeated inconsequential application of the stimulus from loss of arousal as a consequence of repeated presentation of the stimulus in a consequential manner, as in repeated iteration of conditioning stimuli in the Pavlovian paradigm, as has been mentioned. In the first case, the arousal reducing capability of the signal is stimulus-bound and is subject to variation by slight variation in the stimulus parameters. In the second case, the internal inhibition in the sense of Pavlov produced is global in the behavior of the subject and may persist for long periods of time.

When inhibition of reflex activity occurs in the Pavlovian paradigm, whether by differential conditioning, or by extinction, the process is active. That is, the non-reinforced response does not "die-out" but is suppressed. (The Russian term is "tormozhenie"
or "braking"). This effect extends not only to the reflex suppressed
but also to other reflexes, as was first pointed out by Pavlov, and
continues with continued repetition of the conditioning sequence
until it becomes global and a sleep-like state is produced. This is
different from the effects of non-conditioning, inconsequential
repetition of a stimulus which may produce sleep but which does
not generalize its inhibitory effects to unrelated stimuli.

The situation described in the experiments of the
Pensacola group may be thought of in the light of an avoidance condi-
tioning paradigm. Certainly the distressing effects of vestibular
stimulation are avoidance motivation enough. The inhibition of the
responses, and the extension of that inhibition to other stimuli
(which would release nystagmus) may be a manifestation of the
conditioned nature of the response, rather than its habituated nature.

The release from vestibular stimulation after the rotation
run would tend to bring out the compensatory conditioned response
which occurred during the rotation in response first to the early
portion of vestibular stimulation and then to cues in the internal
or external environment which were associated with the vestibular
stimulation during the run, but which now exist alone. With the
passage of time this reflex would be extinguished, but since "once
a conditional reflex is formed it cannot be removed" in the sense
that fewer trials are required to reconstitute it than were required in its initial formation, it will readily reappear at a lower level of adequate stimulation than was originally required.

On the other hand, since this reflex represents one of a second order, it would not tend to appear spontaneously as often as does a conditioned reflex of the first order.

It is conceivable that in experiments with the vestibular system in human adult subjects, we are dealing with a previously conditioned vestibular system, and that the drowsiness of continued vestibular stimulation represents the effects of too prolonged a conditioning sequence.

It is not inconceivable that the induction of nausea by visual objects and by sound may reflect a conditioning process associated with the vestibular system.

The compensatory response is probably associated with the consistency of the vestibular effects produced by head movement over a long period of time, and would not be expected to occur in the usual situation in which motion sickness occurs, associated with a greater variety of movements. This exception, however, would not hold for maintained slow rotation in a space station or capsule, where both adaptive and post-rotatory (compensatory) effects would be expected.
These considerations suggest two testing experiments. The first would establish the general nature of the reflex inhibition produced by the conditioned adaptation to motion, and would differentiate it from habituation by observation than another conditioned reflex, unrelated to vestibular stimulation is inhibited simultaneously. The second would be designed further to establish the conditioned reflex nature of the post-rotatory compensatory response by repeating the adaptation experiment in the identical subjects and determining the time required to re-adapt to motion in the Slow Rotation Room.

C. Vestibular Disturbances in the Space Environment

1. Vertigo

Ref: 31, 52

Vertigo has not been described as a prominent component of motion sickness, but conceivably may arise as a result of organic changes in the vestibular system as a result of unusual increments or decrements of neural signal input, as exemplified in the work of Hamberger and Hyden. (81, 82) It may be useful, therefore, to consider some of the varied syndromes in which vertigo may suddenly be present. It will become evident that the report of vertigo on an operational or simulated mission should not lead to premature
conclusions concerning the etiological significance of motion.

This is particularly important in training and determination of
the efficacy of conditioning procedures in the elimination of
vestibular symptoms in the individual Astronaut.

The most common form of vertigo encountered is undoubtedly
positional in type, that is, vertigo and associated nystagmus are
related to head position. **Nylen type I positional vertigo**, or direction-
changing positional vertigo and nystagmus may be the only sign of
central nervous system disease. (31) Characteristically the onset
is abrupt and paroxysmal, frequent during the active phase of
involvement, but sustaining long semissions. Caloric responses
are often normal, and cochlear signs are present rarely or not
at all. **Nylen type II positional vertigo**, or positional nystagmus
of the benign paroxysmal type with non-changing direction of
nystagmus, has been shown to be correlated with degeneration of
the maculae of the otolith organs. Characteristically, its onset is
abrupt, paroxysmal, with long remissions. Each individual attack
is brief (generally not more than one minute), is dependent upon
head position, and repeated placement of the head in the vertigo
inducing position results in diminution of the severity of symptoms,
until the effect cannot be obtained at all. This is attributed to
"loose otoliths" floating in the endolymph of the utricle and eventually
achieving a stable position. The pathological basis of this disease has recently been confirmed by temporal bone necropsy. The etiological basis has been shown to be circulatory and to be related to a specific occlusion of a portion of the labyrinthine circulation, and may be related to trauma or infection.

Classic Meniere's disease presents the triad of tinnitus, vertigo, and deafness, is abrupt and paroxysmal in onset with nausea and vomiting, and sustains long remissions. There is no postural effect. Caloric responses are abnormal in 90% of cases. Customarily cochlear signs are present and severe, tinnitus always being present, response to amplification poor, loudness recruitment always being present. The deafness is variable, however. The pathological basis of this disorder is distention of the membranous labyrinth (''hydrops of the labyrinth'') due to unknown causes. Characteristically, structures of the vestibular system central to the labyrinth are not affected.

"Atypical Meniere's Syndrome" and "Pseudo-Meniere's Syndrome" are terms which have been used to characterize paroxysmal vertigo where normal hearing was present, as a rule, and where postural dizziness and positional nystagmus were fairly common. These terms conceal a variety of involvements and etiologies (viral, toxic, circulatory) and may represent early forms of the previously mentioned syndromes.
Epidemic vertigo occurs acutely, and is associated with nausea, vomiting, headache asthenia, and nystagmus. The patient is generally febrile. Symptoms may last from weeks to months. Recovery is usual, however. This syndrome is associated with gastrointestinal or upper respiratory involvement, and occasionally oculomotor paresis may occur. Caloric and audiologic tests are characteristically normal. The cerebrospinal fluid, however, may occasionally reveal a lymphocytic pleocytosis. Although the clinical picture suggests infection, an etiological agent has not been isolated. The precise pathological locus has not been demonstrated, but it has been suggested that "an affection of the brain stem...a lesion of the second vestibular neuron including the brain stem as in vestibular neuronitis (vide infra)...seems to be the most plausible cause of epidemic vertigo. However...we cannot exclude...that the localization may vary from patient to patient, both in the central and peripheral nervous system."

Acute toxic labyrinthitis is associated characteristically with acute febrile diseases -- pneumonia, cholecystitis, influenza, and a wide variety of noxaw including overindulgence, fatigue, or drug ingestion. The onset of symptoms is gradual, and they reach a zenith in 24-48 hours with severe vertigo, nausea and vomiting. Etiology and pathogenesis are unknown.
Vestibular neuronitis is characterized by "blackouts" or "drop seizures" rather than vertigo. Attacks are frequent during the active stage, but recovery or long remission is the usual course. No positional effect or cochlear manifestations are evident. Abnormal caloric responses are present in 100% of cases, and often bilaterally. Galvanic responses are altered, suggestive of a lesion central to Scarpa's ganglion. Follow-up has revealed some of these cases to represent an early onset of disseminated sclerosis, thus accounting for the remitting nature of the involvement. It is thus maintained that the disease is probably a specific affection of the vestibular nerve, and perhaps should be classified as another manifestation of the demyelinating disorders.

Tumors of the cerebellopontine angle rarely produce vertiginous paroxysms, and, as may be expected symptoms of imbalance are persistent, and though slight initially, are progressively severe. Positional vertigo is rare. Caloric responses are abnormal in 100% of cases, cochlear signs are always present, deafness being prominent, though tinnitus may be variable. The deafness may respond well to amplification, and loudness recruitment is generally absent, a differentiating point from Menier's Disease. The complex effects of tumorous growth may include circulatory occlusion and resultant end-organ degeneration, or ganglionic and vestibular neuronal pressure degeneration.
In view of the relationship of the posterior portion of the temporal lobe to the vestibular pathway, control of optokinetic movements, and its relationship to directional preponderance, circulatory involvement of the carotid system, tumors vascular malformation, and the like may be expected to induce vertiginous episodes.

Further causes of vertigo are a ceruminous impaction in the external auditory meatus, or fenestration procedures. In summary then, an abrupt onset of vertiginous sensations has been associated with circulatory, toxic-infective, and demyelinative effects. They may or may not be associated with varying head position. Evaluation of reports of vertiginous sensations, particularly on longer missions, must include consideration of these possibilities. There is no known method for prediction of the majority of these abnormalities.

Evaluation of habituation processes to motion or the tendency for "space sickness" to occur under prolonged space environmental conditions, must also involve consideration of the possibility of anatomical in addition to functional change in the vestibular system resulting in a syndrome similar to those established otologically. The more information available on what has occurred the more rational an evaluation of what is occurring in an operational situation.
can become, and the more realistic operational programming or emergency advice can be. In an operational situation audiometry and determination of loudness recruitment may reasonably be arranged. The determination of the precise relationship of position to the vertiginous sensation and the determination of the presence of nystagmus in relation to position and its changing direction with head positional change or not, (via television) may further add precision to the diagnostic technique, if knowledge of the motion characteristics of the space capsule are available. In fact, these procedures, taken together with other clinical considerations (tinnitus, fever) can reasonably differentiate between Meniere's Disease Vestibular Neuronitis, Nylen's positional vertigos Type I and II, and perhaps acute toxic labyrinthitis. In the operational situation it may turn out that one of these changes occur in the usual "sporadic" fashion, but that they will be related in some way as yet obscure to the space environment, particularly to alterations in the labyrinthine circulation. Thus, provision for these examinations in an operational experiment may provide useful information for the future concerning labyrinthine function, and about disturbance of such function, whether reversible or irreversible.
2. Relevant Radiation Effects

Ref: 65, 66, 88, 106, 139

Radiobiologic effects of extremely energetic particulate radiation found in the space environment should be considered as possibly producing either vestibular malfunction or evoking emetic responses from direct damage to medullary centers. From the earliest days of radiation research it has been demonstrated that irradiation of the head produces a myriad of sensory and motor disorders. (44, 45, 58) One of the principal clinical signs (depending upon the portion of the head which is irradiated) are acute disturbances in space orientation. The target structures appear to be either the lateral cerebellum, the vestibular nucleus, or the inner ear. The response manifests itself within minutes to hours after exposure to doses from 4 - 8 kilorads. There appears to be rapid recovery from sub-threshold irradiation. (75) In the cat cerebellum granule layer neurons are selectively hit and the same is true in monkey and rabbit. (105, 45) There is also good evidence that direct damage is done to the inner ear itself. (75) Unilateral irradiation of the tympanic bulla (inner ear and lateral cerebellum being hit) caused head tilting and nystagmus in hamsters when a threshold dose of about 6 Krad of X-rays.
Thus it appears that the dose needed to produce acute or even delayed damage to the inner ear and its neural components sufficient to produce clinical symptoms is far beyond the expected exposure in planned flight. The RBE for high energy particles such as are found in the space environment has not been fully determined. Even with an RBE of 2, which is in excess of most experimentally determined RBE's for high energy protons (the most numerous of cosmic particles), it is reasonable to assume that radiation damage should not be a factor in motion sickness resulting from CNS or receptor damage.

Cacton studying the effect of selective placement of lesions in the lower brain stem structure on X-irradiation emesis in the dog found that the doses need to evoke emesis from brain irradiation to be in the kilorad range whereas a few hundred rad to the stomach would actuate the mechanisms to evoke emesis. Clinically patients during G.I. irradiation therapy often have emetic responses after doses as low as 200 rad. The possibility of exposure at this level in multi-orbital flights should be considered although protraction or fractionation of dose would markedly reduce the effect. In such damage to neural or sensory structures by ionizing radiation resulting in symptoms akin to motion sickness would only take place at supralethal dose ranges. Chance of localized hits by highly
energetic heavy ions with their extremely dense ionization might produce effects but the probability of this is highly unlikely. A more likely target structure is the G.I. tract which is sensitive at much lower (but still high) dose ranges.

D. Mechanical Aspects of the Vestibular System

As early as 1931 Steinhauser showed that the semicircular canals and cupular mechanisms can be viewed as three damped torsional pendulums, the mass being the mass of the endolymph, the spring being the elasticity of the water-tight cupula. Damping is introduced most likely by viscosity of the cupular tissue. Experimental verification of the torsional pendulum analogy was accomplished by Von Egmond, et al showing the following model of the canal (presumably that which lies almost in the horizontal plane.) (106)

Their model had the form:

\[ (I \dot{\theta} + BD + K) \dot{\theta}(t) = \ddot{\theta}(t) \]

where \( \dot{\theta}(t) \) can be taken as angular displacement of the endolymph or of the cupula as a function of time

\[ \ddot{\theta}(t) \] is angular acceleration of the body

\[ D = \frac{d}{dt} \] the differential operator

I, B, and K are inertial, viscous, and elasticity parameters
Experimentally they assumed that instantaneous velocity of the slow component of nystagmus is proportional to cupula displacement produced by angular acceleration. This assumption was partially justified by the later findings of Groen, Lowenstein and Vendrik that angular deflection of the cupula generates a proportional afferent pulse rate for angles \( \angle \). The equation of Von Egmond et al can also be written* in the form of a functional:

\[
\phi(t) = \frac{k}{(T_1d+1)(T_2d+1)}
\]

Their data show \( T_1 \) to approximate 10 sec while \( T_2 \) approximates 1/10 second in man. This means the natural frequency is 1 cps and the damping ratio is 5.

Niven and Hixon put this model to extensive tests under high level angular accelerations of human subjects. (130) They rotated their subjects with sinusoidally varying angular displacements, at frequencies from 0.02 to 0.20 cps, all with peak angular acceleration of 40 degrees per sec\(^2\). They recorded eye motions by corneoretinal potential. Measuring response with respect to points of zero slow component of nystagmus, they obtained phase shift as a function of frequency. From best fit curves, they derived natural frequencies which varied from 3.6 to 6.7 for six subjects, and damping ratios which varied from 0.75 to 1.9. A seventh subject whose measured

*A second order equation can be factored into two exponential lags if damping exceeds unity.
parameters differed by a factor of two, indicated extremely poor balance and was unusually resistant to motion sickness. This suggested a potential application of this measuring technique in screening individuals clinically.

Certain new evidence regarding vestibular function and oculomotor control has become available. A functional separation of the pursuit or slow component of optokinetic response, from the quick or saccadic component was accomplished by Young. He utilized a discontinuous or sampled data model with a 0.2 sec. sampling rate to describe both pursuit and saccadic systems. Melville-Jones and Milson, however, suggest that the pursuit mode is mediated by the vestibular mechanism in a continuous sense. They point out that with the \( C \) values given in the Von Egmond et al. equation, as confirmed by Niven and Hixon, in the range of 1 - 10 radians/sec. (the range of normal head movements) \( \delta(\chi) \) is proportional not to acceleration but to head velocity. In practice eye velocity due to vestibular stimulation is only about half the head velocity, they suggest. The optokinetic feedback supplies the other half -- and in some cases, overcompensates.

Essentially all of the above-described experiments in vestibular and optokinetic function were performed with movements in the horizontal plane. Anatomical evidence shows that such motion should
cause forces in more than one canal, necessarily involving co-
ordinate transformation. Further, $T_i$ in the model can change
as a function of plane of rotation, which means different canals
have different time constants. Whether all of the foregoing con-
clusions of various investigations is also true with regard to head
and eye motions in other than the horizontal plane is not clear.

Further refinements in the model of the semicircular canal
function are expected to involve other tests for linearity and second
order forms, including step responses in acceleration and velocity,
both on and off. Evidence from various sources and in other
sensory contexts suggests an asymmetry in response to outset with
respect to termination of stimulus. Vestibular afferent rate should
give expected transient response and confirm natural frequency and
damping values previously obtained. Vestibular time constants for
various planes of rotation, both parallel and oblique to the planes
of semicircular canals should be studied. Such experiments have
obviously been contemplated by present investigators, and should
proceed.
References to Bibliography

**ERRATA**

<table>
<thead>
<tr>
<th>Paper cited in text as No.</th>
<th>Should be No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>27</td>
<td>28</td>
</tr>
<tr>
<td>28</td>
<td>27</td>
</tr>
<tr>
<td>28a</td>
<td>29</td>
</tr>
<tr>
<td>29</td>
<td>30</td>
</tr>
<tr>
<td>30</td>
<td>31</td>
</tr>
<tr>
<td>31</td>
<td>32</td>
</tr>
<tr>
<td>32</td>
<td>33</td>
</tr>
<tr>
<td>33</td>
<td>34</td>
</tr>
<tr>
<td>34</td>
<td>35</td>
</tr>
<tr>
<td>35</td>
<td>36</td>
</tr>
<tr>
<td>36</td>
<td>37</td>
</tr>
<tr>
<td>37</td>
<td>38</td>
</tr>
<tr>
<td>38</td>
<td>39</td>
</tr>
<tr>
<td>39</td>
<td>40</td>
</tr>
<tr>
<td>40</td>
<td>41</td>
</tr>
<tr>
<td>41</td>
<td>42</td>
</tr>
<tr>
<td>42</td>
<td>43/44</td>
</tr>
<tr>
<td>43</td>
<td>45</td>
</tr>
<tr>
<td>44</td>
<td>46</td>
</tr>
<tr>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>etc</td>
<td>etc.</td>
</tr>
<tr>
<td>181</td>
<td>183</td>
</tr>
</tbody>
</table>