Motion sickness: a synthesis and evaluation of the sensory conflict theory[1]

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"Motion sickness" is the general term describing a group of common nausea syndromes originally attributed to motion-induced cerebral ischemia, stimulation of abdominal organ afferents, or overstimulation of the vestibular organs of the inner ear. Seasickness, car sickness, and airsickness are commonly experienced examples. However, the identification of other variants such as spectacle sickness and flight simulator sickness in which the physical motion of the head and body is normal or even absent has led to a succession of "sensory conflict" theories that offer a more comprehensive etiologic perspective. Implicit in the conflict theory is the hypothesis that neural and (or) humoral signals originate in regions of the brain subserving spatial orientation, and that these signals somehow traverse to other centers mediating sickness symptoms. Unfortunately, our present understanding of the neurophysiological basis of motion sickness is incomplete. No sensory conflict neuron or process has yet been physiologically identified. This paper reviews the types of stimuli that cause sickness and synthesizes a mathematical statement of the sensory conflict hypothesis based on observer theory from control engineering. A revised mathematical model is presented that describes the dynamic coupling between the putative conflict signals and nausea magnitude estimates. Based on the model, what properties would a conflict neuron be expected to have?

Key words: motion sickness, nausea, vestibular, vision, mathematical models.

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Le « mal des transports » est le terme générique pour décrire un ensemble de syndrômes communs de nausée originellement attribués à l'ischémie cérébrale induite par un mouvement, à la stimulation des fibres afférentes des organes abdominaux ou à la surstimulation des organes vestibulaires de l'oreille interne. Le mal de mer, le mal d'auto et le mal de l'air sont des exemples courants. Toutefois, l'identification d'autres situations, telle l'expérience du simulateur de vol où le mouvement physique de la tête et du corps est normal ou même absent, a mené à une succession de théories de « conflits sensitifs » qui offrent une perspective étiologique plus complète. La théorie des conflits ports implicitement l'hypothèse que les signaux neuronaux et (ou) humoraux prennent leur source dans des régions du cerveau liées à l'orientation spatiale, et que ces signaux se déplacent dans des centres médiant les symptômes du malaise. Malheureusement, notre compréhension actuelle des fondements neurophysiologiques du mal des transports est incomplète. Aucun processus ou neurone de conflit sensitif n'a encore été physiologiquement identifié. Cet article révise les types de stimuli qui provoquent le malaise, et formule mathématiquement l'hypothèse du conflit sensitif basée sur la théorie de l'observateur en automatique. On présente un modèle mathématique décrivant le couplage dynamique entre les signaux conflictuels putatifs et l'estimé de l'amplitude de la nausée. D'après ce modèle, quelles devraient être les propriétés d'un neurone conflictuel?

[Traduit par la revue]

Introduction

Motion sickness in humans is a nausea and vomiting syndrome elicited by certain kinds of real or apparent body movements. It is characterized by physical signs such as vomiting and retching, pallor, cold sweating, yawning, belching, flatulence, and decreased gastric tonus and subjective symptoms such as stomach discomfort, nausea, headache, feeling of warmth, and drowsiness. It has a significant incidence in civil and military transport. Virtually everyone is susceptible to some degree, provided the stimulus is appropriate and lasts long enough. Many other animal species exhibit susceptibility (Money 1970). The physiological, behavioral, and pharmacological motion sickness research literature has been well reviewed collectively by Tyler and Bard (1949), Chinn and Smith (1955), Money (1970), Reason and Brand (1975), Graybiel (1975), and Miller (1988). The purpose of the present paper is to synthesize the "sensory conflict" theory for motion sickness from a contemporary mathematical modelling perspective.

Until a century ago, physicians commonly attributed motion sickness to reduced cerebral blood flow or mechanical stimulation of abdominal afferents owing to motion of the viscera. These ideas, termed "blood and guts theories" by Reason and Brand (1975), were eventually discounted after it was noted (James 1882) that individuals who lack inner ear vestibular function are immune to motion. The view became widely held that motion sickness results from overstimulation of the vestibular organs produced by "unnatural" body motions. The role of abdominal afferents was largely discounted. Many assumed that one could accurately predict whether sickness would occur or not in any given situation simply by assessing the magnitude, axis, and frequency content of the physical stimulus to the vestibular system. However, over the past 25 years, researchers have concluded that the "vestibular overstimulation" notion alone does not provide an adequate explanation for the disorder, since it cannot account for several important facts concerning susceptibility. Among these are the following.

Previous experience in a particular motion environment usually confers a useful degree of immunity.

Past experience factors being equal, the pilot of an aircraft or the driver of a car who is in active control of his vehicle is much less susceptible to sickness than the passengers.

People regularly stimulate their vestibular organs vigorously

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when they actively run, jump, or dance, but these activities, which produce "endogenous" (self-generated) sensory stimulation, almost never produce sickness. In contrast, comparable "exogenous" (externally generated) motion stimuli often seem to make people sick.

Sickness can occur under some conditions where the physical body motion stimulus is normal or even completely absent. For example, people who are fitted with new spectacles that significantly distort their vision commonly report nausea and other symptoms during the first several days of wear. Spectators of very wide screen movies also occasionally report symptoms. Experienced military pilots who train in flight simulators equipped with wide field of view computer-generated "out the window" displays frequently complain of sickness, even though there is no actual motion stimulus to their vestibular organs. In these cases, the provocative stimulus seemed related to the visual rather than vestibular component of stimulation.

These facts clearly contradicted the vestibular overstimulation hypothesis. A more comprehensive etiologic theory was needed. Most investigators concluded that the actual trigger for sickness was an as yet unidentified signal in the "orientation brain" whose magnitude somehow depended not only on sensory cues to motion, but also on previous experience living in the abnormal environment and whether the stimulus was self-generated or not. When this internal neural or humoral signal was present, it somehow coupled over to the "emetic brain," eventually producing symptoms and signs. Many workers undoubtedly assumed that the linkage would be easily identified once the anatomy, electrophysiology, and pharmacology of spatial orientation and emetic pathways in the CNS were better understood.

Physiological basis of motion sickness

As of this writing, however, the physiological mechanisms underlying motion sickness remain relatively poorly defined. Although progress is being made, in some respects we know less today about the emetic linkage than we thought we did 5 years ago.

Classic postwar studies of canine susceptibility to swing sickness (Wang and Chinn 1956; Bard et al. 1947) indicated that the cerebellar nodulus and uvula, portions of the central vestibular system, are required for susceptibility. Many neurons in the central vestibular system that subserve postural and oculomotor control are now known to respond to a variety of spatial orientation cues, including visual ones, as reviewed by Henn et al. (1980). A brainstem "vomiting center" was identified by Wang and Borison (1950) and Wang and Chinn (1954), which has been found to receive convergent inputs from a variety of other central and peripheral sources, including the diencephalon and gastrointestinal tract. Nausea sensation in man has been commonly assumed to be associated with activity in this vomiting center (Money 1970). The integrity of both the vomiting center and an adjacent "chemoreceptive trigger zone" (CTZ), localized in area postrema on the floor of the fourth ventricle, was found to be required for motion sickness (Wang and Chinn 1954; Brizzee and Neal 1954). Ablation experiments indicated the cerebellar nodulus and uvula were also involved. It was believed that signals originating somewhere in the "orientation brain" somehow traversed, probably via the cerebellum, to the chemoreceptive trigger zone, which in turn activated the vomiting center. Wang and Chinn (1953) and Crampton and Daunton (1983) found preliminary evidence in animals suggesting that all or part of the stimulus to the CTZ might be due to ventricular flow or diffusion of a emetic agent in cerebrospinal fluid. However, an emetic linkage via cerebrospinal fluid (CSF) transport is arguably not fast enough to easily account for the very short latency vomiting that is observed experimentally with intense or prolonged repeated stimulation. The possibility of multiple emetic pathways (see below) and significant interspecies differences in mechanism must be considered.

Just as a working hypothesis for the emetic linkage was beginning to emerge, other experimenters who were attempting to replicate and extend some of the traditional ablation experiments began to question the essential role of the CTZ and cerebellum. As reviewed in other papers in this symposium, several recent attempts to demonstrate motion sickness immunity in area postrema ablated and cerebellar nodulectomized and uvulectomized animals have not been successful (Miller and Wilson 1983*a*, 1983*b*; Borison and Borison 1986; Wilpizeski et al. 1986), and workers now doubt that medullary emetic centers are discretely localizable.

Certainly some aspects of the physiology of the "output" pathways in motion sickness are better understood. The act of emesis itself involves the somatic musculature. The coordination of the diaphragm, intercostal, and abdominal muscles has been experimentally defined (e.g., Miller et al. 1987). That so many respiratory, vasomotor, and gastric responses are consistent signs of motion sickness indicates that areas in the reticular core of the brainstem traditionally associated with autonomic regulation are coactivated. Although decerebrate animals and people can be made motion sick, the limbic system and associated hypothalamus – pituitary – adrenal cortex (HPA) neuroendocrine outflow pathway is also clearly normally involved in mediating responses: increases in circulating levels of such stress-related hormones as epinephrine and norepinephrine, antidiuretic hormone, ACTH, cortisol, growth hormone, and prolactin have been found during sickness (e.g., Eversmann et al. 1978; Kohl 1985).

The question of where antimotion sickness drugs exert their action is far from resolved. There is no substantial evidence that effective drugs act on the vestibular end organs themselves or exert major effects on orientation perception or movement control. More likely, their sites of action are at or beyond the "linkage" mechanism to the emetic brain, such that they simply raise the threshold for sickness. Antimotion sickness drugs could be acting directly on brainstem emetic centers. Alternatively, they may shift the fundamental adrenergic–cholinergic balance in the limbic system (e.g., Janowsky et al. 1984).

Historical development of the sensory conflict theory

Although we do not yet have a complete physiological definition of motion sickness, the development of a succession of "sensory conflict" theories for motion sickness has provided a much broader etiologic perspective on the syndrome. The conflict theory has been widely accepted, and as a result, most workers now view seasickness, car sickness, airsickness, spectacle sickness, wide-screen movie sickness, flight simulator sickness, less common forms (such as space and camel sickness), and the nausea and the vomiting produced by vestibular end-organ disease simply as different examples of a single "sensory conflict" related nausea and vomiting syndrome.

Claremont (1931) observed that motion sickness symptoms result whenever there is a discrepancy between the information given us by one set of sensations, and that given by another set." He noted that "normally the two sets 'agree' with one another, or rather their occurrence in a given conjunction we are accustomed to we regard as normal. This normality is disturbed on board ship. Our eyes here tell us that we are stationary, since we are moving with the room." But our other sensations tell us we are moving. This basic conflict notion has since become known as the "sensory conflict hypothesis." The theory has been revised and extended by numerous authors (including Steele 1968; Guedry 1965, 1968, 1978; Melvill Jones 1974; and Reason 1969, 1978). It is important to note that until recently, statements of the conflict theory did not detail how the output pathways in motion sickness respond to the putative conflict signals. As discussed in later sections of this paper (Experiments on the dynamic character of symptoms and signs, and A revised model for symptom dynamics), additional assumptions are needed. Thus, these statements of the conflict theory do not themselves represent complete conceptual models for motion sickness.

An additional difficulty was that the essential idea ("sensory conflict") was at first only loosely defined. In early statements of the theory, conflict signals were assumed to result from a direct comparison of signals provided by different sensory modalities (e.g., "the signals from the eye and ear do not agree"; "canal–otolith" and "visual–inertial" conflicts). Papers from the era list taxonomies of the various types of intermodality conflicts. This approach has intuitive appeal. However, in 1978, this definition underwent a major revision: Reason (1978) noted that in terms of the actual processing of signals in the CNS, a direct intermodality comparison of afferent information is simply not appropriate. This is because signals from the various sense organs have different "normal" behaviour (in terms of dynamic response and coding type), and whether they can be said to "conflict" or not actually depends on coding, context, and previous sensory-motor experience. Reason argued that the essential conflict must be between actual and anticipated sensory signals. He rejected the "intermodality conflict" theories and proposed a "neural mismatch" hypothesis based on the "reafference principle" (see below). Reason's (1978) "neural mismatch" revision was the first, and is today probably the best known, of a newer group of theories sometimes collectively referred to as "sensory–motor" or "efference copy" conflict theories for motion sickness. Readers are cautioned, however, that variants of the older "intermodality conflict" theory still do appear in the contemporary literature. Authors of reviews sometimes casually interject older intermodality conflict notions even when discussing the newer sensory–motor theories.

In formulating his "neural mismatch" hypothesis, Reason drew on the well known "reafference principle" of von Holst (1954) and the prism adaptation experiments and models of R. M. Held and co-workers (Held 1961; Hein and Held 1961). Reason argued that the brain probably evaluates incoming sensory signals for consistency by computing the component of sensory signals that is new and unexpected, given knowledge of ongoing movement commands. The brain is postulated to maintain a "neural store" (a memory bank or dictionary) of paired sensory input and motor command "memory traces" that are continuously updated based on experience interacting with the physical environment. As a body movement is commanded, the CNS is assumed to fetch from the neural store the associated normally anticipated sensory input. These fetched traces, Reason noted, correspond to the "efference copy" signals postulated by von Holst. Actual sensory input and retrieved sensory memory traces are continuously subtractively compared. The difference is a "senory conflict" signal. The specific stimulus for motion sickness, a "neural mismatch signal," was proportional to the number and magnitude of sensory conflict signals. Reason noted that any stimulus situation or environment that effectively changed the rules relating motor outflow to sensory return (conditions which were called "sensory rearrangements" by Held) would therefore be expected to produce prolonged sensory conflict and result in motion sickness. Adaptation to "sensory rearrangement" was hypothesized to involve updating of the neural store with new sensory and motor "memory trace" pairs.

Reason's (1978) model had several significant shortcomings. It was not obvious why certain stimuli such as passive vertical low frequency linear acceleration were nauseogenic. The model was only qualitative, making simulation and quantitative prediction beyond its reach. Key structural elements such as the "neural store" and "memory traces" were only intuitively defined. The model did not really address the question of why the CNS should have to compute a sensory conflict signal, other than to make one sick, or what functional properties conflict signals might have such that they could be identified in a physiological experiment. Also, Reason's scheme focussed only on sensory conflict and did not incorporate "emetic brain" output pathway dynamic elements, which must be present to account for the latency and peculiar time course of symptoms.

A mathematical definition of sensory conflict

In general, quantitative "as if" mathematical models have proven to be useful tools for scientific investigation, because they compel one to more concisely describe the important functional elements in a system under study, and to see whether the resulting model can correctly predict (and thus interrelate) the results of previous experiments. Even when the models are primarily heuristic, the intellectual process often suggests new insights, "critical" experiments, and further model improvements.

To address some of the deficiencies in Reason's "neural mismatch" formulation, the present author (Oman 1978, 1982) formulated a version of the contemporary sensory–motor conflict theory from a mathematical modelling perspective. The model incorporated and extended Reason's hypothesis and contained emetic linkage output pathway dynamics, as required for a formally complete motion sickness model. The conflict theory portion of the model was synthesized by application of observer theory concepts from control engineering to the neural information processing task faced by the CNS in actively controlling body movement using a limited set of noisy sensory signals. Thus, the model can also be considered an extension of the "optimal control" model in the field of manual control (Baron and Kleinman 1968) and in the field of spatial orientation research, an extension of "Kalman filter" models (Young 1970; Borah et al. 1978). The latter have been used to predict orientation perception in passive observers with some success. In these previous models, however, "sensory conflict" was not defined in the same sense as that used by Reason and myself.

In the design of guidance, control, and navigation systems,