Chapter 35

MOTION SICKNESS

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SUMMARY

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INTRODUCTION

Motion sickness, or kinetosis, is a condition characterized by pallor, nausea, and vomiting. It is brought about by exposure to real or apparent, unfamiliar motion to which the individual is not adapted. Many different motion environments lead to nausea and vomiting, and these are identified by terms such as seasickness, airsickness, carsickness, space sickness, simulator sickness, virtual reality sickness, ski sickness, and even camel and elephant sickness. Despite the apparent diversity of the causal stimuli, there are common features in the nature of the provocative motion stimuli and in the signs and symptoms evoked; all are manifestations of the motion sickness syndrome. Motion sickness is in certain respects a misnomer, for the word *sickness* carries the connotation of disease. The term obscures the fact that motion sickness is a normal response of a healthy individual to certain motion stimuli. Indeed, only the few who completely lack functional balance organs of the inner ear are truly immune.[1]

There are considerable differences among individuals in their susceptibility to motion sickness. For a particular motion environment, say that of a boat in rough seas, within a representative population some will be incapacitated by the motion, others will vomit from time to time but will carry out their allotted duties, and others will have no symptoms and no impediment other than that produced by the motion on their locomotor and postural activities (Figure 35-1). Because motion sickness can have an impact on operational effectiveness, the topic is of importance in the context of military medicine. Apart from the degradation of performance of trained personnel during land, sea, or air

Fig. 35-1. Motion sickness is not unique to modern travelers. Winslow Homer's 1867 wood engraving entitled *Homeward Bound* portrays passengers (and crew, in the background) on the rolling deck of a ship on rough seas. The crew members that we can see seem relatively unaffected, in that they seem to be performing their duties. The passengers, on the other hand, seem to personify a spectrum of seasickness from miserable (the seated women and children along the left side of the ship) to few or no symptoms (the man at the right of the picture, perhaps looking at dolphins through binoculars). Wood engraving: Reproduced with permission from Sterling and Francine Clark Art Institute, Williamstown, Mass.

operations, motion sickness can cause attrition during training and interfere with the acquisition of skills. Severe seasickness can also jeopardize the survival of those who have to escape to life rafts in rough seas.

SIGNS AND SYMPTOMS

On exposure to provocative motion of sufficient intensity and duration, the development of the motion sickness syndrome follows an orderly sequence, although there is considerable individual variability in the dominance of certain signs and symptoms.[2,3] This individual response pattern tends to be consistent and invariant of the causal motion environment.[4] The earliest symptom is typically an unfamiliar sensation of abdominal (mainly epigastric) discomfort, best described as *stomach awareness*. With continued exposure to the provocative motion, well-being deteriorates with the onset of nausea and may be preceded by a feeling of warmth and a desire to seek cool air. Some people experience skin flushing (vasodilation), but more commonly pallor and cold sweating are the harbingers of vomiting. Pallor is most apparent in the facial area and is a manifestation of heightened activity of the sympathetic nervous system. Sweating, another autonomic response, is usually confined to those areas of skin where thermal, as opposed to emotive, sweating occurs. Recordings of sweat production (Figure 35-2)

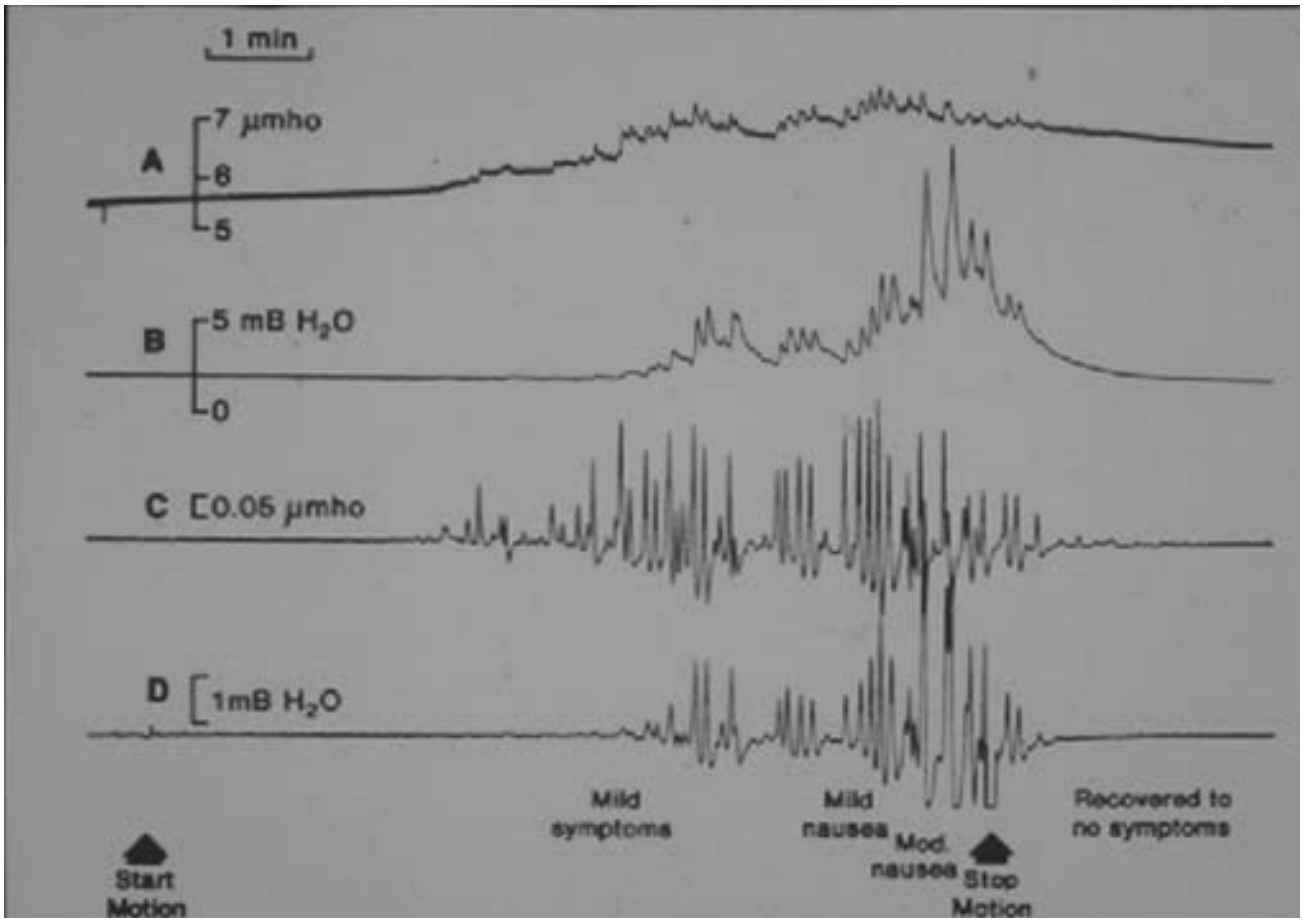


Fig. 35-2. Recordings of sweat production from the forehead of a subject during low-frequency linear oscillation. Tracings B and D show water vapor concentrations in an aspirated capsule on the forehead (DC-coupled in B and AC-coupled in D). Tracings A and C show skin conductance from forehead electrodes (DC-coupled in A and AC-coupled in C). Note both the progressive increase in sweating activity with increasing severity of symptoms and the rapid return to baseline after motion is stopped. Reproduced with permission from Golding JF. Phasic skin conductance activity and motion sickness. *Aviat Space Environ Med*. 1992;63:167.

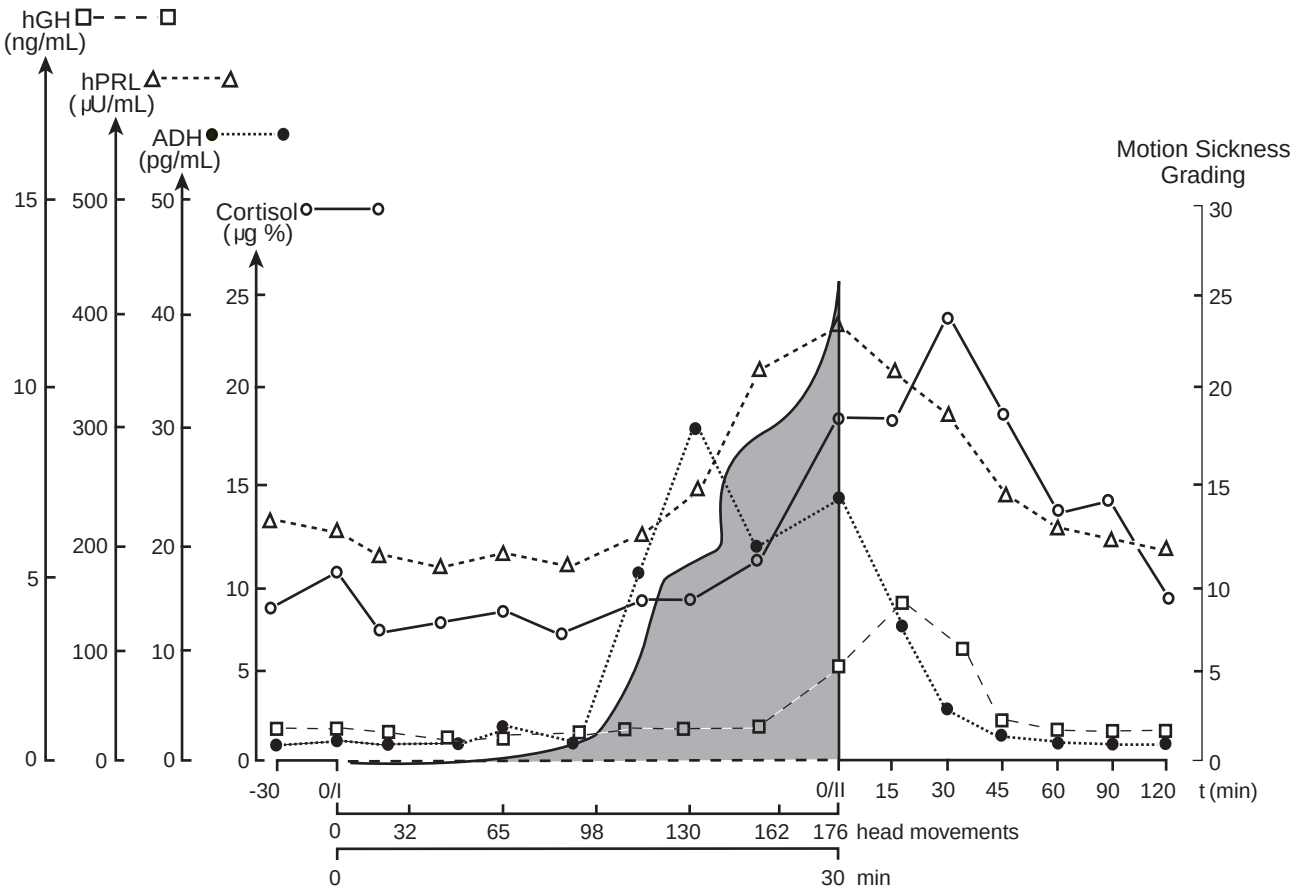


Fig. 35-3. Secretion of pituitary hormones (hGH: human growth hormone; hPRL: human prolactin; ADH: antidiuretic hormone) and cortisol in a subject in response to 30-minute cross-coupled (Coriolis) stimulation of increasing intensity (0/I to 0/II on the abscissa). The gray area, center, represents the development of motion sickness symptoms, which are scaled on the ordinate on the right. Reproduced with permission from Eversmann T, Gottsmann M, Uhlich E, Ulbrecht G, von Werder K, Scriba PC. Increased secretion of growth hormone, prolactin, antidiuretic hormone and cortisol induced by the stress of motion sickness. *Aviat Space Environ Med*. 1978;49:55.

show irregularly increasing sudomotor activity with pulses of sweat production that tend to accompany each wave of nausea.[5] Vomiting often brings some symptomatic relief, but with continued exposure, nausea again increases and culminates in vomiting or, if all gastric contents have been expelled, retching. This cyclical pattern of waxing and waning symptoms, recurrent vomiting and anorexia, may last for several days given continued exposure, as in storm conditions at sea or in the atypical force environment of space flight. However, most people in such circumstances adapt to the motion and are eventually symptom-free after 2 to 3 days.[6]

In addition to what may be identified as the cardinal signs and symptoms of motion sickness (ie, pallor, sweating, nausea, and vomiting), a number of other symptoms commonly, if not consistently, occur. Headache is a variable prodromal symptom, usually frontal in distribution, and may be accompanied by an ill-defined dizziness. Other early symptoms are increased salivation, belching, and flatulence.

Changes in respiratory rhythm with sighing and yawning are not uncommon precursors to vomiting, and hyperventilation sometimes occurs, particularly in those who are anxious and apprehensive about the motion environment. In those exposed to motion of insufficient severity to evoke frank malaise, excessive drowsiness and extended duration of sleep may be the sole symptoms. The condition was first reported[7] in subjects living in a rotating room (in which head movements were provocative) and given the name *sopite syndrome* by the investigators. More-important changes in behavioral state are the apathy and depression that can accompany severe motion sickness and render the victims incapable or unwilling to carry out allotted duties or even to take basic steps to ensure

the safety of themselves or their colleagues. An old adage holds that those aboard a boat in a storm first fear that the waves will wash them overboard; then after awhile, when motion sickness has taken hold, they wish that they *would* be washed overboard.

In addition to the symptoms experienced by those suffering from motion sickness, there are changes in physiological function that reflect alteration in the activity of the autonomic nervous system.[2,8] Motility and tonus of the stomach and gut decreases and bowel sounds (transduced by microphone or stethoscope) tend to disappear. Electrical activity of the gut (measured by the electrogastrogram, EGG) can be recorded by surface electrodes placed over the stomach. In those becoming motion sick, the EGG shows a reduction in amplitude and an increase in the basic electrical rhythm from the normal 3 cycles per minute to 5 to 7 cycles per minute.[9] The increase in frequency of the electrical activity seen on the EGG, termed tachygastria, correlates with the severity of symptoms and is associated with decreased gastric motility, as the EGG reflects pacemaker potentials of the stomach and not gastric contraction per se.

Cardiovascular changes are mainly confined to changes in vasomotor tone. The pallor caused by vasoconstriction of cutaneous vessels is accompanied by vasodilation of deeper vessels and increased muscle blood flow.[10] There may also be a modest elevation of heart rate and blood pressure, but these changes are variable and idiosyncratic and not highly correlated with the level of malaise.

Motion sickness is associated with increased excretion of anterior and posterior pituitary hormones. Most pronounced is the elevation of the antidiuretic hormone (ADH), which is responsible for the oliguria that accompanies motion sickness. Other pituitary hormones—notably adrenocorticotropic hormone, growth hormone, and prolactin—are also increased, although proportionately not to the same extent as ADH (Figure 35-3).[11] The change in secretion of pituitary hormones, in particular of ADH, correlates well with the severity of symptoms during both the motion challenge and recovery. Adrenal hormones, epinephrine and noradrenaline, are also elevated and, like the reduction in thyroid stimulating hormone, may be considered to be a nonspecific stress response.

ETIOLOGY

The pivotal role of the balance organ of the inner ear—the vestibular apparatus—in motion sickness has been recognized for more than a century, following the observation that some deaf-mutes are immune.[1] Subsequent efforts to evoke motion sickness in humans and animals deprived of vestibular function have consistently failed, and even partial destruction of vestibular receptors confers a degree of immunity, at least until central nervous system (CNS) compensation for the sensory loss has occurred.[12] The importance of the vestibular system in motion sickness led to the concept that the condition was due to overstimulation.[6] There was argument about the relative roles of stimulation of the receptors of the semicircular canals, which transduce angular movement of the head, and of stimulation of the otolith organs, which transduce linear motion and the orientation of the head to gravity (Figure 35-4). However, the overstimulation hypothesis is untenable, for some quite-strong motion stimuli (eg, those experienced by a rider of a galloping horse) are not provocative, whereas weaker stimuli (eg, those associated with head movement while turning slowly) can be highly nauseogenic. Furthermore, vestibular overstimulation does not account for the induction of motion sickness by purely visual stimuli in the absence of any motion of the observer and stimulation of vestibular receptors, as occurs in some static flight simulators or when

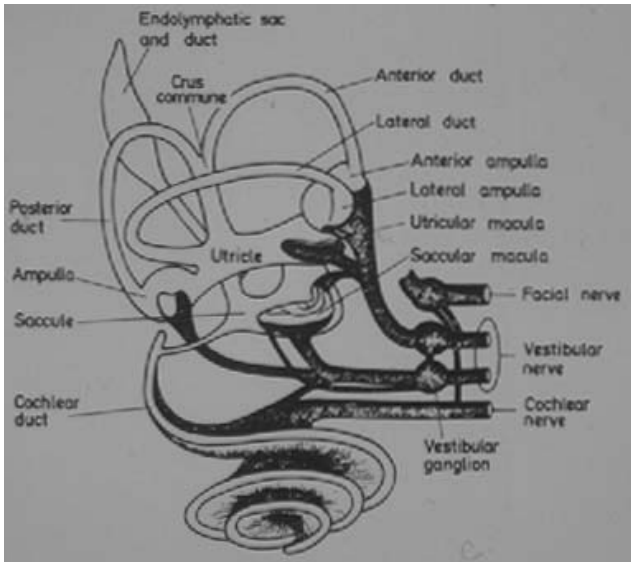


Fig. 35-4. The principal structures of the membranous labyrinth and its neural connections. Receptors in the ampulla of each semicircular duct are stimulated by angular accelerations acting in the plane of the duct. Receptors in the utricular and saccular maculae—the otolith organs—are stimulated by linear accelerations acting in the plane of the macula. Adapted with permission from Lindeman HH. Studies on the morphology of the sensory regions of the vestibular apparatus. *Ergebinsse der Anatomie und Entwicklungsgeschichte*. 1969;42:27.

watching dynamic scenes depicted on a large motion picture screen (Cinerama or Imax sickness). Nor does it account for the adaptation that occurs during continued or repeated exposure to provocative motion, nor the recurrence of symptoms on return to a familiar motion environment (eg, terrestrial) after having adapted to an atypical one (eg, weightlessness).

Neural Mismatch Theory

An alternative, and today widely accepted, explanation is that motion sickness is the response of the organism to discordant sensory information about bodily orientation and motion. The importance of *sensory conflict* as the principal etiologic factor was proposed more than a century ago,[13] but more cogently described by Guedry[14] and by Reason[15,16] in his neural mismatch, or sensory rearrangement, theory. Hypothesis would be a more appropriate term, as the neurophysiological substrate of the brain mechanisms proposed have not been elucidated, nor does Reason's theory provide a metric of neural mismatch that would allow a prediction to be made of the nauseogenic potential of a given motion environment. Despite these deficiencies, neural mismatch is a unifying theory that permits the identification of different categories of mismatch that, in practice, are known to be provocative. However, it does not explain why humans, in common with many other animals (eg, monkeys, dogs, cats, even fish), respond to certain motion stimuli by vomiting. Emesis is clearly of benefit to an animal as a means of getting rid of ingested poison. Treisman[17] postulated that brainstem mechanisms subserving orientation and motion also detect neurophysiological dysfunction caused by a neurotoxin and initiate the teleologically beneficial response of vomiting. He further hypothesized that in motion sickness, vomiting occurs because this protective mechanism interprets conflicting sensory signals as neural dysfunction caused by poisoning. Support for this hypothesis comes from the demonstration that surgical removal of the vestibular apparatus abolished or reduced the emetic response to lobeline and L-dopa, whereas vomiting following the injection of apomorphine was unchanged.[18]

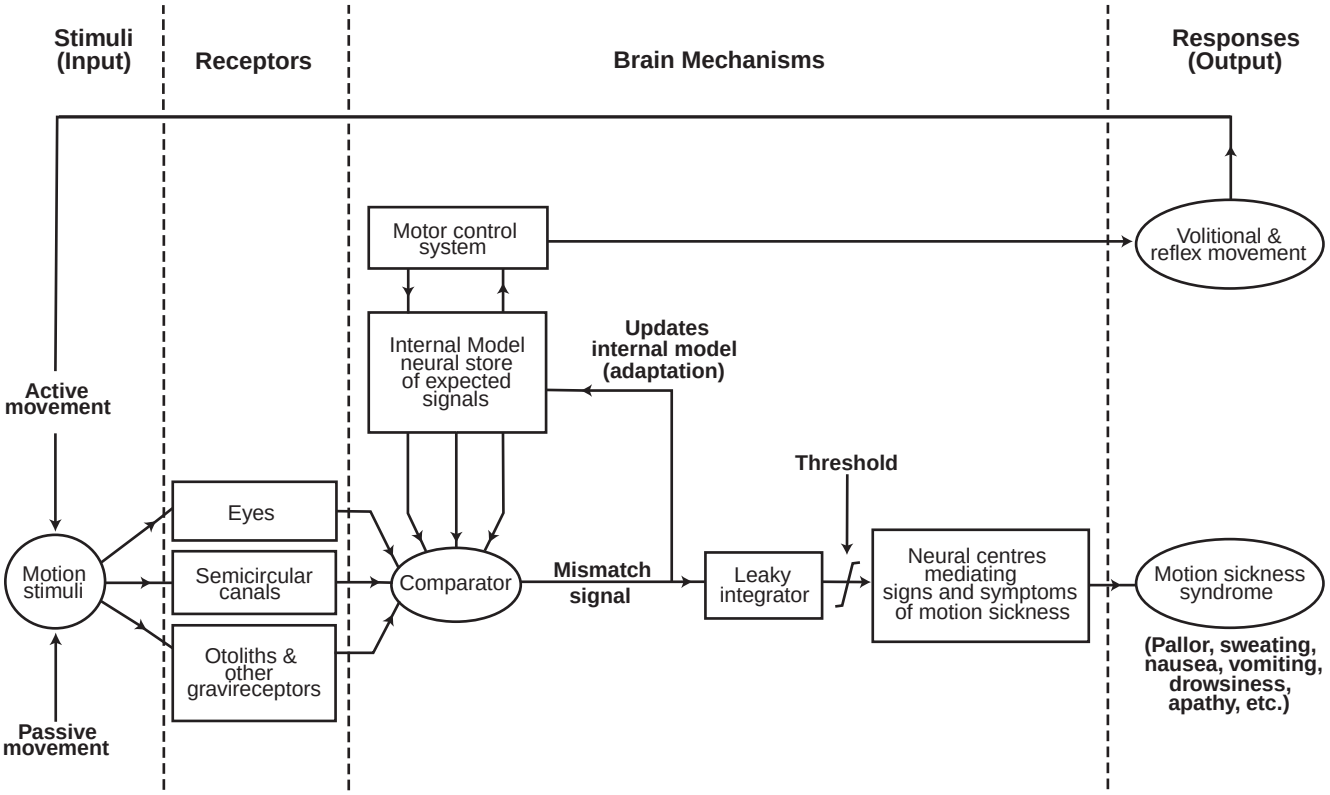


Fig. 35-5. A heuristic model of motor control, motion detection, and motion sickness based on the neural mismatch theory. Reproduced with permission from Benson AJ. Motion sickness. In: Dix MR, Hood JD, eds. *Vertigo*. Chichester, England: John Wiley & Sons, Ltd; 1984: 397.

The principal features of the neural mismatch theory are shown diagrammatically in Figure 35-5. Essential to the theory is the presence within the brain of a representation of afferent and efferent activity associated with bodily movement. This internal model is built up from information acquired during normal locomotor activity and the control of balance and posture. Afferent information about bodily orientation and movement comes from sensory organs stimulated by bodily motion, notably the eyes; the specialized receptors of the semicircular canals and otolith organs; and mechanoreceptors in the skin, capsules of joints, and muscles. These widely distributed receptors respond to forces acting on them and hence provide information about the orientation of the body to the gravitational vertical or, more precisely, to its orientation to the ambient gravito-inertial force. (In certain circumstances, as in aircraft in a coordinated turn, the resultant gravito-inertial force is not aligned with gravity and the otolith organs and the other mechanoreceptors no longer signal the orientation of head and body to the true vertical.)

An essential component of the neural mismatch theory is that any disparity between incoming signals from the sensory systems monitoring bodily motion and orientation, and the pattern of signals expected on the basis of past experience, leads to the generation of a mismatch signal. Transient mismatch is common during normal locomotor activity (eg, when one trips or is unexpectedly pushed); in such circumstances, the mismatch signal is used to initiate a corrective postural response. However, the presence of a sustained or repeated mismatch, as occurs on exposure to an unfamiliar motion environment, indicates that the internal model is inappropriate and requires modification.

It is postulated[15] that the mismatch signal brings about an updating of the internal model and, in a manner analogous to negative feedback, a reduction in the degree of mismatch. This mechanism—a primitive form of learning—underlies the process of adaptation to the atypical motion environment. The other postulated role of the mismatch signal is to excite neural centers that mediate the motion sickness syndrome. The nature of the coupling between the comparator and these neural centers is not known. Nevertheless, the relatively slow development of the syndrome and the persistence of malaise after withdrawal of the provocative stimulus suggest that there is some form of storage and progressive accumulation of the coupling agent; this is represented in Figure 35-5 by a leaky (or partial) integrator. A threshold is also required in this pathway to account for the acquisition of adaptation to atypical motion without the development of malaise. The setting of this threshold and the time constants of the leaky integrator may play a part in determining an individual's susceptibility, although, as discussed below, other factors may be of greater importance.

Figure 35-6 represents the time course of the postulated mismatch signals on transfer from one motion environment to another. Inputs from sensory receptors accord with the internal model in the normal pedestrian environment, but a large mismatch signal occurs on initial exposure to a novel, unfamiliar environment. The mismatch signal slowly decays, probably with an exponential time course, as the internal model is updated. On reaching zero magnitude, the individual may be considered to have adapted to the atypical motion environment; new patterns of sensory–motor coordination will have been established, and signs and symptoms of motion sickness will have dissipated. On return to the familiar motion environment, mismatch again occurs because the internal model is no longer appropriate, and motion sickness may recur. This *mal de débarquement* (sickness of disembarkation) can also be accompanied by the persistence of patterns of postural control and sensory–motor coordination that were appropriate for life in the atypical environment but are inappropriate on return to the familiar. In addition, transient illusory sensations of motion may occur and be perceived either as self-motion or as motion of the visual scene. In general, readaptation proceeds more quickly than the initial adaptation to the atypical environment, because configurations of the internal model established by long experience are more readily retrieved (recalled from memory) than new ones acquired. By the same argument, adaptation to a motion environment to which a person had previously adapted is likely to be more rapid than on initial exposure, because copies are retained in memory.

In the diverse conditions in which motion sickness occurs, two main categories of neural mismatch can be identified according to the sensory systems involved. In the first, conflict is between motion cues provided by visual and inertial receptors. This will be referred to as visual–vestibular conflict, as the principal inertial receptors are those of the vestibular apparatus (although the contributions of nonvestibular mechanoreceptors, as discussed above, cannot be ignored). The second category of neural mismatch is between information provided by the semicircular canals and receptors stimulated by linear accelerations; for brevity, this is called canal–otolith conflict. In each of these cat-

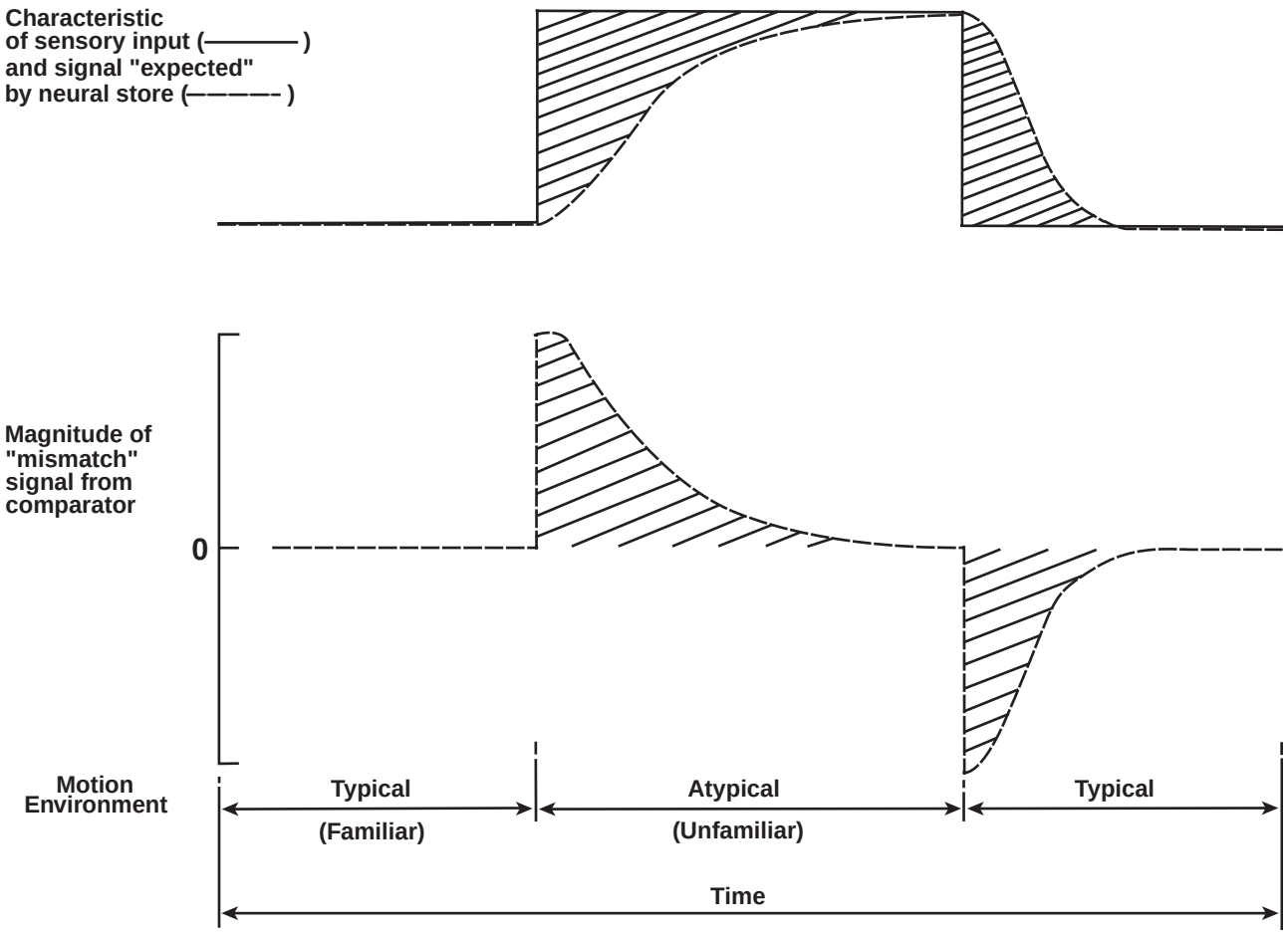


Fig. 35-6. The diagram illustrates both the time course and the magnitude of the mismatch signal, and changes in the internal model on exposure to a new and unfamiliar (atypical) motion environment and on return to the familiar (typical) environment. Adapted with permission from Reason JT, Brand JJ. *Motion Sickness*. London, England: Academic Press; 1975: 170.

egories, two types of neural mismatch can occur: Type 1 when both sensory systems concurrently signal contradictory or uncorrelated information, and Type 2 when one system signals information in the absence of the expected signal from the other system (Table 35-1). Readers should keep in mind, however, that most provocative motion environments involve more than one type of sensory conflict.

Visual–Vestibular Mismatch

Type 1. Uncorrelated visual and vestibular inputs are present when an observer on a moving vehicle cannot see an object or scene that provides stable orientational reference to the true vertical or horizontal. Vestibular and somatosensory receptors signal motion of the vehicle (whether a ship, aircraft, or land vehicle), but if the occupant of the vehicle is using an unstabilized optical device, such as hand-held binoculars or an optical sight, some motion of the visual scene will not be correlated with vestibular information. Even minor changes in the perceived visual scene (eg, wearing eyeglasses with new lenses) can, in the presence of normal head movements, evoke mild symptoms of motion sickness. More dramatic distortion of vision produced by, for example, prisms that laterally reverse the visual scene (so that it moves to the right, rather than to the left, with a head movement to the right) can be highly provocative if the wearer of such a device executes head movements and attempts to walk about. Sickness induced by reading a hand-held map or book while being driven over rough roads or in turbulent flight is another example of Type 1 visual–vestibular conflict.

TABLE 35-1

CLASSIFICATION OF NEURAL MISMATCH IN PROVOCATIVE ENVIRONMENTS

	Category	
Type	**Visual (A)/Vestibular (B)**	**Canal (A)/Otolith (B)**
Type 1: A and B signals simultaneously give contradictory information	Watching waves from a ship Use of binoculars in a moving vehicle Making head movements when vision is distorted by an optical device Reading hand-held material in a moving vehicle Cross-coupled (Coriolis) stimulation Simulator sickness (moving base)	Making head movements while rotating about another axis (Coriolis, or cross-coupled, stimulation) Making head movements in an abnormal acceleration environment, which may be constant (eg, hyper- or hypogravity) or fluctuating (eg, linear oscillation) Space sickness (fast head movement) Vestibular disorders (eg, Ménière's disease, acute labyrinthitis, trauma)
Type 2a: A signals are received but expected B signals are absent	Simulator sickness (fixed base) Cinerama / Imax sickness Haunted swing* Circular linear vection	Space sickness (slow head movement) Pressure (alternobaric) vertigo Caloric stimulation of semicircular canals Vestibular disorders (eg, cupulolithiasis, round window fistula)
Type 2b: B signals are received but expected A signals are absent	Looking inside a moving vehicle without external visual reference Reading in a moving vehicle	Low-frequency (< 0.5 Hz) translational oscillation Rotating linear acceleration vector (eg, "barbecue-spit" rotation; rotation about an off-vertical axis)

*Haunted swing: a device in which the swing is stationary and the visual surround swings

Type 2a. Situations in which visual motion stimuli are not accompanied by commensurate and expected movement of the body can provoke Type 2a mismatch. However, severe symptoms are rarely engendered by the dynamic visual stimuli afforded by projected displays (Cinerama, Imax) or the computer-generated imagery of flight or road vehicle simulators. Visual stimuli that are meaningful to the observer and accord with previous real-world experience (eg, an aircraft entering a steep turn or an automobile decelerating hard) are most likely to provoke a response, but sickness can also be evoked by steady movement of nonrepresentational visual stimuli (eg, a pattern of bars or random spots). Such an *optokinetic* stimulus evokes an illusory sensation of turning, called circularvection, which, when not accompanied by concordant vestibular information, is a source of sensory mismatch.

Type 2b. The converse of Type 2a mismatch, Type 2b mismatch occurs when vestibular and other gravireceptors are stimulated by vehicular motion but the expected visual motion cues are absent. This type of conflict is present in all kinds of passive transportation wherein the occupant does not have a clear view of a stable, external, visual scene. Aboard ship in rough seas, an individual on deck with a good view of the horizon is less likely to suffer from seasickness than one who is below deck. The latter receives visual information only about his movement within the cabin and not the actual motion of the vessel as transduced by his nonvisual sensory systems. Sensory conflict is reduced by closing the eyes, which can increase tolerance to the provocative motion. Conversely, performance of a visual task decreases tolerance, especially if it involves visual search, such as the identification of targets on a map or radar display.[19] Tasks involving visual tracking of a moving target in the presence of whole-body motion have been shown in laboratory experiments[20] to be more provocative than when only a stationary target was observed.

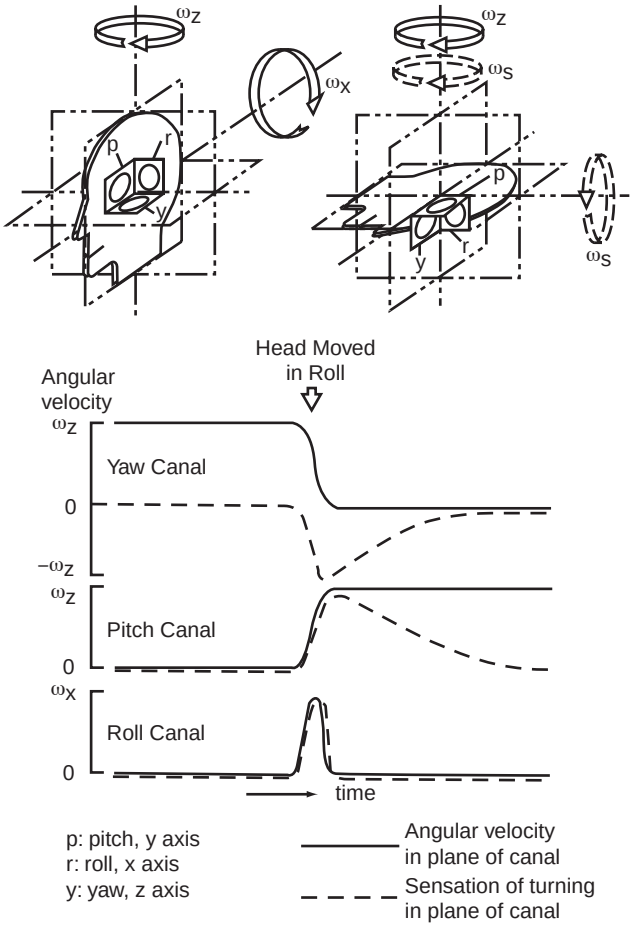


Fig. 35-7. Cross–coupled (Coriolis) stimulation of the semicircular canals by a head movement of 90° in roll (x axis) having a maximum angular velocity of ω_x while also rotating at a constant velocity (ω_z) about a vertical axis. The six semicircular canals are represented by an idealized three-canal system (labeled y, p, and r in figure) orthogonally disposed to transduce angular movements of the head in the yaw (y), pitch (p), and roll (r) axes. The lower half of the figure shows the angular velocity, as a function of time, in the plane of each canal (——) and the sensation of turning (– – –) engendered by the angular stimulus. Note that in the steady state (ie, ω_z constant for 30 s or more), none of the canals signal rotation. However, when the head is moved in roll, the yaw canal is taken out of the plane of rotation and generates an illusory sensation of rotation about an Earth horizontal axis that is in conflict with information from the otoliths and other gravireceptors that signal a stable, left-ear-down, head position. Initially, the pitch canal signals veridically the vertical axis rotation of magnitude (ω_z), but as the speed of the vertical axis rotation is constant, the sensation decays, as does the erroneous sensation from the yaw canal. The plane of the roll canal does not change during the head movement, hence it is not influenced by the vertical axis rotation (ω_z) and it signals correctly the time course and angular velocity of the roll movement. Reproduced with permission from Benson AJ. Spatial disorientation: Common illusions. In: Ernsting J, Nicholson AN, Rainford DJ, eds. *Aviation Medicine*. 3rd ed. London, England: Butterworths; 1999: 445.

Intravestibular (Canal–Otolith) Mismatch

Vision is not essential for the induction of motion sickness, for the blind, like sighted individuals with eyes closed or in darkness, are susceptible.

Type 1. Type 1 neural mismatch, in which receptors of both the semicircular canal and the otolith organs each signal motion of the head, occurs when active or passive head movements are made in a vehicle that is turning, or is undergoing motion that exposes those aboard to an atypical force environment (ie, other than 1*g* vertical). When an angular head movement is made while exposed to sustained rotation about some other axis, the semicircular canals receive a cross-coupled, or Coriolis, stimulus. Figure 35-7 illustrates how three idealized orthogonal, semicircular canals are stimulated when a 90° head movement is made in *roll* (ie, movement about the front-to-back, or x, body axis) is made during a sustained turn in *yaw* (ie, the head-to-foot, or z, body axis). The head movement is correctly transduced by the roll canal, but the *pitch* (ie, the side-to-side, or y, body axis) and yaw canals experience changes in velocity, which give rise to erroneous sensations of turning in these planes and which take many seconds (typically 5–10 s) to decay. During the period the canals are generating *false* sensations, the otoliths provide *correct* information about the orientation, and the change in orientation, of the head with respect to gravity; there is, therefore, a mismatch that in practice can be highly provocative. In susceptible individuals, just one head tilt through 90° in roll, while rotating in yaw at 30 rpm, can evoke symptoms, even vomiting. In everyday life, however, such high rates of sustained rotation are rarely experienced outside the fairground or research laboratory. More commonly, sickness is induced by repeated head movements in a vehicle executing slow turns, with concomitant changes in the force environment.

Cross-coupled stimulation is not the only cause of neural mismatch associated with head movement. When the head is moved in an atypical force environment (ie, one in which the gravito-inertial force is greater or less than 1*g* [where *g* is a unit of acceleration equal to Earth's gravity, 9.81 m/s^2]),

otolithic afferent information about the change in orientation of the head differs from that generated when the same head movement is made in the normal 1*g* environment. Neural mismatch occurs because the semicircular canals correctly transduce the angular movement of the head. Their sensitivity is but little, if at all, influenced by the force environment, whether this be the hypogravity of orbital flight or the hypergravity achieved by tight turns in combat aircraft.

The nausea, vomiting, and malaise suffered by those with acute vestibular disorders occur in the absence of motion and are, by definition, not motion sickness. Nevertheless, the signs and symptoms, often exacerbated by head movement, are in most respects identical to those of motion sickness, and they share a common etiology, namely a Type 1 mismatch of afferent signals from the canals and otoliths. For example, severe disturbance of afferent signals from vestibular receptors is associated with sudden unilateral loss of vestibular function by trauma or labyrinthectomy. Likewise, pathological processes such as Ménière's disease can cause a sudden change in the resting discharge of canal and otolithic receptors, an alteration of their stimulus response characteristic, or both.

Type 2a. Neural mismatch due to the absence of expected signals from the otoliths when the canals signal motion has been adduced as a primary cause of space sickness.[6,21] In weightlessness, movements of the head will be correctly transduced by the canals, but provided the head movement does not involve high angular accelerations, the linear acceleration of the otoliths will be insufficient to stimulate them, and a Type 2a intravestibular mismatch will occur. However, if an astronaut, for example, makes rapid head movements similar to those made on Earth, where angular accelerations of 400 degrees per second squared ($°/s^2$) to $500°/s^2$ are commonly achieved, the otoliths will be stimulated in an atypical manner and a Type 1 mismatch will occur.

Stimulation of semicircular canal receptors in the absence of concomitant otolithic stimulation can be caused by change in ambient pressure. During ascent, aircrew and divers sometimes experience sudden vertigo, hence the name *pressure* or *alternobaric vertigo*. The vertigo and associated nystagmus are commonly short-lived but in some individuals, symptoms may persist and be accompanied by nausea and malaise. Other conditions in which the canals are selectively stimulated are positional alcohol vertigo (PAV) and benign paroxysmal vertigo (BPV).[22] In both of these conditions, the semicircular canals may become sensitive to linear acceleration, and hence their orientation to gravity, owing to a change of density between the cupula and endolymph within the semicircular canals. The diffusion of alcohol from the blood into the cupula, rendering it less dense than the endolymph, may be responsible for the initial phase of PAV. The transient vertigo that occurs in BPV on moving the head to a right- or left-ear-down position has been attributed[23] to the lodgment of otoconial debris on the cupula (cupulolithiasis), which makes it more dense than the endolymph.

Type 2b. When signals from otolithic and somatosensory gravireceptors are not accompanied by the expected signals from the semicircular canals, Type 2b canal–otolith mismatch (the converse of Type 2a) occurs. Selective stimulation of the otoliths can readily be achieved by exposing an individual to rotation at a steady speed about a nonvertical axis. Once the effect of the initial angular acceleration has abated, the canals fail to signal rotation but the otoliths are stimulated by the continued reorientation of the head and body to gravity. Continuous rotation about an Earth-horizontal axis that is aligned with the z axis of the subject's body (as on a barbecue spit) is highly provocative, nausea being induced in most subjects within a few minutes when rotated at 10 rpm.[24] Otolithic stimulation produced by rotation of the specific force vector, as in barbecue spit rotation, is a feature of certain aerobatic maneuvers and fairground rides. Considerably more common are those situations in which motion sickness is induced by repetitive translational (linear) acceleration, such as is experienced aboard a heaving ship, an aircraft flying through turbulent air, or a motor vehicle that is repeatedly accelerated and braked.

A number of experiments carried out on vertical and horizontal oscillators, modified lifts, and parallel swings (reviewed by Guignard and McCauley[25] and Griffin[26]) demonstrated that the incidence of motion sickness bears an inverse relation to the frequency of oscillation (Figure 35-8). These laboratory studies accord with observations made in aircraft and ships. Aircraft with a high (0.8–0.9 Hz) natural frequency of response to turbulence produced less sickness than aircraft with a low (0.4 Hz) natural frequency. Similar observations have been made aboard ships,[27] and they accord with anecdotal reports that car sickness is more common in vehicles with a soft, low-frequency suspension than in those with firmer springing and a higher natural frequency.

The nature of the neural mismatch that causes motion sickness during linear oscillation at 0.2 Hz but not at 1 Hz is not immediately apparent. It may be explained[22] by consideration of the correlation of canal and otolithic activity established during normal

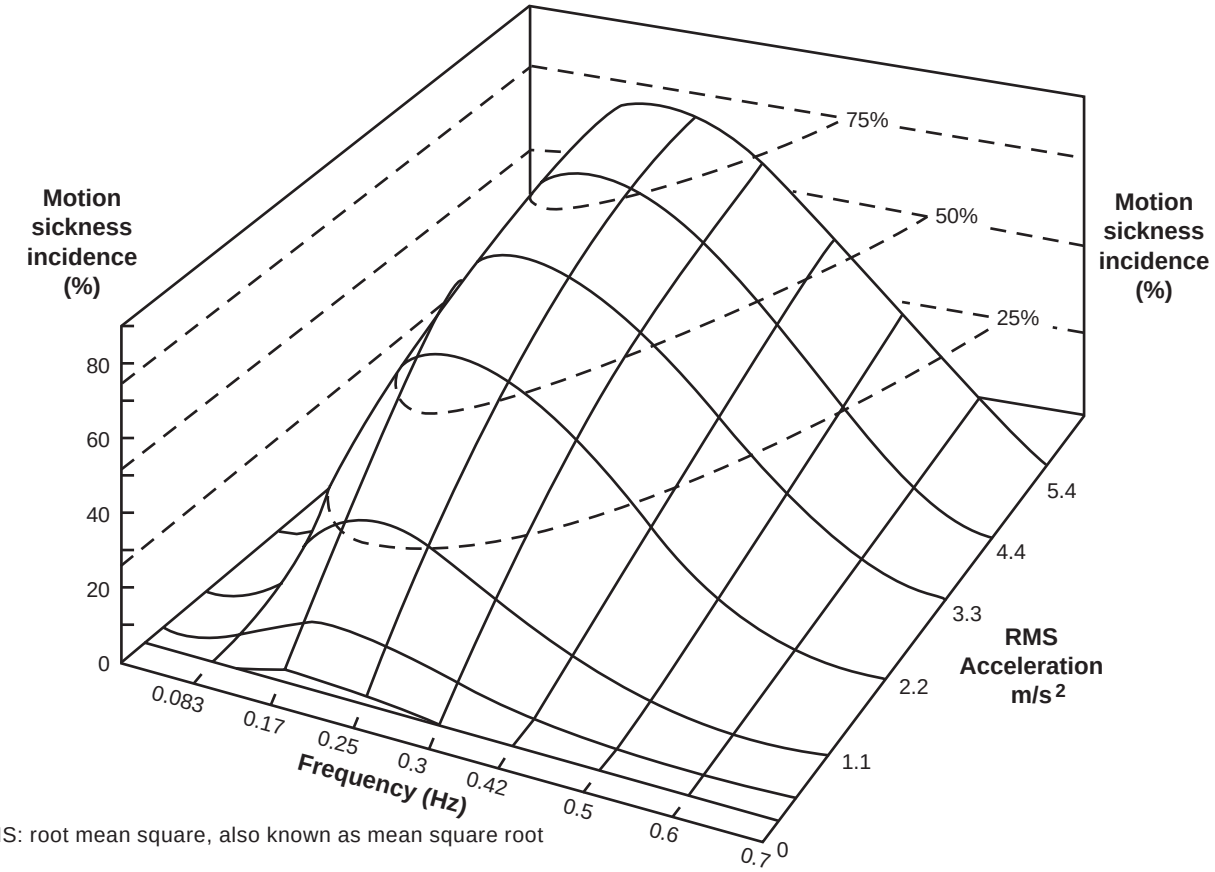


Fig. 35-8. Oscillation about an earth-vertical axis at a frequency of about 0.2 Hz produces the highest incidence of motion sickness. At higher and lower frequencies the stimulus is progressively less provocative. The incidence of sickness increases as a function of the intensity of the oscillation, but even a stimulus having an RMS amplitude of less than 1 m/s^2 is provocative at 0.2 Hz. Adapted with permission from McCauley ME, Royal JW, Wylie CP, O'Hanlon JF, Mackie RR. *Motion Sickness Incidence: Exploratory Studies of Habituation, Pitch and Roll and the Refinement of a Mathematical Model.* Santa Barbara, Calif: Human Factors Research, Inc; 1976: 39. Technical Report 1733-2.

locomotor activities. The dominant frequencies of head motion during walking, running, jumping, and so forth lie in the range 0.5 to 10 Hz, so it is in this frequency domain that the canals and otoliths signal angular and linear motion in a dynamic but not necessarily correlated manner. At lower frequencies, however, a change in the head's orientation to gravity in the pitch and roll planes is signaled by the otoliths acting in their "static," position-sensing role, and the canals contemporaneously signal the angular movement. Thus, when otoliths and other gravireceptors are stimulated by a slowly changing force vector, the CNS expects concomitant and concordant information from the canals. During linear oscillation, the otoliths but not the canals are stimulated; Type 2b mismatch occurs and motion sickness may result.

An alternative explanation, although one still dependent on a mismatch between afferent information and that which the CNS expects to receive, was proposed by Stott.[28] He pointed out that during natural locomotor activity over periods of more than about 1 second, the average intensity of the linear acceleration of the head has a magnitude of 1*g* and therefore defines "downward." Conditions in which the otoliths and other gravireceptors signal slowly changing linear acceleration (eg, during linear oscillation at frequencies < 1 Hz) depart from the normal invariant pattern of sensory input and hence constitute a potentially provocative neural mismatch.

The well-defined inverse relation between the incidence of motion sickness and the frequency of linear oscillation implies the presence of a low-pass

filter in either the comparator or the relay of the mismatch signal to the neural centers mediating the motion sickness syndrome. The characteristics of this postulated filter at frequencies below 0.2 Hz is a matter for conjecture. Sickness does not occur when stationary (ie, frequency = 0) in normal gravity but has a high incidence during "parabolic" flight, in which periods of 0*g* and 2*g* alternate at a frequency of about 0.05 Hz.[29] This, however, is a powerful stimulus and the gain of the low-pass filter is probably less than at 0.2 Hz. Flight experiments involving vertical oscillation at 0.1 Hz, with an acceleration of ± 0.3*g*, produced incapacitating motion sickness when the investigator made head movements.[30] Provocation decreased as the period of oscillation increased and was insignificant at 0.02 Hz, ± 0.1*g*.

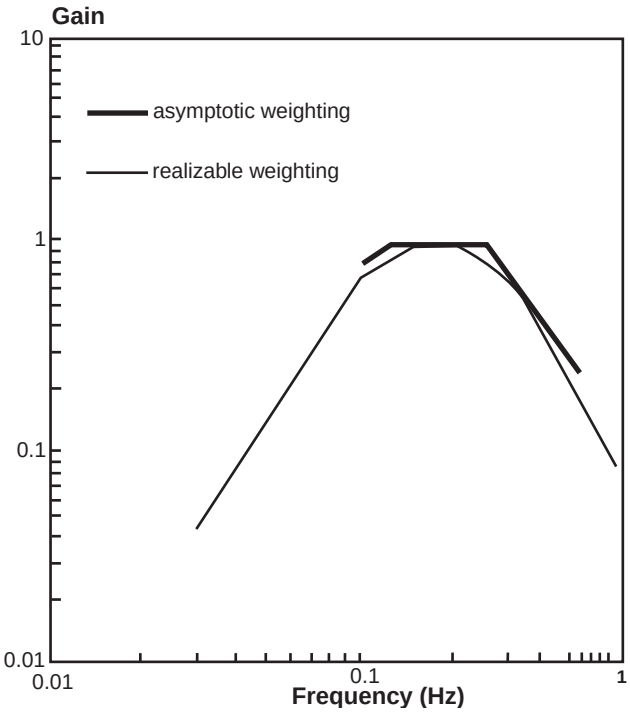


Fig. 35-9. Bode plot of the filter characteristic required to provide the frequency weighting (W_f) used to calculate the motion sickness dose value ($MSDV_z$) in the equation $MSDV_z = a \bullet W_f \bullet t^{1/2}$ (Equation 1 in the chapter). The graph shows a straight-line "asymptotic approximation" used to define the weighting function, as is required in the specification of measuring instruments, and the "realizable weighting" that can be achieved by conventional electronic filters. The weighting function has the characteristic of a band-pass filter with the greatest sensitivity in the octave 0.125–0.25 Hz with rapid attenuation in sensitivity at higher and lower frequencies. Reproduced with permission from Griffin MJ. Physical characteristics of stimuli provoking motion sickness. In: *Motion Sickness: Significance in Aerospace Operations and Prophylaxis*. Neuilly-sur-Seine, France: Advisory Group for Aerospace Research and Development, North Atlantic Treaty Organization. 1991; Paper 3:3-11. AGARD Lecture Series 175.

Etiologic Factors Affecting Incidence

The frequency and severity of symptoms in a group of people exposed to provocative motion is governed by a number of factors, of which the most important are the physical characteristics of the motion and the differences between individuals in their susceptibility to motion sickness.

Physical Characteristics of the Motion Stimulus

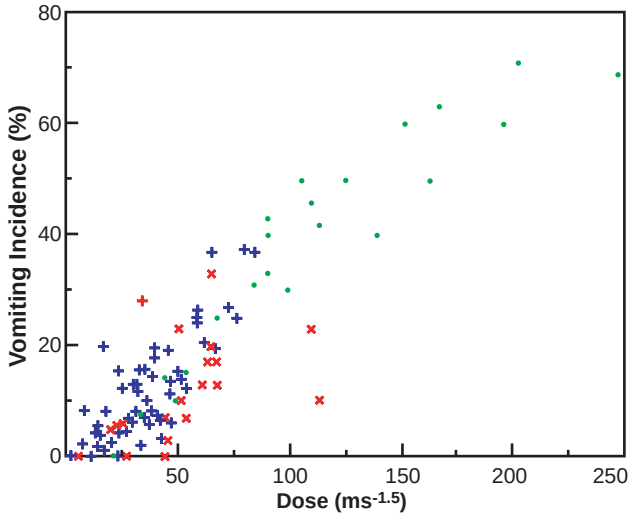


Fig. 35-10. Relation between motion dose, calculated in accordance with $MSDV_z = a \bullet W_f \bullet t^{1/2}$ (Equation 1 in the chapter), and the incidence of vomiting. The data points are from reports published by Alexander et al (1947, x) and McCauley et al (1976, •), who provoked sickness by vertical oscillation; and Lawther and Griffin (1986, +), who used data from ships' passengers on 6-hour voyages. Reproduced with permission from Lawther A, Griffin MJ. Prediction of the incidence of motion sickness from the magnitude, frequency and duration of vertical oscillation. *J Acoust Soc Am*. 1987;82:963.
x: Alexander SJ, Cotzin M, Klee JB, Wendt GR. Studies of motion sickness, XVI: The effects upon sickness rates of waves and varioius frequencies but identical acceleration. *J Exp Psychol*. 1947;37:440–447.
•: McCauley ME, Royal JW, Wylie CP, O'Hanlon JF, Mackie RR. *Motion Sickness Incidence: Exploratory Studies of Habituation, Pitch and Roll and the Refinement of a Mathematical Model*. Santa Barbara, Calif: Human Factors Research Inc; 1976. Technical Report 1733-2.
+: Lawther A, Griffin MJ. The motion of a ship at sea and the consequent motion sickness amongst passengers. *Ergonomics*. 1986;29:535–552.

The limited number of studies that have correlated the incidence of sickness with measures of the physical characteristics of the provocative motion confirm what is known from everyday experience, namely that the intensity, frequency, and duration of the motion are of prime importance. In most ships, aircraft, and land vehicles, there is motion with six degrees of freedom: three *angular* (pitch, roll, and yaw), and three *linear* (surge, heave, and sway). But in an extensive study in which ship motion was related to the incidence of sickness among passengers,[31] the best predictor of sickness was found to be the intensity of the linear acceleration of the vertical, z axis motion (heave) of the vessel, duly weighted for the frequency of the motion. Lawther and Griffin[31] proposed that the incidence of motion sickness for exposures of up to 6 hours could be predicted by the motion sickness dose value ($MSDV_z$), which is related to stimulus intensity and duration by the following formula (Equation 1):

$$1. \qquad MSDV_z = a \bullet W_f \bullet t^{1/2}$$

where *a* represents the root mean square (rms) heave acceleration in m/s^2, W_f represents a frequency weighting factor, and *t* represents the duration of exposure in seconds. The frequency weighting is based on laboratory experiments by O'Hanlon and McCauley[32] (see Figure 35-8) and takes the form shown in Figure 35-9. The greatest weight is given to frequency components in the octave 0.125 to 0.250 Hz, frequencies above and below this range being progressively attenuated. The time dependency of $t^{1/2}$ is also based on the McCauley experiments. These showed that for motion exposures of up to 2 hours, the incidence of sickness did not exhibit a linear relation to the duration of exposure but one that was better fitted by a power law function with an exponent of 0.5.

Lawther and Griffin[31] proposed a linear relation between the incidence of sickness and the $MSDV_z$ (Equation 2):

$$2. \qquad V = k \bullet MSDV_z$$

where *V* represents the predicted percentage incidence of vomiting and *k* represents a factor, estimated at one third, for the general population. Figure 35-10 shows the relation between MSDV and the incidence of vomiting in laboratory and field studies. Prediction of an "illness rating" (I) on a scale of 0 = "I feel all right," to 3 = "I feel dreadful" may also be made using the following formula (Equation 3):

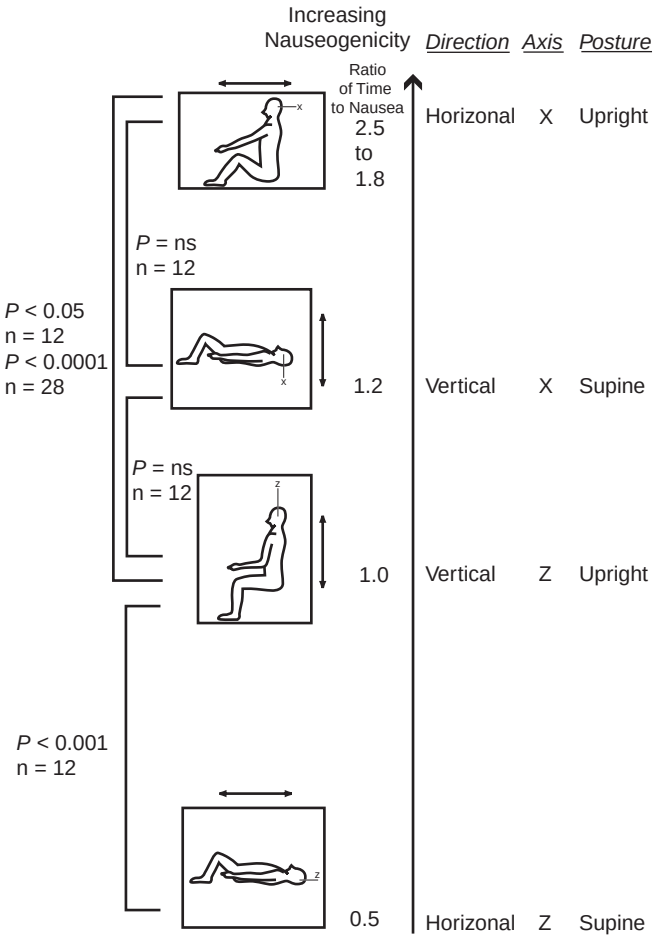


Fig. 35-11. Acceleration with the body in certain positions results in more-rapid onset of motion sickness. The nauseogenicity of a low-frequency linear oscillation varies with the posture of the subject (upright or supine) and the orientation to gravity of both the subject (horizontal or vertical) and the axis of motion (x or z). Statistical significance (*P*) of differences in nauseogenicity and numbers of subjects (n) used in each study are indicated along the brackets to the left of the figure. Reproduced with permission from Golding JF, Harvey HM, Stott JRR. Effects of motion direction, body axis, and posture on motion sickness induced by low frequency linear oscillation. *Aviat Space Environ Med*. 1995;66:1050.
ns: not significant

$$3. \qquad I = (0.045 \bullet V) + 0.1$$

The studies on which these three predictive formulas are based were confined to vertical, linear oscillation, principally acting in the head-to-foot (or z) body axis. The orientation of the body with respect to the direction of the linear motion can influence its nauseogenic potential, as can the direction of the

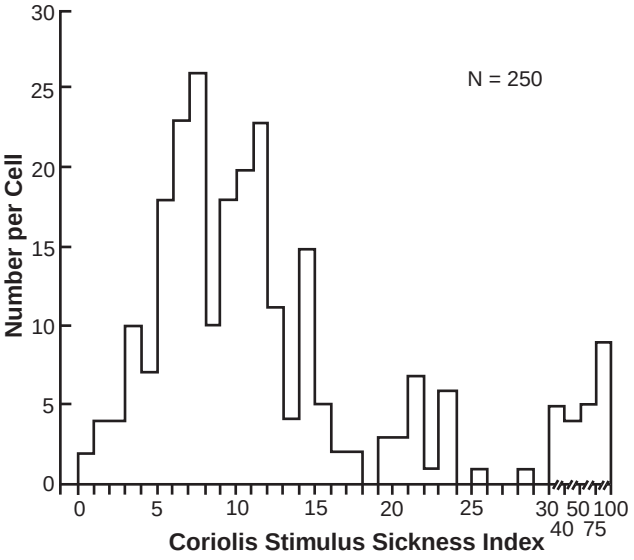


Fig. 35-12. Histogram showing the distribution, in 250 normal subjects, of susceptibility to motion sickness induced by cross-coupled (Coriolis) stimulation. The distribution of susceptibility is highly asymmetrical and perhaps bimodal. The measure of the magnitude of the stimulus (the Coriolis stimulus sickness index) is nonlinear, being a combination of the duration of exposure and the turntable speed, which increased with time. Note the presence of a small number of subjects who were highly resistant to the provocative stimulus. Reproduced from Miller EF, Graybiel A. The semicircular canals as a primary etiological factor in motion sickness. In: *Fourth Symposium on the Role of the Vestilinear Organs in Space Exploration*. Washington DC: National Aeronautics and Space Administration; 1970: 77. Report SP-187.

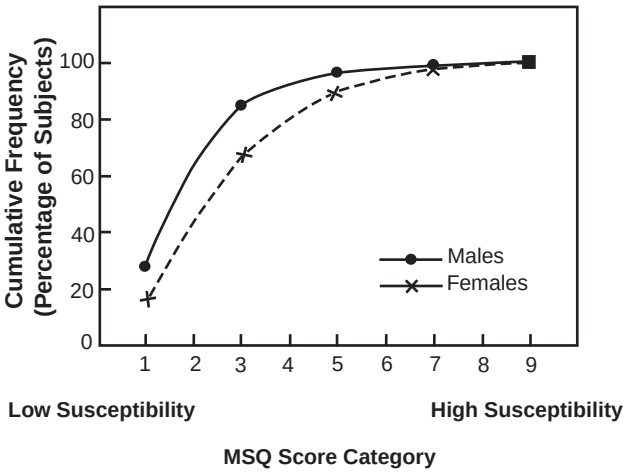


Fig. 35-13. Cumulative frequency distributions of the motion sickness questionnaire (MSQ) scores of 2,432 university students. The graph shows that the male students had a higher frequency of low MSQ scores than the female students, with median scores of 1.5 and 2.3 for men and women, respectively. Data source: Lentz JM, Collins WE. Motion sickness susceptibility and related behavioral characteristics in men and women. *Aviat Space Environ Med*. 1977;48:317.

motion relative to the gravitational vertical. The findings of experiments[33] in which body orientation to gravity and to stimulus direction were systematically varied suggest that for a given intensity of low-frequency linear oscillation, the incidence of sickness is higher (*a*) when the stimulus acts in the x (antero–posterior) than in the z (head–foot) body axis and (*b*) when the individual is upright rather than supine. This is shown diagrammatically in Figure 35-11, in which the nauseogenicity of the stimuli is related to the z axis (ie, the vertical, upright condition).

Although there is some, albeit not consistent, evidence that restricting angular head movements in provocative motion environments reduces the incidence of sickness,[34,35] there is no support for the potentiation of a linear stimulus (typically vertical axis, heave motion) by concomitant angular rolling or pitching motions, such as occur aboard ship. These angular motions have frequency spectra with peaks close to those of the dominant heave motion. Volitional or passive angular head movements made in the presence of such cyclical angular movements do not evoke erroneous cross-coupled (Coriolis) sensations, and they should not be provocative. Sustained angular motion, in which head movements are known to be provocative, does not commonly occur in transportation devices; notable exceptions, however, include aircraft in a steady turn, a spinning parachutist, or a tumbling space vehicle. The intensity of the sensations and the nauseogenic effect of an out-of-axis head movement depend on (*a*) the angle through which the head is moved and (*b*) a power law function of the steady rate of turn, having an exponent between 1.7 and 2.1.[36] Thus, a head movement made when turning at, say, 20°/s is roughly 4-fold more provocative than one made at 10°/s. As most individuals can make several large-amplitude head movements while rotating at 60°/s without becoming sick, we can infer that only the most sensitive are likely to suffer symptoms during sustained procedural turns in aircraft, as these rarely exceed 10°/s.

Individual Differences in Susceptibility

One notable feature of motion sickness is the

large difference between individuals in their susceptibility to provocative motion. On leaving harbor and heading into rough seas, some among those aboard develop symptoms and vomit within minutes, others tolerate the motion for half an hour or more, and a minority are unaffected. However, in extreme conditions the only people who will not succumb to motion sickness are those without functional vestibular systems.[1,17,37] The wide scatter in susceptibility is illustrated in Figure 35-12, which shows the number of subjects who developed significant signs and symptoms of motion sickness as a function of the intensity of a provocative cross-coupled (Coriolis) stimulus. Departure from a simple normal distribution is caused by a small, particularly resistant group of the population. It may be that the distribution in susceptibility is truly bimodal, but as the test employed a rotational stimulus that was increased incrementally, the high-tolerance tail of the distribution may be attributed to those subjects who had both low intrinsic susceptibility and the ability to adapt to the prolonged repetitive stimulus. Subjects with low tolerance had little opportunity to adapt before the test was terminated by the advent of their malaise. A bimodal distribution in susceptibility has, however, been adduced by Shepard and colleagues,[38] whose contention that susceptibility is a heritable trait is supported by the finding of differences in the α_2-adrenergic receptor gene in the subjects designated high- and low-susceptibles.

Susceptibility to motion sickness changes with age. Motion sickness is rare below the age of 2 years, but thereafter susceptibility increases to reach a peak between the ages of 4 and 12 years. Tolerance progressively increases over the next decade or so, so that beyond the age of 25 years, susceptibility is perhaps half of what it was at 17 to 19 years.[39] With increasing age, sensitivity declines further. The elderly are not, however, immune, as studies[27] of passengers in aircraft and ships have shown, but the reduction in sensitivity from that of the general population (ie, the value of k in Equation 2) has not been quantified.

A number of studies employing questionnaires show that women are more susceptible to motion sickness than men of the same age[6,40,41] (Figure 35-13). In passengers aboard a seagoing ferry, a higher incidence of seasickness was reported by female than by male passengers in the ratio of about 1.7:1 (ie, the value of k, in Equation 2 estimated at 0.33 for the general population, would be 0.25 for men and 0.42 for women).[27] The reason for this gender difference is not known. It may be that women are more ready to report symptoms than men; on the other hand, hormonal factors may be significant, as women are reported to have higher susceptibility during their menses. In contrast, comparison of the incidence of space sickness and tolerance to ground-based provocative tests in male and female astronauts[42,43] has failed to show a gender difference; on average, the female astronauts had a slightly lower, albeit not significantly lower, incidence of space sickness than their male colleagues. Hormonal factors may also explain why men who had a high degree of aerobic fitness and, presumably, higher levels of endorphin, had a lower tolerance of provocative motion than those who had not participated in a physical training program.[44,45]

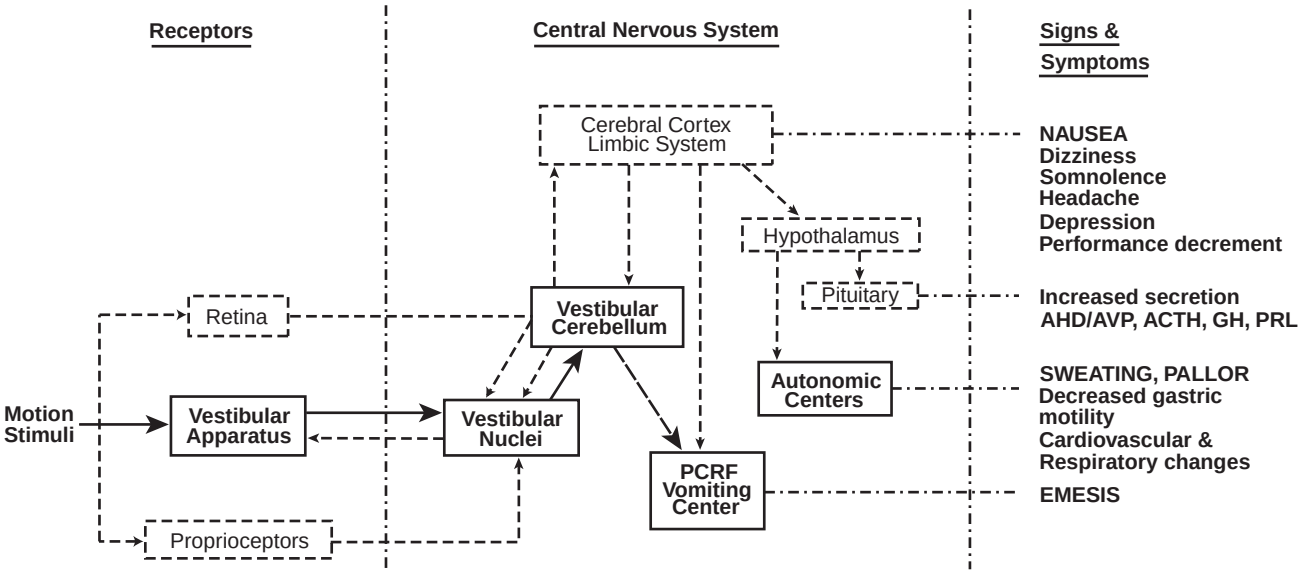
In a group of men or women of similar age and exposure to provocative motion, there are still large differences in susceptibility, differences that are largely enduring traits of the individual. With the known importance of the vestibular sensory system in motion sickness, we might have expected a correlation between measures of vestibular function and susceptibility. However, no clear relation having predictive power has been established despite numerous investigations (reviewed by Kennedy, Dunlap, and Fowlkes[46]). Interestingly, one of the few consistent findings was the presence of greater asymmetry in responses to caloric stimuli in those with a high susceptibility to seasickness and airsickness.[47,48]

As individual differences cannot be accounted for by differences in the transduction of bodily motion by receptor systems, they must be due to processes within the CNS. Reason and Graybiel[49] proposed that a large part of individual variation in susceptibility was due to the strength or weakness of three factors: (1) receptivity, (2) adaptability, and (3) the retention of adaptation. Receptivity refers to the internal scaling of sensory information. In terms of the motion sickness model, those who have high receptivity would be expected to have a more-intense mismatch signal and a higher susceptibility to motion sickness. Adaptability describes the rate at which an individual adapts, by updating the internal model, on exposure to an atypical motion environment. Those who adapt slowly will have a more-prolonged mismatch and are more likely to become sick than those who are fast adaptors. These concepts of receptivity and adaptability permit explanation of how a person may react on first exposure to provocative motion. His or her response on reexposure depends on how well the protective adaptation is retained (ie, on the degree of retentivity).

These three factors all influence susceptibility but are not of equal importance in an operational context. Evidence in an individual of high receptivity implies that sickness will occur on initial exposure to unfamiliar provocative motion, but if he or she is a fast adaptor and has high retentivity, then sickness is unlikely to be a persistent problem. Conversely, a person with low adaptability and poor retention is likely to suffer chronic motion sickness.

The idea that psychological factors are of prime importance in the etiology of motion sickness has had many advocates over the years, yet the weight of evidence (see reviews by Money,[2] Reason and Brand,[6] Mirabile,[39] and Tyler and Bard[50]) favors the conclusion that psychological factors and psychopathology play only a minor role in determining susceptibility. Nevertheless, there is experimental evidence[51] that mental stress and anxiety can heighten susceptibility. Attempts to correlate motion sickness susceptibility with psychological traits, as revealed by personality inventories, have yielded conflicting results, although significant correlations have been found in a number of tests (see reviews by Collins and Lentz[52]; Kennedy, Dunlap, and Fowlkes[46]; and Mirable[39]). In general, susceptible individuals are more prone to anxiety and have high neuroticism scores; in addition, they are more self-contained or introverted. The nonsusceptible tend to be tough and aggressive and are better able to cope with stress in a nonemotional manner.[52] Susceptible individuals, on the other hand, are more likely to manifest autonomic reactions (eg, increased heart rate, sweating) in stressful situations.

The extent to which these dimensions of personality are causally related to susceptibility is a matter for conjecture. The demonstration that introversion and neuroticism are associated with slow adaptation[49] suggest a possible mechanism for the lower tolerance found in individuals with high scores of these traits. Furthermore, a neurotic indi-



ACTH: adrenocorticotropic hormone
ADH/AVP: antidiuretic hormone/arginine vasopressin
GH: growth hormone
PCRF: parvicellular reticular formation
PRL: prolactin

Fig. 35-14. Neural structures involved in motion sickness. The bold-faced boxes and arrows indicate structures and pathways considered to be essential, whereas the broken boxes and arrows identify structures and pathways that can be involved in the development of the syndrome but are not essential. The dot-dash lines link the signs and symptoms with the neural structures thought to be involved. (They also guide the eye to indicate the separation of receptors from the central nervous system and the list of signs and symptoms.) Reproduced with permission from Benson AJ. Operational aviation medicine. In: Ernsting J, Nicholson AN, Rainford DJ, eds. *Aviation Medicine*. 3rd ed. London, England: Butterworths; 1999: 464.

vidual is more likely to be aroused and made anxious by what may be perceived as a life-threatening environment, such as aerobatic flight or storm conditions at sea. Heightened anxiety will degrade the acquisition of protective adaptation and may even prevent adaptation altogether.

NEURAL CENTERS AND PATHWAYS

Although the neural mismatch theory postulates certain neural processes within the CNS, it tells us little about which centers and pathways mediate the signs and symptoms of the motion sickness syndrome, nor about the process of adaptation. Knowledge about the neurophysiological mechanisms involved is far from complete, although some have been identified by experimental studies. Figure 35-14 summarizes the principal elements and pathways that are thought to be involved and relates them to the physiological and behavioral responses that characterize the motion sickness syndrome.

Essential for the development of motion sickness is the presence of a functional vestibular system, namely the semicircular canals and otolith organs in the membranous labyrinth and the vestibular nuclei. The importance of the vestibular projections to the cerebellar uvula and nodules is less certain. Early studies[53,54] indicated that ablation of these structures abolished swing sickness in dogs, but this was not confirmed by Miller and Wilson,[55] who demonstrated continued susceptibility of cats after large lesions of the cerebellar vermis were made.

The location of the mismatch comparator is a matter for conjecture, although it is most likely to lie in those structures where vestibular, visual, and proprioceptive signals converge, namely the vestibular nuclei and the cerebellum. The activity of cells in the second-order neurones of the vestibular nuclei can be influenced by optokinetic stimuli and by joint movement.[56] There is, however, no evidence to date for the presence of neurones that signal disparity of motion information. In contrast, Purkinje's cell activity of the flocculus of the cerebellum has been shown[57] to reflect the difference between retinal and vestibular signals of motion. The cerebellum is also of importance in adaptation to sensory rearrangements that typically evoke motion sickness. Removal of the vestibular cerebellar cortex prevents adaptive modification of vestibular–ocular control in animals whose vision was "reversed" by prisms[58] and inhibits habituation to vestibular stimuli.[59]

Supratentorial neural systems are not required for motion sickness to occur, as decerebrate animals retain their susceptibility. Nevertheless, the cerebral cortex is involved in the expression of symptoms (eg, nausea, dizziness, somnolence, and depression) and the establishment of aversive and conditioned responses to motion. Attention has also been directed toward the role of the telencephalic limbic system as another possible location for the identification of sensory mismatch and for the acquisition of protective adaptation.[60] The mesencephalic components are connected to visceral sensory centers in the reticular formation of the brainstem by both ascending and descending pathways. The latter probably play an important role in mediating the changes in autonomic activity, manifest as the vasoconstriction (pallor), sweating, and reduction in gastric motility that consistently occur in motion sickness. Involvement of the diencephalic component of the limbic system, the hypothalamus, must also be inferred from the increased secretion of pituitary and adrenal hormones found in subjects exposed to provocative motion stimuli.[11] It must be acknowledged, however, that ablation experiments[61] have shown that neither the hypothalamus nor the pituitary gland is essential for the induction of motion sickness.

The relatively slow development of the physiological correlates of motion sickness and the persistence of signs and symptoms after withdrawal of provocative motion suggest that the activation of autonomic centers and finally the act of vomiting are achieved by the accumulation of a neurohumoral agent released by the center or centers that identify sensory mismatch. Support for this concept came from experiments in which animals were rendered refractory to motion sickness when a plastic barrier was placed over the area postrema of the medulla or when the sylvian aqueduct was blocked. The findings are, however, not conclusive, and alternative explanations can be adduced (see Crampton[62] for a review of this topic). Furthermore, the role of the area postrema and its chemoreceptive trigger zone (CTZ), once thought to be essential for the emetic response in motion sickness, has been negated by careful ablation studies.[63] The CTZ is necessary for vomiting to be induced by various drugs, chemicals, and poisons, but it is not an essential component of the neural structures mediating motion sickness.

Emesis, a coordinated motor act involving contraction of the diaphragm and abdominal muscles, relaxation of the cardiac sphincter, and gastric stasis, appears to depend on the integrity of a zone of the parvicellular reticular formation (PCRF) in the me-

dulla. Electrical stimulation in this area elicits vomiting as well as prodromal signs and led to its being identified as a central coordinating mechanism for emesis.[64] For convenience, the PCRF has been called a vomiting center, although this belies the fact that the area is not well localized.[55] The PCRF is located ventral to the vestibular nuclei and is traversed by an extensive vestibular commissural system. It also receives multiple descending afferents from cortical and subcortical structures, which would explain why an emetic response can be elicited by electrical stimulation of the frontal cortex, thalamus, amygdala, and limbic system structures.[65] The relevance of these centers for the development of motion sickness in humans is inchoate, like so much of our knowledge about the neurophysiological processes involved.

INCIDENCE OF MOTION SICKNESS

Airsickness

In military aviation, the incidence of airsickness is highest in student aviators during initial training flights. In US Navy flight officers, 74% ofcadets reported experience of airsickness during basic training and 39% had vomited at least once; however, the incidence of sickness and vomiting fell during advanced training and was lower still in the Fleet Readiness squadron (Table 35-2).[66] Data from the Royal Air Force[67] indicate that 50% of navigators of high-performance aircraft suffered from airsickness during training, and some 39% of student pilots were also affected, symptoms being sufficiently severe in 15% to cause a training sortie to be modified or abandoned. In the Israeli Air Force, self-reports from flight cadets revealed that 46% experienced nausea at least once during their first five flights.[68]

Trained pilots rarely suffer from motion sickness when they control the aircraft's flight trajectory, although they may get sick, like other crew members and passengers, when they do not have hands-on control of the aircraft. A US Air Force study[69] revealed that 76% of aerial gunners and 57% of electronic warfare officers had experienced airsickness during operational duties. The highest incidence of airsickness appears to be among aviators engaged in hurricane-penetration flights. Severe turbulence caused symptoms in 90% of those with previous experience of such flights, whereas all of those who had not flown this type of sortie before were airsick, with one third reporting severe symptoms.[70] Airsickness is a relatively common problem among troops being transported by air when, for operational reasons, flight is at low level in turbulent conditions. A study of Mexican Air Force paratroopers[71] found that 64% of students were airsick on the first training flight (Figure 35-15), although the incidence fell steadily on consecutive daily flights; by the fifth day only 25% of the students were affected. Among trained paratroopers, 35% were airsick during a 1-day proficiency exercise. A recent study[72] of passengers on short hauls (average duration = 46 min) in small turboprop aircraft found that 0.5% vomited, 8.4% had nausea, and 16.2% felt ill.

Seasickness

TABLE 35-2

INCIDENCE OF AIRSICKNESS IN US NAVY STUDENT PILOTS

Training Phase	Students (N)	Sorties Flown (N)	Incidence of Airsickness (% of Sorties)		
			Symptomatic	Vomited	Performance Degraded
Basic	796	10,759	19.4	9.2	12.7
Advanced	543	9,299	11.9	4.9	4.2
Fleet Ready	372	8,325	7.6	3.0	3.6
Total—all phases	796	28,383	13.5	5.9	7.3

Adapted with permission from Hixson WC, Guedry FE, Lentz JM. Results of a longitudinal study of air sickness incidence during naval flight officer training. In: *Motion Sickness: Mechanism Prediction, Prevention and Treatment*. Neuilly-sur-Seine, France: Advisory Group for Aerospace Research and Development, North Atlantic Treaty Organization. 1984; Paper 30:4. AGARD Conference Proceedings 372.

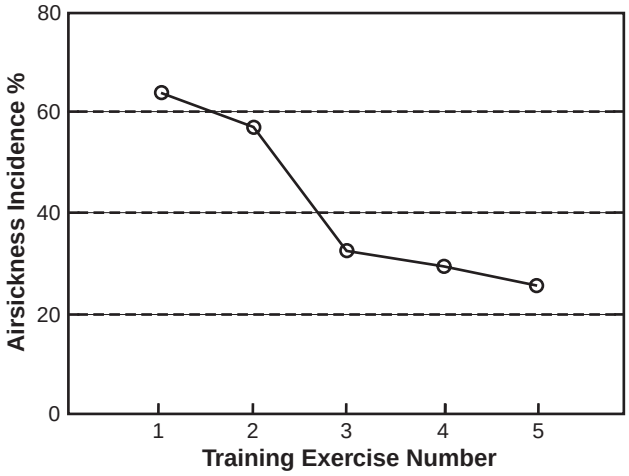


Fig. 35-15. Incidence of symptoms of airsickness in a group of 45 trainee paratroopers on consecutive daily exercises. The incidence of symptoms decreased more than 60% over the five daily training exercises, with the most dramatic change occuring between the second and third. Adapted with permission from Antuñano MJ, Hernandez JM. Incidence of airsickness among military parachutists. *Aviat Space Environ Med*. 1989;60:794.

The incidence of seasickness varies between a fraction of 1% to 100%. It depends primarily on the intensity of the motion stimulus and the extent to which those aboard the vessel are adapted to the motion. The motion stimulus is a function of the state of the sea and the size of the vessel and its sea-keeping properties.

In an extensive study[73] carried out aboard a 16,000-ton troop ship on trans-Atlantic crossings, the incidence of vomiting ranged from 20% to 41%. Similar sickness rates have been reported in other military transport ships (see review by Griffin[27]). Questionnaires completed by sailors of the Royal Navy revealed that 70% had been seasick during their careers and that 42% had been sick in the past 12 months[73] (Table 35-3). These data also showed a relation between incidence of sickness and vessel size, which yielded a mathematical model that predicted sickness incidences of 67% to 29% as vessel size increased from 200 to 20,000 tons. These figures accord with an observed sickness rate of 62% of sailors in Israeli SAAR Missile Boats (300–500 tons).[74]

The motion of life rafts in rough seas is highly provocative and all but the most resistant succumb in storm conditions. In a life raft trial conducted in a wave tank, 55% of subjects had vomited and a further 21% were nauseated after 1 hour of exposure.[75] In totally enclosed, motor-propelled, survival craft (TEMPSC) used for escape from drilling rigs, seasickness occurred in more than 75% of the occupants. In one TEMPSC, all were sick except the coxswain, who was the only one who had a view out.[76]

Confirmation that the incidence of seasickness is positively correlated within the motion of the vessel—more specifically its linear, vertical acceleration—has come from a limited number of studies. The most extensive was carried out by Lawther and Griffin[31] and embraced data from 20,029 passengers aboard six ships, which varied in size from 67 m to 130 m (1,255–7,003 tons); two hovercraft; and one hydrofoil craft. The relation that they found between the motion dose ($MSDV_z$), calculated according to Equation 1, and the incidence of vomiting can be seen in Figure 35-10. Although there is still a good deal of scatter in the data, the positive correlation is highly significant, as is the relation between illness rating and $MSDV_z$.

The location of passengers and crew aboard ship can also materially influence the incidence of sick-

TABLE 35-3

INCIDENCE* OF SEASICKNESS AS A FUNCTION OF SEA STATE

	Frequency† of Sickness (%)			
Sea State	**Always**	**Often**	**Occasionally**	**Not at all**
Calm	0	0	4	94
Moderate	1	3	25	71
Rough	6	16	44	34

*Among 466 Royal Navy personnel aboard two ships: HMS *Gurkha* and HMS *Hermione*
†Percentage of sailors who had suffered seasickness during career: 70%; during past year: 42%
Adapted with permission from Pethybridge RJ, Davies JW, Walters JD. *A Pilot Study on the Incidence of Seasickness in RN Personnel on Two Ships.* Alverstoke, Hants, United Kingdom: Institute of Naval Medicine; 1978: 5. Report 55/78.

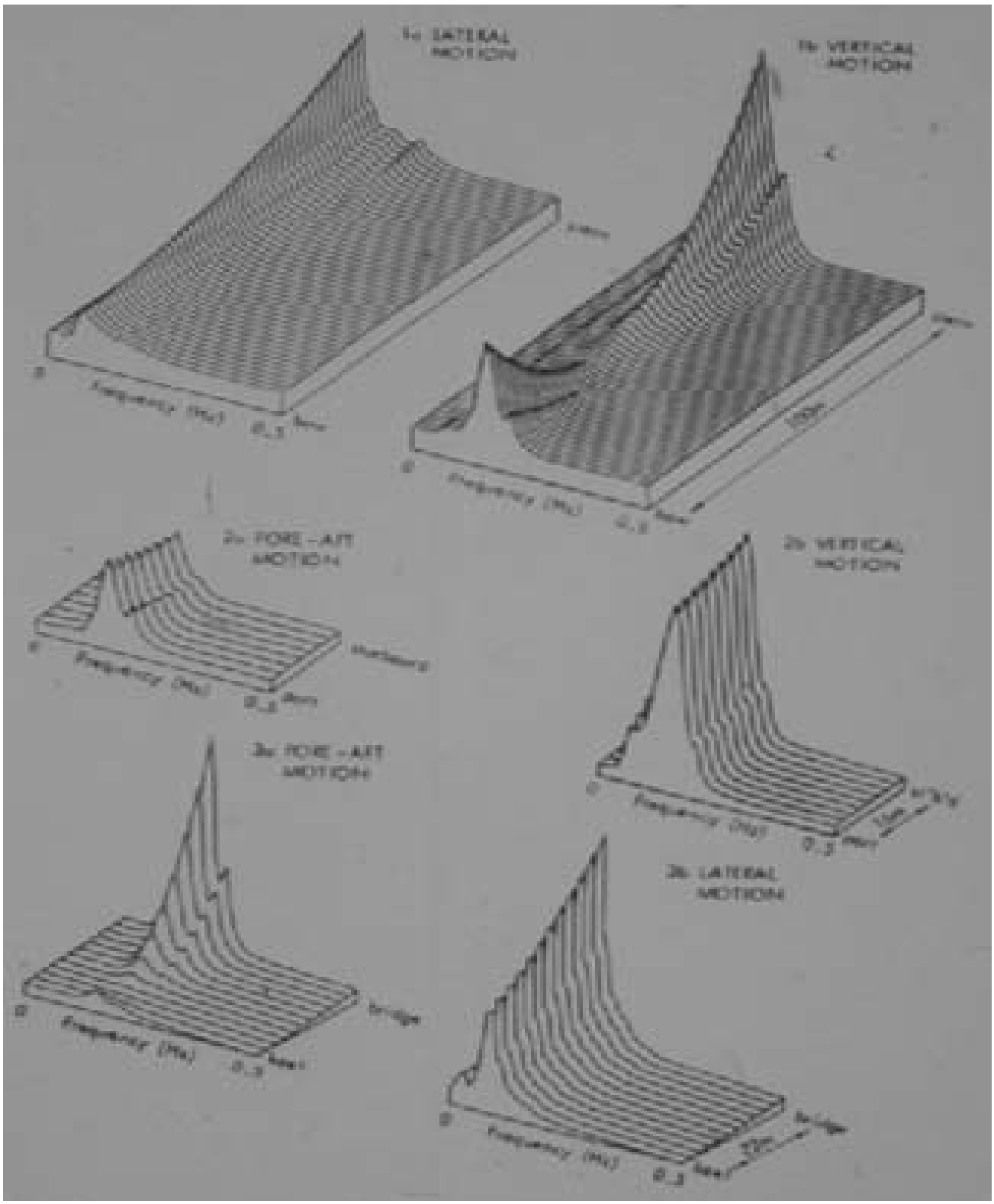


Fig. 35-16. Effect of location aboard ship on the magnitude of the motion stimulus. The graphs show the power spectra of the linear acceleration at incremental locations from bow to stern (1a and 1b), port to starboard (2a and 2b), and keel to bridge (3a and 3b). Reproduced with permission from Griffin MJ. Motion sickness. In: *Handbook of Human Vibration*. London, England: Academic Press; 1990: 314.

ness. Sickness was least among those quartered amidships, where the vertical motion is substantially less than at the bow or stern (Figure 35-16). Amidships, low in the ship, is clearly the most favorable position for minimizing the motion stimulus, but this benefit may be negated by loss of external, visual, orientational cues.

Simulator Sickness

The first reports of symptoms resembling motion sickness in pilots flying a helicopter simulator appeared in 1957. Nausea, vomiting, blurred vision, and other unpleasant symptoms tended to occur within the first 10 minutes of a simulator sortie and were experienced by 78% of those who flew the simulator. Over the ensuing 40 years, a number of studies have been conducted of what has come to be known as simulator sickness (see the review by Kennedy, Hettinger, and Lilenthal[77]). Some of the symptoms, commonly reported by those who fly aircraft simulators or drive tank and automobile simulators, are characteristic of the motion sickness that occurs in vehicular transportation (eg, airsickness, seasickness), notably, stomach awareness, nausea, vertigo, sweating, pallor, and drowsiness. However, severe nausea, vomiting and retching are rare. Other symptoms in those who fly or drive simulators, but which are not common features of motion sickness, are eyestrain, blurred vision, and difficulty in focusing, which may be coupled with reports of headache, difficulty in concentrating, vertigo, and disorientation. The relative incidence of some of these symptoms in 10 US Navy flight simulators studied by Kennedy and colleagues[78] is shown in Table 35-4. The incidence of symptoms of simulator sickness varied from 10% to 60%. These figures embrace the incidence rates found in other flight simulators with synthetic displays of the external scene subtending large visual angles, most of which were equipped with a moving base to provide whole-body motion cues. The highest incidence of simulator sickness was found in a US Air Force air-to-air combat simulator, in which 88% of pilots had experienced one or more symptoms.

In addition to symptoms experienced during simulated flight, a number of postexposure effects have been described. These include disturbances of postural control, illusory sensations of motion, visual flash backs, disorientation, and dizziness. Typically, these sensory and motor disturbances are short lived and rarely last more than 12 hours, but some individuals have described delayed effects lasting up to several weeks.[77]

The incidence of simulator sickness is usually highest among student pilots with no prior experience of the simulator, and in most, the symptoms decrease with repeated exposure. In some studies,[79] pilots with extensive experience of the real aircraft but little of the simulator were most troubled during initial simulator flights. Reason and Brand[6] suggested in 1975 that the higher incidence in the experienced pilots is due to a greater disparity between motion cues that are provided by the visual display and motion base of the simulator, and those that their experience has led them to expect on executing particular flight maneuvers. The inexperienced pilots have a less structured internal model and expectancy of motion cues, so neural mismatch and the consequent motion sickness is accordingly less.

Virtual reality systems may be considered a particular type of visual simulation: one in which the observer sees only the external scene without any frame of reference, such as that provided by the aircraft cockpit in a flight simulator. In contemporary systems, the quality of the visual display—with regard to resolution, geometric distortion, and update lags—is inferior to that of flight simulators. As all of these factors have been implicated in the generation of the mismatch responsible for simulator sickness, it is to be expected that simulated movement through a virtual visual world will induce symptoms. One

TABLE 35-4

SYMPTOMS REPORTED BY PILOTS FOLLOWING SORTIES IN FLIGHT SIMULATORS*

Symptoms	Frequency (%)
"Motion Sickness"	
Drowsiness	26
Sweating	16
Nausea	10
Stomach awareness	8
Vertigo	5
"Eyestrain"	
Eyestrain	25
Headache	18
Difficulty in focusing	11
Difficulty in concentrating	10
Blurred vision	3

*Data based on 2,500 pilots' reports at 10 flight simulator facilities Data source: Kennedy RS, Hettinger LJ, Lilienthal MG. Simulator sickness. In: Crampton GH, ed. *Motion and Space Sickness*. Boca Raton, Fla: CRC Press; 1990: 323.

study[80] found that of 150 subjects immersed for 20 minutes in a virtual reality system, 61% reported symptoms at some time during the test. Symptoms decreased after the exposure but were still present in 30% of the subjects 10 minutes after the visual display was removed. Nausea was the most significant symptom, followed by disorientation and oculomotor problems.

Space Motion Sickness

Since the first report by the cosmonaut G. S. Titov (who in 1961 was the first to experience sustained weightlessness in orbital flight) of seasickness-like symptoms on making head movements in the weightless environment of orbital flight, the occurrence of sickness in astronauts and cosmonauts during the first few days in orbit has been well documented. The incidence of what has come to be called *space sickness* (or *space adaptation syndrome*, a euphemism that does not subsume space sickness as just another form of motion sickness) has been well documented; the incidence for the first 20 years of space flight is summarized in Table 35-5. There was no report of sickness from astronauts in the small Mercury and Gemini capsules, but in the larger vehicles, where astronauts or cosmonauts could move about, many experienced symptoms. An analysis of space sickness in astronauts who flew in the Space Shuttle[42] (Table 35-6) revealed that 67% had symptoms, which were severe in 13%. On average, the incidence was slightly lower in astronauts on their second flight and was lower in female than in male astronauts, but neither of these differences is

TABLE 35-5

INCIDENCE OF SPACE MOTION SICKNESS IN ASTRONAUTS AND COSMONAUTS

Space Vehicles	Incidence (%)
USA	
Mercury	0
Gemini	0
Apollo	33
Skylab	56
Apollo–Soyuz Test Project	0
Shuttle	52
USSR	
Vostock	13
Voskhod	60
Soyuz/Salyut (1 & 4)	55
Apollo–Soyuz Test Project	0
Salyut 6	44
Salyut 7	40

Data source: Homick JL, Reschke, ME, Vanderploeg JM. Space adaptation syndrome: Incidence and operational implications for the space transportation system program. In: *Motion Sickness: Mechanism Prediction, Prevention and Treatment*. Neuilly-sur-Seine, France: Advisory Group for Aerospace Research and Development, North Atlantic Treaty Organization. 1984; Paper 36:36-2. AGARD Conference Proceedings 372.

TABLE 35-6

SPACE MOTION SICKNESS IN SPACE SHUTTLE ASTRONAUTS

	Frequency (%) of Space Motion Sickness as a Function of Severity			
Crew Member (Number)	None	Mild	Moderate	Severe
All (85)	33	30	24	13
Male (77)	30	33	23	14
Female (8)	63	12	25	0
Commander/Pilot (24)	3	29	25	13
Mission Specialist (41)	41	32	20	7
Payload Specialist (20)	15	30	30	25

Data source: Davis JR, Vanderploeg JM, Santy PA, Jennings RT, Stewart DF. Space motion sickness during 24 flights of the Space Shuttle. *Aviat Space Environ Med*. 1988;59:1186, 1187.

statistically significant.

Typically, astronauts report the onset of symptoms shortly after they begin moving about in the vehicle. With continued activity, stomach awareness and nausea usually precede vomiting, which, not infrequently, is projectile. Headache and anorexia are common, while the relative absences of cold sweating and pallor are the principal differences in the symptomatology of space sickness and that of terrestrial motion sickness. There are, however, more similarities than differences. Vomiting typically brings some transitory lessening of malaise; adaptation takes place over the first 2 to 4 days in weightlessness, after which time head movements can be made with impunity; drugs that are beneficial in motion sickness (eg, scopolamine, promethazine) also attenuate the symptoms of space motion sickness.[81,82]

Motion Sickness in Land Vehicles

Motion sickness in automobiles and buses is relatively common among the highly susceptible young and even some adults. A survey conducted on 3,256 passengers on coach journeys over a variety of routes in the United Kingdom with durations of 0.5 to 6.5 hours revealed that, overall, 22% felt "slightly unwell," 4% felt "quite ill," and 2% felt "absolutely dreadful." Nausea was reported by 13% of passengers, and 1.7% vomited.[83] There is a paucity of data on the incidence of sickness in automobiles and other land vehicles. Apart from one report[74] of motion sickness in tanks, in which 20% of subjects experienced nausea, only anecdotal and unquantified information supports the notion that motion sickness is a problem in fighting vehicles.

OPERATIONAL SIGNIFICANCE OF MOTION SICKNESS

Seasickness

The scientific literature does not convey a consistent picture of the effect of motion sickness on human performance.[74,84] Without doubt, the act of vomiting has a direct effect on performance, but this is transitory; some aviators and sailors maintain their ability to carry on their allotted tasks despite periodic vomiting. Others, however, in whom the classical signs and symptoms of motion sickness are less severe, are overcome by apathy and depression. Rolnick and Gordon[74] describe a *helplessness reaction,* which causes a decrement in performance through cognitive, emotional, and motivational deficits. Support for the dissociation of the nausea and depressive components of the motion sickness syndrome is afforded by the finding that decrement in performance at sea was not correlated with physiological signs of seasickness but was significantly correlated with feelings of helplessness.[74]

For those who suffer from severe seasickness in life rafts, the depression and erosion of motivation can impair the will to survive and to take positive steps to aid survival. In addition to these behavioral consequences, the dehydration and loss of electrolytes (metabolic alkalosis) brought about by repeated vomiting and retching can only reduce the ability of those in a life raft to withstand the privation, exposure, and other stresses of a hostile marine environment.

Airsickness

The principal operational impact of airsickness is in aviator training. As discussed above, there is a high incidence of airsickness in student pilots during initial flights. Fortunately, the majority adapt quite quickly, but there is a minority, estimated at 3% to 11%,[66,67] whose training is compromised because sorties have to be modified or curtailed. With continued airsickness, the student fails to make the required progress—sometimes interpreted as a lack of aptitude—and he or she is suspended from the training program. Yet airsickness is rarely given as a reason for rejection from training. Data from the air forces of the United States, France, and Belgium indicate that only 1% of students were removed because of airsickness when the overall attrition rate was on the order of 33%.[85] However, in a French Air Force study, of the 40 students who had consulted their flight medical officer because of airsickness, the attrition rate was 70%.[85]

Simulator Sickness

Simulator sickness, like sickness in actual flight, can interfere with training, although I am not aware of simulator sickness being so severe as to lead to removal of a student from flying training. However, the presence of malaise can direct the student's attention away from the task at hand and delay learning. Those who experience symptoms may individually or collectively develop a negative attitude toward simulation and may try to avoid further exposure in the simulator. Furthermore, behavior learned in the simulator to avoid symptoms, such as reducing head movements, may not be appropriate or safe behavior in actual flight.[86] Alteration of the simulator's motion-

base dynamics to reduce provocative low-frequency components may also engender patterns of control behavior that do not transfer positively to the real aircraft. Flight safety may be compromised by simulator sickness aftereffects if the aviator pilots a real aircraft shortly after leaving the simulator. The presence of sensory disturbances (eg, disorientating sensations, flashbacks, and dizziness) may increase the likelihood of loss or inappropriate control and an orientation-error accident. On the ground, aftereffects are a potential hazard insofar as the disequilibrium could cause a fall and injury during normal locomotor activity, whereas sensory disturbances could interfere with the aviator's ability to drive an automobile safely.

Space Motion Sickness

Despite the extensive training of spaceflight crews and their high motivation to perform allotted tasks, those who become space sick suffer a degradation in performance. Vomiting interrupts ongoing activities, and the loss of well-being can have a deleterious effect on task performance. Awareness of the provocative nature of rapid head movements brings about a restriction of the amplitude and velocity of volitional head and body movements, which leads to tasks being performed more slowly. Those who experience severe symptoms tend to limit their activities to essential tasks and attempt to maintain a fixed orientation within the vehicle with good tactile support.[87]

Most astronauts' and cosmonauts' signs and symptoms of space motion sickness dissipate over the course of 2 to 4 days. Head movements can then be made with impunity, and the new patterns of sensory–motor integration, acquired as the space travelers adapt to weightlessness, allow tasks to be performed in an expedient manner, sometimes more efficiently than on Earth. Unfortunately, a small proportion of astronauts, perhaps cosmonauts too, fail to adapt fully. They continue to experience symptoms whenever provocative head and body movements are made, and their performance does not return to preflight levels.

Emesis within the space vehicle may be unpleasant for the individual who vomits and for nearby crew members, but it is not life-threatening. However, vomiting within the enclosed helmet and pressure suit worn during extravehicular activity (EVA) is potentially lethal. It is therefore essential that EVA is performed only by astronauts and cosmonauts who have adapted to weightlessness and are no longer space sick.

Mal de débarquement phenomena, notably disturbance of postural control, illusory sensations of bodily motion, dizziness, and nausea, have the potential to degrade performance during re-entry and landing. Most apparent is the disequilibrium that some astronauts experience on assuming an erect posture on leaving the spacecraft an hour or so after landing. Such individuals would be severely compromised if required to escape in an emergency on landing. Head movements can also be provocative on return to Earth, and in a few susceptible individuals can be sufficiently provocative to cause vomiting and significant incapacitation for a few days. The astronauts and cosmonauts who have serious mal de débarquement phenomena tend to be the same individuals who are badly affected by space sickness at the beginning of an orbital flight.

PREVENTION AND TREATMENT

The surest way to prevent motion sickness is to avoid exposure to provocative motion environments. Although this may be an option in civilian life—even if few are prepared to forego travel by car, airplane, or boat—it is not an option that is available to military personnel. Prevention, or at least reduction in the severity and incidence, of motion sickness may be achieved either by (*a*) lessening the intensity of the provocative stimulus or (*b*) increasing individual tolerance to provocative motion.

Reduction of Provocative Stimuli

Hull design can materially influence the response of a vessel to different sea states and the amplitude of motion in the critical 0.1- to 0.3-Hz frequency band. Stabilization of the vessel in roll may make life more comfortable for those aboard, but it does little to reduce either heave acceleration or pitching movement, with their attendant high linear accelerations at bow and stern. In general, the larger the ship or aircraft, the lower the intensity of provocative motion; however, the ride quality of aircraft is governed by factors other than size.[27] Wing loading influences the response of the aircraft to turbulence, and control system characteristics determine the maximum vertical accelerations during automatic terrain following, although topographical features and ground speed govern the amplitude and frequency of the stimulus. The design of the suspension of fighting vehicles can influence ride quality and the frequency spectra of vertical motion, but the principal determinants of the mo-

tion stimuli to the occupants are the irregularity of the terrain and the manner in which the vehicle is driven (eg, rate of cornering, harshness of acceleration and braking).

Design factors relating to the occupants of the vehicle can also influence the incidence of motion sickness, such as the occupants' location and orientation to the dominant motion. Consideration should be given to the ability of those aboard to see out and obtain veridical, visual cues for orientation. Provision of adequate restraint can be important, as the restriction of head movement has been shown[34] to decrease the incidence of sickness in some situations.

Operator and Passengers

Those within a vehicle, whether in control or passengers, can adopt strategies that will reduce the intensity of provocative motion and sensory conflict and hence the likelihood of motion sickness. Those in control can, if operational constraints permit, steer a course that avoids the roughest seas, the most turbulent air, or the most irregular ground. They can also reduce the intensity of motion stimuli by making changes of speed and direction in a smooth and well-tempered manner. Passengers and others aboard who do not directly control the vehicle's motion trajectory may have the option to position themselves within the vehicle where the low-frequency heave acceleration is least (eg, aboard ship, near the center and low down; in aircraft, near the wing roots).

As noted above, restriction of head movements may or may not be advantageous in reducing the incidence of sickness produced by low-frequency, heave oscillation. There is no doubt, however, that head movements are provocative and should be avoided in the transient weightlessness of parabolic flight[29] and during the first few days of a space flight. The benefit of a recumbent posture at sea is also somewhat equivocal, but it is a common observation that those suffering from seasickness are more comfortable if made to lie down with the head supported. When recumbent, less postural activity is required, and conflicting visual cues are absent when the eyes are closed.[35]

Other behavioral measures can also reduce the incidence of motion sickness. Passengers and those who have to work in an enclosed cabin should, whenever feasible, avoid tasks involving prolonged visual search (eg, reading a map or book). Those able to see out should direct their visual attention to a stable orientational reference (eg, a distant point on the road ahead, or the horizon at sea); they should not focus on nearby objects that may be in motion (eg, waves or other vehicles). It is also advantageous to be involved in tasks that minimize introspection and attention to bodily sensations. Best is the task of controlling the motion trajectory of the vehicle, for of those aboard, the skipper, driver, or pilot is the least likely to suffer motion sickness. For those not at the controls, involvement in some absorbing task, even singing, is better than preoccupation with endogenous sensations and self-pity.

Increasing Individual Tolerance

Adaptation

Some of the measures described above can be of immediate value to those exposed to provocative motion, but in the long term, adaptation is the most potent prophylactic. This is *nature's own cure* and, where practicable, acquiring protective adaptation is preferable to administering anti–motion sickness drugs to military personnel. The basic principle governing the acquisition and maintenance of protective adaptation is that there should be gradual and incremental exposure to progressively more-intense provocative motion. Adaptation, once achieved, should be maintained by regular and repeated exposure to the motion stimulus. Unfortunately, for most of the population at risk, the intensity and duration of exposure to provocative motion cannot be controlled, and so the acquisition and retention of adaptation cannot be optimized. Student aviators are a possible exception, for in this group steps can be taken to grade exposure to provocative flight maneuvers and to provide regular flight experience. Even so, not all aviators develop sufficient protective adaptation, and they have to be withdrawn from the flying program. Their withdrawal may be only temporary, for many aviators who continue to be troubled by airsickness can be helped by a treatment program of the type first employed by Dowd[88] and Dobie[67] in the 1960s.

This *desensitization therapy* typically involves a ground-based phase with twice-daily exposure to provocative, cross-coupled (Coriolis) stimulation of progressively increasing intensity. This is followed by a flying phase in which the process of incremental adaptation is continued by the progressive introduction of more-stressful and provocative flight maneuvers. Some flight medical officers have regarded vestibular adaptation as an essentially physiological process[89] and have not employed supportive psychotherapeutic procedures, such as cognitive–behavioral therapy, which Dobie and May[90]

regard as an essential element of the program. There is experimental evidence[91] that autogenic feedback training (ie, a combination of biofeedback and autogenic therapy, which develops an individual's ability to control autonomic responses) can increase tolerance to provocative motion. However, the reduction in susceptibility achieved by autogenic therapy alone is inferior to that achieved when it is combined with incremental exposure to cross-coupled stimulation.[92,93]

Variants of desensitization therapy include the use of other adapting stimuli, such as vertical linear oscillation and moving visual patterns (optokinetic stimuli), in the belief that there will be better generalization of the adaptation to the flight environment than that achieved when only cross-coupled stimulation is employed in the ground-based phase of therapy.[89]

The literature on desensitization therapy (see reviews by Stott[35,92] and Dobie and May[90]) is confined to the treatment of flying personnel. It is in this group that the therapy is cost-effective: first, because of the financial investment in selection and training; and second, on return to flying, adaptation will likely be sustained by continued exposure to provocative flight maneuvers. There is anecdotal evidence of the successful desensitization of a chronically seasick sailor, but I am not aware of any systematic use of desensitization therapy on other military personnel. Apart from the cost of therapy, the irregularity of storm conditions at sea does not favor the maintenance of protective adaptation.

Acupressure and Acustimulation

Stimulation of the P6 (or Nei-Kuan) point on the anterior aspect of the wrist is believed by acupuncturists to be of prophylactic benefit in motion sickness. Commercially available elasticized bands, each with a plastic button that can apply steady pressure to the P6 point, have failed to show any benefit in controlled trials.[94–96] In contrast, acustimulation provided by cyclical manual pressure[96] or electrical stimulation[97] has had a statistically significant prophylactic effect. If these reports are substantiated by more-extensive field trials, acustimulation may become the method of choice for short-term prophylaxis, as there are no deleterious side effects such as those that arise with certain drugs.

Selection

In critical military tasks where motion sickness would impede mission effectiveness, personnel with low susceptibility can be selected. Reviewing the extensive literature on predictive tests, Kennedy, Dunlap, and Fowkles[46] conclude that assessment of susceptibility to motion sickness in an operational environment has the highest predictive validity. This is followed, in rank order, by laboratory provocative tests, motion sickness history, psychological factors (personality and perceptual style), and physiological measures (autonomic and sensory functions). Defense organizations in some countries (eg, France, Israel, the United Kingdom) employ an operational selection test for flying personnel. Candidates are exposed to provocative flight maneuvers, and only those who are not overcome by motion sickness are accepted for flight training. If there is no shortage of able candidates, this method of selection is acceptable, but wasteful: some, perhaps many, of those who become sick on initial exposure to unfamiliar motion may adapt quite adequately during subsequent flights. Although provocative tests, performed either in the operational environment or in laboratory simulations, give information about susceptibility at the time the test is performed, no well-validated test of the important attributes of adaptability and retentivity is available that would aid prediction.

When known to be used for selection, data from motion sickness questionnaires should also be treated with caution, as they are not always answered honestly. In the Royal Air Force, a questionnaire administered to candidates before selection for flying training yielded a history of motion sickness in 3.6%, but when the same confidential questionnaire was completed later by the same group, after they had been established in the flying training program, 59% gave an affirmative response.[67]

Drug Treatment

Over the years, many remedies have been recommended for the prophylaxis of motion sickness (reviewed by Reason and Brand[6]), but few have been proven in laboratory or field trials to be more effective than a placebo. The demonstration of therapeutic value is complicated by the need to control for a placebo effect. With motion sickness, the placebo effect can be large if the individual knows that he or she is taking a substance or following a procedure (eg, the application of pressure to the P6 point) with alleged therapeutic benefit. Trials also have to allow for differences between drugs in the mode of administration and in the rate of absorption and dosage, as well as to the timing, intensity, and duration of the provocative motion challenge.

Many drugs have been tested against motion sick-

TABLE 35-7

DOSAGE AND DURATION OF ACTION OF ANTI–MOTION SICKNESS DRUGS

Drug	Route	Adult Dose	Time of Onset	Duration of Action (h)
Scopolamine	oral	0.3–0.6 mg	30 min	4
Scopolamine	injection	0.1–0.2 mg	15 min	4
Scopolamine (Transderm Scop)	patch	one	6–8 h	72
Promethazine	oral	25–50 mg	2 h	15
Promethazine	injection	25 mg	15 min	15
Promethazine	suppository	25 mg	1 h	15
Dimenhydrinate	oral	50–100 mg	2 h	8
Dimenhydrinate	injection	50 mg	15 min	8
Cyclizine	oral	50 mg	2 h	6
Cyclizine	injection	50 mg	15 min	6
Meclizine	oral	25–50 mg	2 h	8
Buclizine	oral	50 mg	1 h	6
Cinnarizine	oral	15–30 mg	4 h	8

ness[98,99] but of those that are beneficial (Table 35-7), none provide complete protection and none is without side effect (see review by Stott[100]). Of the currently available drugs, the centrally active, muscarinic cholinergic antagonist, scopolamine (ie, *l*-hyoscine), is probably the most effective single drug. It is rapidly absorbed and reaches a peak concentration in the body at about 1 hour after ingestion but has a short half-life of 2.5 hours that limits its duration of action to about 4 hours. Side effects after ingestion of scopolamine in doses larger than 0.6 mg are frequent, particularly sedation, dry mouth, blurring of vision (due to impairment of accommodation), and lightheadedness. The drug is not well tolerated by children and should not be taken by the elderly, especially those with glaucoma or obstruction of the bladder neck. Side effects tend to be accentuated if the drug has to be taken repeatedly at 4- to 6-hour intervals for prolonged prophylaxis. With the scopolamine transdermal patch, protection can be provided for up to 72 hours after a patch has been applied to the skin behind the ear. The transdermal patch provides a loading dose of 200 μg of scopolamine and controlled release of the drug at 20 μg/h for up to 3 days. Therapeutic blood levels of scopolamine are not reached until 6 to 8 hours after application of the patch, so it is necessary either to anticipate the requirement for prophylaxis or, if more immediate protection is required, to take an oral dose of scopolamine when the patch is applied. Scopolamine may be given by injection for the treatment of established motion sickness when vomiting and gastric stasis prevent or impede absorption of an orally administered drug. It should be noted that when injected, blood levels of the drug are 4- to 6-fold higher than when it is taken orally because there is no initial first pass through the liver, as occurs when the drug is absorbed from the gut.

Scopolamine, like atropine, has a broad affinity for the five muscarinic receptor subtypes that have so far been identified. With the availability of selective antimuscarinic drugs, there exists the possibility of targeting the neural processes of motion sickness without incurring the side effects produced by blockade of other muscarinic receptors. Studies[101] have shown that the unmarketed drug zamifenecin, which has high affinity for M_3 and M_5 receptors, is as effective as 0.6 mg scopolamine in increasing tolerance to cross-coupled stimulation in humans. On the other hand, the unmarketed drug idaverine, which has high affinity for M_2 and lower affinity for M_1 receptors, was without effect on motion sickness in cats.[102]

A number of drugs that were developed and marketed primarily for their antihistaminic properties have also been shown to be effective in motion sickness prophylaxis.[103,104] These are promethazine, dimenhydrinate, cyclizine, meclizine, and cinnarizine. All of these drugs can cross the blood–brain barrier and have some central anticholinergic activity as well

as being histamine H_1-receptor antagonists. Both promethazine and meclizine have strong anticholinergic properties and a long duration of action (12–24 h). Dimenhydrinate, cyclizine, and cinnarizine are shorter acting and somewhat less effective than promethazine. All of these antihistaminic drugs cause drowsiness, promethazine and dimenhydrinate being the most sedative. Other side effects, dizziness, dry mouth, and blurred vision, which are attributable to the anticholinergic action of the drugs, occur but to a lesser extent than with scopolamine.

The central sympathomimetic (adrenergic) agent *d*-amphetamine phosphate was used empirically in combination with scopolamine for motion sickness prophylaxis in World War II. Yet not until the 1960s was amphetamine by itself shown to increase tolerance to provocative motion and also to have an additive effect in therapeutic effectiveness when combined at a dose of 5 to 10 mg with scopolamine or promethazine.[105] A further benefit was a reduction of some of the side effects of scopolamine, notably drowsiness and performance decrement, but dry mouth was increased. Unfortunately, *d*-amphetamine is a potentially addictive drug and is liable to abuse, so its general use in motion sickness prophylaxis cannot be justified. Ephedrine (15–30 mg) is almost as good as *d*-amphetamine in enhancing the efficacy of anti–motion sickness drugs and can be used in conjunction with scopolamine (0.6 mg) or promethazine (25 mg) when optimum protection of short or medium duration is required.

The observation that electroencephalographic changes in acute motion sickness have features in common with those that occur in minor epilepsy led to the experimental evaluation of the analeptic drug phenytoin for motion sickness prophylaxis. At plasma concentrations of 10 to 20 μg/mL (anticonvulsant therapeutic levels), the drug was highly effective in both laboratory and sea trials in increasing tolerance to provocative motion.[106,107] However, tests carried out 3 to 4 hours after a single 200-mg dose of the drug showed only a slight increase in tolerance and no reduction in symptom score.[108] Phenytoin has a narrow therapeutic index, the relation between dose and plasma concentrations is nonlinear, and it has potentially serious side effects and drug interactions; accordingly, its general use for motion sickness prophylaxis is not recommended.

In concluding this review of prophylactic drugs, mention should be made of some drugs that are both widely used and effective in the treatment of nausea and vomiting but are without proven benefit in motion sickness. Examples are the phenothiazine, prochlorperazine; the dopamine antagonist, metoclopramide; and the $5HT_3$ receptor antagonist, ondansetron.

Treatment of Severe Motion Sickness and Vomiting

Individuals with severe symptoms and vomiting cannot benefit from orally administered anti–motion sickness drugs because of impaired absorption from the gastrointestinal tract due to gastric stasis and emesis. The preferred treatment is an intramuscular injection of promethazine (25–30 mg), although scopolamine, cyclizine, and dimenhydrinate may also be given by injection. Therapeutic blood levels of scopolamine are achieved through the buccal absorption of the drug,[109,110] and this offers an alternative, albeit slower, rate of drug delivery. Promethazine and cyclizine may also be administered by means of rectal suppositories.

Repeated vomiting and an attendant inability to retain ingested fluids carry a risk of dehydration and electrolyte imbalance, especially if potentiated by high insensible fluid loss, as in a hot environment. Usually, once vomiting is controlled, fluids can be replaced by mouth, but in those rare cases where vomiting has not been controlled, as can occur on board a life raft, an intravenous infusion of fluid and electrolytes may be necessary.

SUMMARY

Exposure to unfamiliar motion produces a syndrome consisting of pallor, nausea, and vomiting. Provocative stimuli may be produced in land vehicles, at sea, in the air, and during space flight. A related condition occurs in simulators ranging from large-screen movies to sophisticated virtual-reality laboratories. Susceptibility to motion sickness shows a large degree of variation within and between individuals and usually follows a reliable pattern, progressing from stomach awareness to nausea, a feeling of warmth, flushing of the skin, and sweating before vomiting, which may offer transient relief from discomfort.

Motion sickness in all its manifestations depends on the vestibular apparatus of the inner ear. It is widely accepted today that symptoms result from mismatched sensory information regarding body orientation and motion. Normal locomotor activity produces an accustomed pattern of inputs from the eyes, the semicircular canals, and the otoliths, as

well as gravireceptors in the musculoskeletal system. Trouble arises when there is a sustained disparity among these inputs. Two main categories of neural mismatch have been identified, representing (1) conflict between visual and vestibular receptors or (2) mismatch between the canals and the otoliths.

The incidence of motion sickness in a particular set of conditions can be traced to a combination of factors including the physical characteristics of the motion, innate susceptibility, and training or accustomization. Different problems typify airsickness, seasickness, simulator sickness, space motion sickness, and land transportation. Prevention may involve selection and training of resistant individuals, reduction in provocative stimuli, and progressive training programs. Pharmaceutical agents with varying mechanisms of action have been found to offer relief but may produce unacceptable side effects for military purposes.

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