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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.

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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 Gemeni 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

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* 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 in-

dividual 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. (115, 126) 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° to the frontal plane of the body, and the vertical canals on each side make an angle of about 45° with the saggital 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. (**) 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. (¹³⁶)

2. <u>Vestibular Stimulation</u>

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 essentially 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. (¹⁰¹)

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. (130)

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. (15a)

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". (163) 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. (3 2) 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, $(30^{o}C)$ 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 $(44^{o}C)$ 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 dem-

onstrated 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.

(63,107)

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, atributed to proprioceptive influx, may preceed 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. (**132**) 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 anti-peristalsis and psylospasm, and abdominal wall contraction, preceding vomiting. Significant displacement of viscera has not been observed. (**35,154**)

6) <u>Cold sweating,</u> 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 quantitiatively studied, as far as our literature survey has revealed.

7) <u>Respiratory changes</u> 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) <u>Miosis of pupils,</u> followed by mydriasis and hippus, has been observed during rotation, and the retinal vasculature has blanched. Measurements of opthalmic 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) <u>Salivation</u> has been shown to occur to caloric stimulation, perhaps as a result of stimulation of the chorda tympani. (43)

11) <u>Oliguria</u> 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. (**22,35**) Present

theory describes two half-centers as responsible. The first, the chemo-

receptive 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. (170,102)
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. (143)

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 ventricule, 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 CO_2 content, O_2 content, O_2 capacity, or O_2 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 acetycholine 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 in 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 production 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 scending 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. (35). Various medications

have been administered for therapy and prevention. (35) 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. (107)

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. (156) 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. (ιι τ) 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 un-practiced 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. (ιsι) Attempts have been made to study electroencephalo-graphic 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, dermographia, tilt table test, respiratory pattern, blood

pressure, pulse rate, skin temperature, forehead sweating, salivation,

and the like. The Barany chair test was early disregarded. (100)

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. (100)

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. (151) Cupulogram techniques (nystagmus, sensation,

occulogyral illusion) appear to be predictive in that chronically seasick

individuals have steeper cupulograms than normals. (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

ophthalmodynanamometry 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 re-

warding 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 semicircular 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. (151) Violent pitching has been estimated to produce angular velocities of $2^{o}/\sec^{2}$, 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. (158) 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 prorioceptive

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

prorioceptive 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. Concommitant 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. (153) 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 ssytem 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 ab-
normally 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 (103) 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. (113) 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. (90) 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 ap-

propriate 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". (12)

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 temproal 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 Pennsacola 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 attendent 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." (2⁴⁰) 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." (159) "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 un-
successful. 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." (284) 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 sub-

sequent 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 un-

reasonable 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 analagous 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 anti-histaminic 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 ([119]) 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 cupulometric (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". (12)

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. (118)

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. (4ᴸ)

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 (₁₇₄) 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." (₁₇₆)

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. (2 3 4) 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.)."(3 6) 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." (3ⳑ)

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. (١๖೦)

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...despite

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." (160)

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. (¹⁴²) 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. (¹¹⁶) 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.(¹³⁸) Vascular responses to heating and cooling

of the gastric mucosa and the skin and of the epigastric region were

measured by plethysmography. (¹³⁴) 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 re-
inforcement usually leads to a dimunition 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. (¹⁸⁴)

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 attemptst 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, artifically 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. (161) 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. (173)

b. Neurosis

The relation of chronic neurotic inadequacy to motion

sickness remains obscure, as mentioned above, in that a satisfact-

orily normal population is necessary for valid conclusions. Psychi-

atric 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 predelic-

tion 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 suscepti-
bility largely by anecdotal data and by persons experienced in the
assessment of motion sickness. (107) The possible effect of sugges-
tion, 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. (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. (3⁶) There, the avowed purpose of the pro-

gram 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. (16f)

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 respira-
tory 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 extero-ceptive 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

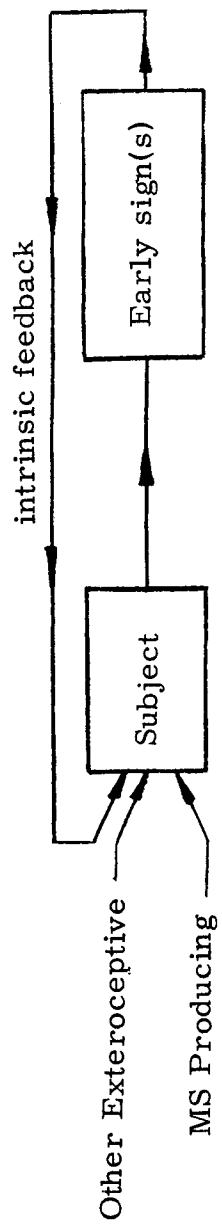"correct" actions are the response.

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 regula-

tion, it is suggested, acts as negative feedback, allowing the

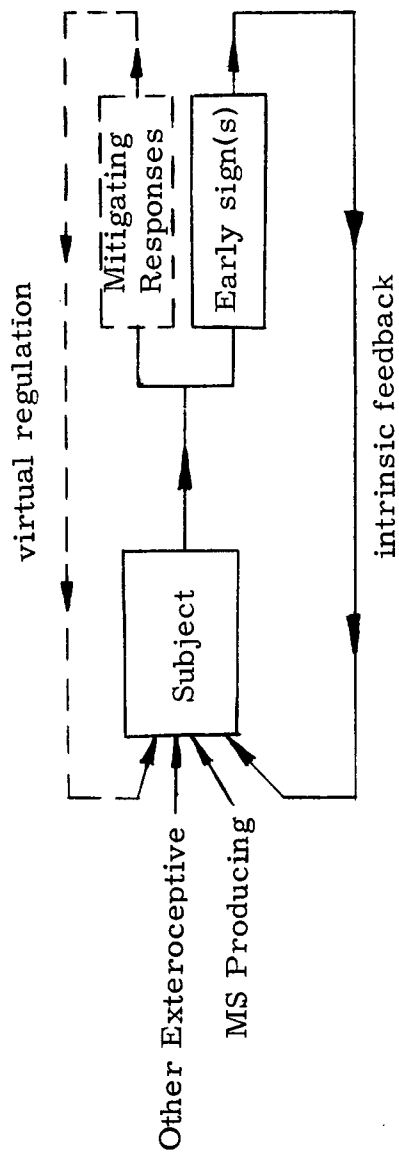diminution or deferment of the symptoms of motion sickness. Thus, through a plausible training regimen, the subject can learn to adapt in a way that preserves physiological and psychological homeostasis.

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 dpeend 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

intrinsic feedback

Subject

Early sign(s)

Other Exteroceptive

MS Producing

EARLY STAGE: POSSIBLE ADAPTIVE MECHANISM

Control I

virtual regulation

Mitigating Responses

Early sign(s)

Subject

intrinsic feedback

Other Exteroceptive

MS Producing
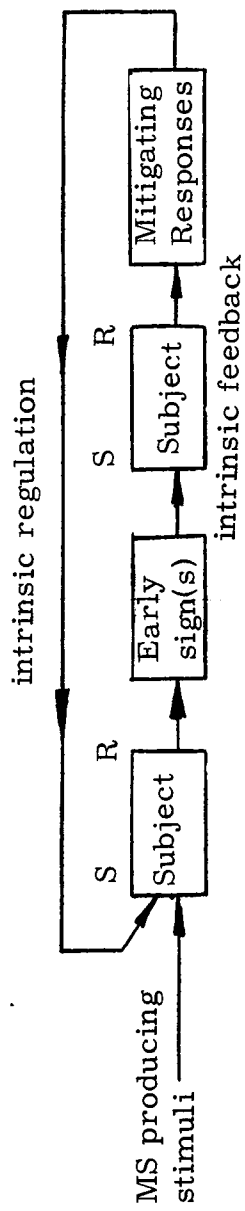
RESULT OF TRAINING

Control II

intrinsic regulation

S   R   S   R

Subject

Early sign(s)

Subject

Mitigating Responses

intrinsic feedback

MS producing stimuli

bio-dynamics, inc.

THE MOTION SICKNESS CYCLE

interoceptive stimulus

Subject

Sight, Hearing & Other Exteroceptive Stimuli

Motion Sickness Producing Stimuli

nausea, vomiting, other late signs & symptoms.

dizziness

drowziness

disturbed peripheral circulation

other early signs & symptoms
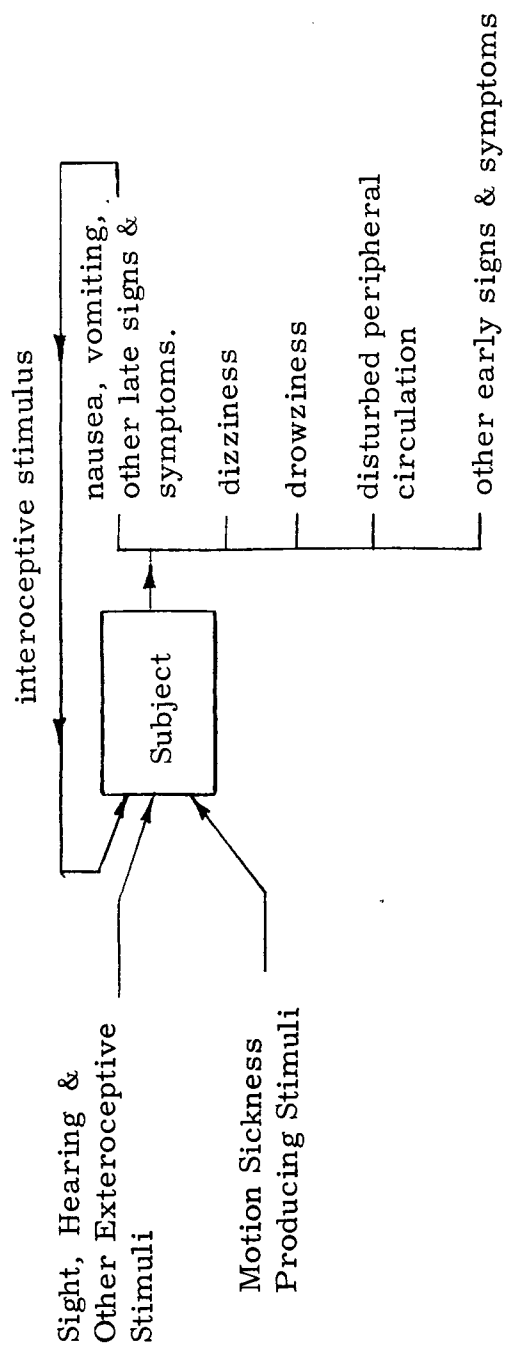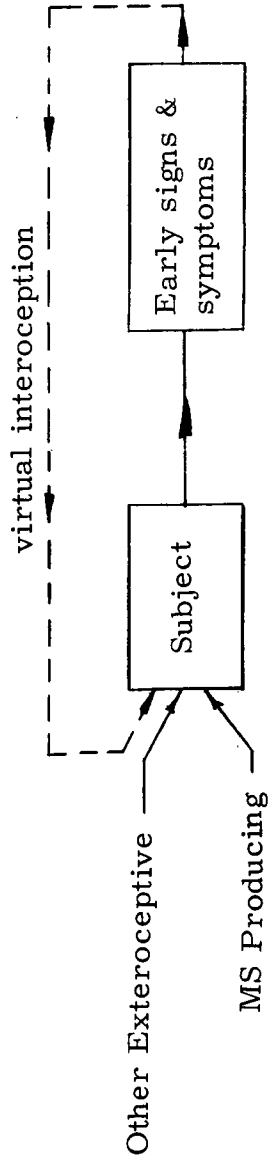
EARLY STAGE OF CYCLE   Detection I

virtual interoception

Subject

Early signs & symptoms

Other Exteroceptive

MS Producing
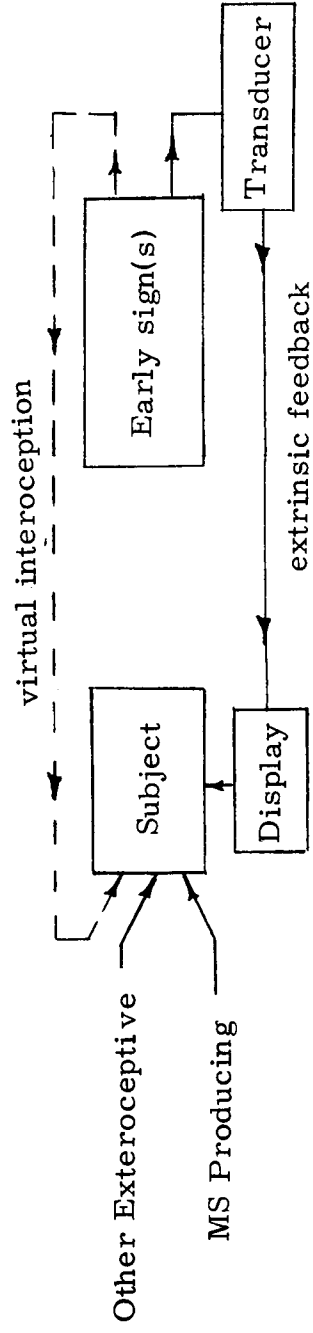
INSTRUMENTED EARLY STAGE   Detection II

virtual interoception

Subject

Display

Early sign(s)

Transducer

extrinsic feedback

Other Exteroceptive

MS Producing

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

System	Symptom	Sign(s)
Central Nervous	drowsiness	EEG
Peripheral circulation	feeling of warmth chill	pallor anomalous skin temperature pulse volume blood pressure
Cardio-vascular	headache fainting	heart rate blood oxygenation blood pressure cerebral blood flow
Gastro-intestinal	vomiting	gut pressure peristalsis gastric pH salivation
Ocular	dizziness disturbed vision	nystagmus pupillary response retinal artery flow electro-oculograph response
Autonomic nervous	feeling of fear feeling of alarm	galvanic skin response heart rate respiration rate
Skeletal musculature	headache "tenseness"	myographic response

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. Like-wise, 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 environ-

ment. 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 defini-
tion 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 interelation 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 indivi-

dual'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 intero-ceptive 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 significand 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.

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PART II

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

sterocilial configuration, though one process from each cell has a

kinocilial structure.   The hair-cells are surrounded by supporting

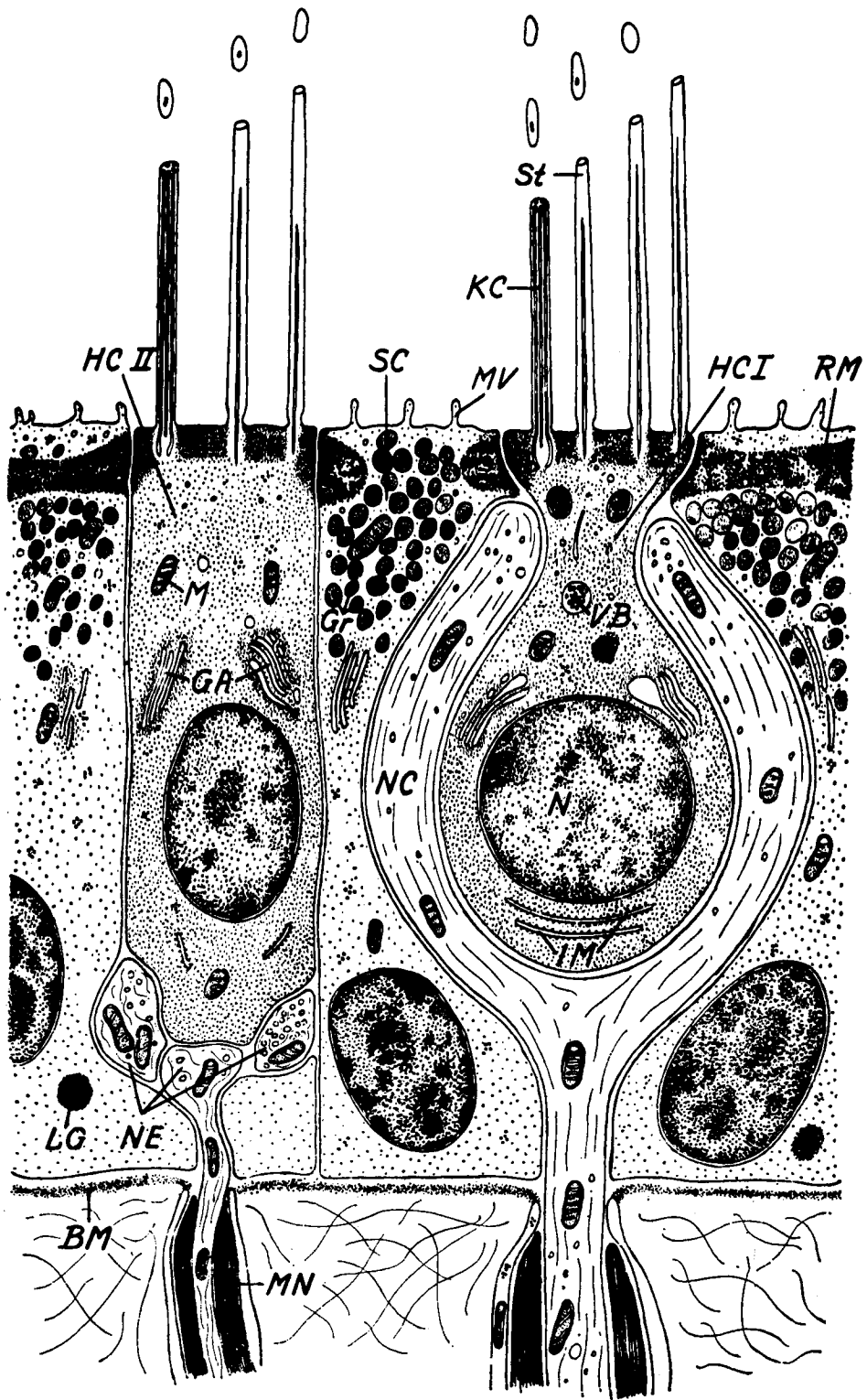cells, which in turn thrust small villous processes into the gelatinous

Figure 3

Brodal, Alf, et al, THE VESTIBULAR NUCLEI AND THEIR
CONNECTIONS, ANATOMY AND FUNCTIONAL CORRELATIONS,
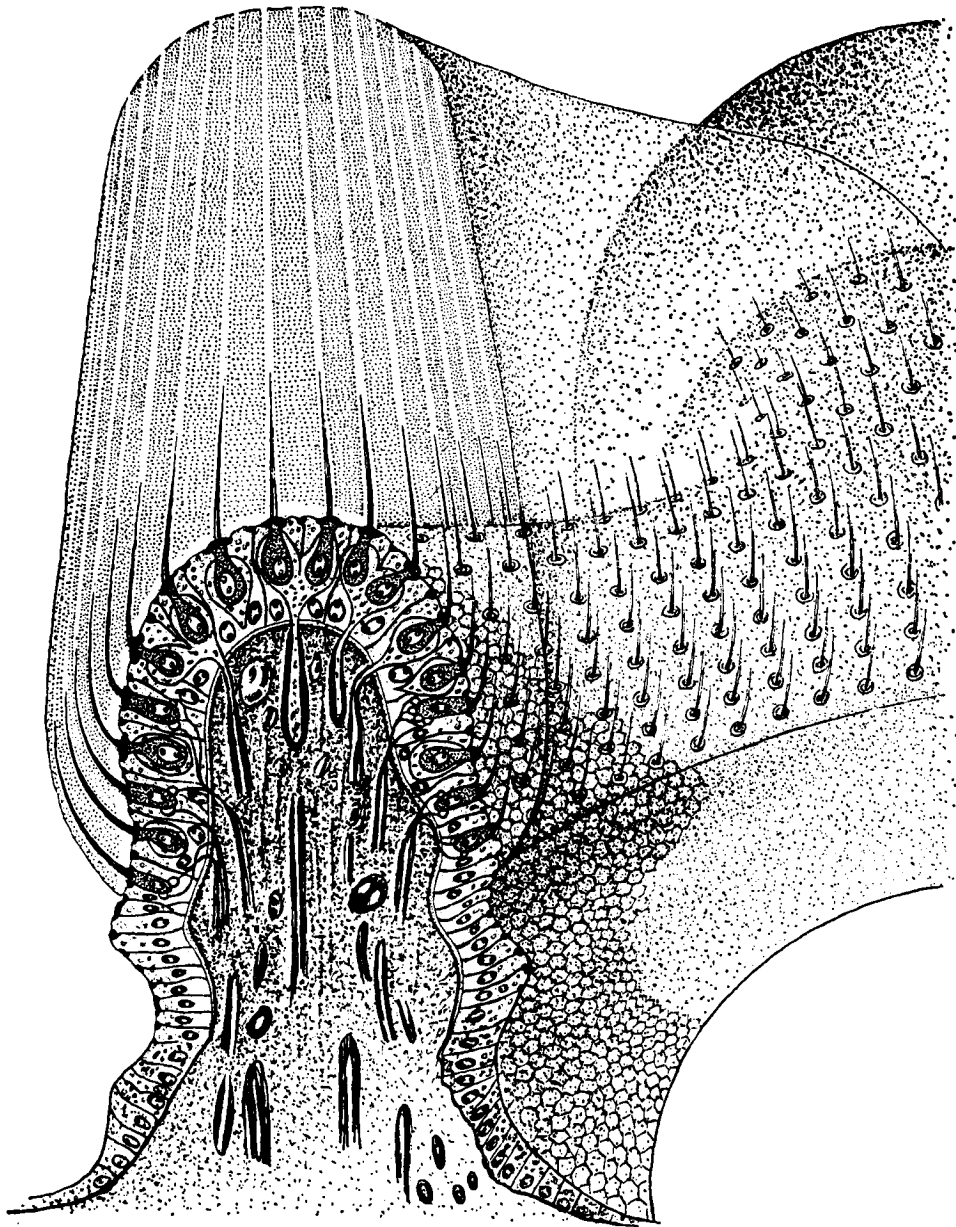1962, courtesy Charles C. Thomas, Publisher, Springfield, Illinois.

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 granulated 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 differentiated 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.

c

Figure 4

Brodal, Alf, et al, THE VESTIBULAR NUCLEI AND THEIR
CONNECTIONS, ANATOMY AND FUNCTIONAL CORRELATIONS,
1962, courtesy Charles C. Thomas, Publisher, Springfield, Illinois.

Figure 4

Schematic drawing of one half of a crista ampullaris, showing innervation of its epithelium. Thick nerve fibres forming nerve c calyces round type I hair cellsa 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. (63) 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 endolympaticus. 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. (32)

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. Radiaoactive
tracer studies reveal active secretion of an S^{35} 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. <u>Neurophysiology of the Vestibular System</u>

    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)

c. Projections of the Vestibular Nuclei and Associated Cell Groups.

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 distince 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 and 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
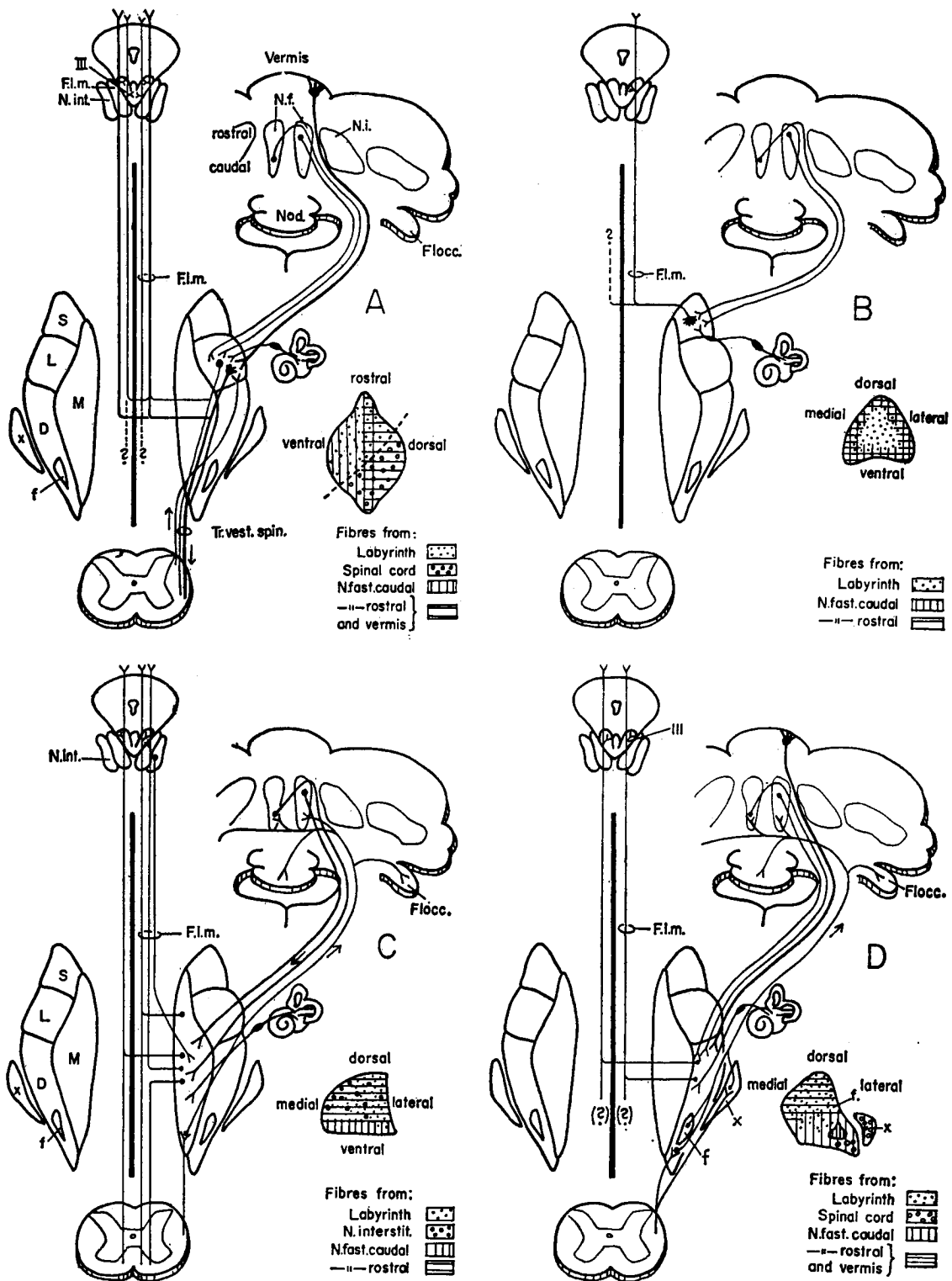
Figure 5

Brodal, Alf, et al, THE VESTIBULAR NUCLEI AND THEIR
CONNECTIONS, ANATOMY AND FUNCTIONAL CORRELATIONS,
1962, courtesy Charles C. Thomas, Publisher, Springfield, Illinois.

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 saggital 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. 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.

Figure 5 (cont.)

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 cristae 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 fascuculus. 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 nucleuproteins 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 inves-

tigators, 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.

$$\ddot{\xi} + \frac{\Pi}{\Theta} \dot{\xi} + \frac{\Delta}{\Theta} \xi = 0 \qquad (1)$$

where $\Theta =$ moment of inertia of the endolymph

$\Pi =$ moment of friction for unit angular velocity

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

$\xi =$ the angular deviation of the endolymph in relation to the skull

$\dot{\xi} =$ the angular velocity of the endolymph in relation to the skull

$\ddot{\xi} =$ the angular acceleration of the endolymph in relation to the skull

The constants: $\frac{\Pi}{\Delta} = 10$, and $\frac{\Theta}{\Delta} = 1$ can be determined as follows: An

approximate solution for impulsive stimulation, that is to say, a

sudden stopping of rotation from constant velocity, γ, is:

$$\xi = \gamma \frac{\Theta}{\Pi} \left[e^{-\frac{\Delta t}{\Pi}} - e^{-\frac{\Pi t}{\Theta}} \right] \qquad (2)$$

with limiting conditions $t=0, \xi = 0, \dot{\xi} = \gamma$

The return of the deflected cupula is determined

by $e^{-\frac{\Delta t}{\Pi}}$, 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, tu,

is given by:

$$t_u = \frac{\pi}{\Delta} \log_1\left(\frac{\epsilon v}{\pi \, s_{min}}\right) \quad approx.$$

(3)

Thus, a plot of an individual's tu vs. log ϵ should be linear with π/Δ

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 character-

istics 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 demon-

strated 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 milliam-

peres 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 audi-

tory 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 labyrinthine 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 <u>direction-changing variety of positional nystagmus</u>. 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 propri-ceptive stimulus, which can be separated from the exteroceptive stimulus by anesthesizing 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 quad-rupedal standing. Autonomic leg reflexes and the labyrinthine reflexes are also present.

In order to differentiate neck from labyrinthine reflexes both laybrinths 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 labyrinthec-tomized monkeys following bilateral removal of the motor and pre-motor 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 prorioceptive 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 huppocampal "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 dimnution 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 amplitued in electrophysio- logic 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 elect-rical events occurs along with the establishment of a behavioral conditioned reflex. In the neorcortex, 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, despire 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 sensative 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 accel- eration 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 electroencephalo-
graphic "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 reduc-
tion 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 stiuation described in the experiments of the Pensacola group may be thought of in the light of an avoidance conditioning 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 cohclear 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 correllated 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 diminituion 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. Characteris-

tically, 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 paryxysmal

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 toxis 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 verti-

ginous paroxysms, and, as may be expected symptoms of imbal-

ance 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 multiorbital flights should be considered although protraction or fractionation of dose would markedly reduce the effect. In su 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:

$$(I D^2 + BD + K)\, \delta(t) = \ddot{\omega}(t)$$

where $\delta(t)$ can be taken as angular displacement of the endolymph or of the cupula as a function of time

$\ddot{\omega}(t)$ is angular acceleration of the body

$D = \dfrac{d}{dt}$ 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 pro-

portional afferent pulse rate for angles $\geq 6^c$. The equation of

Von Egmond et al can also be written* in the form of a functional:

$$\frac{\delta(t)}{\Theta(t)} = \frac{k}{(T_1 D + 1)(T_2 D + 1)}$$

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 corneo-

retinal 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

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*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 τ values given in the Von Egmond et al. equation, as confir-

med by Niven and Hixon, in the range of 1 - 10 radians/sec. (the range

of normal head movements) $\delta(t)$ 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 coordinate transformation. Further, T_1 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 conclusions 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

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