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Subgravity states: Key to understanding the role of terrestrial gravity in human behaviour

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Abstract—The early orbital flights, although undertaken with considerable confidence, involved some uncertainty because of the impossibility of simulating under terrestrial conditions all of the conditions encountered in space. However, space-flight achievements by both the American astronauts and Soviet cosmonauts have firmly established that man, if appropriately selected, trained, and protected by suitable life-support systems, can perform efficiently for long periods of time in the hostile environment of space.

We know that the side effects of vestibular origin pose important problems in space exploration, and the neurophysiological effects of any extensive, rapid adaptation processes in subgravity states have enabled a better understanding of man's compensatory capabilities. With the successful establishment of orbiting research laboratories, an unparalleled opportunity exists that will undoubtedly enable better understanding of the role played by gravity in normal terrestrial activity, not only as it affects our vestibular physiology, but also as it may or may not concern other systems and at different organizational levels in the body.

Introduction

THE MONUMENTAL achievements performed in space by both the American astronauts and Soviet cosmonauts have conclusively demonstrated that with appropriate selection, training, and protective support, man has the capability to live and perform effectively for long periods of time in that hostile environment. The early suborbital and orbital flights, although undertaken with some degree of confidence, involved uncertainty because of the impossibility of simulating under terrestrial conditions all the factors to be encountered in space. Of particular significance in this regard would be the possible effects of long-term exposure to hypogravity, including complete weightlessness; this could be determined only by actual space flight. In spite of lack of knowledge concerning the physiological effects of weightlessness, the space travellers have shown a remarkable capability for habituation, although, as pointed out by Berry [1] this has occurred at some physiological cost. However, the apparent postflight return to a normal healthy state has contributed considerably to our knowledge of man's capability to respond to extremes of stress. Furthermore, a remarkable opportunity now presents itself to enable a better understanding of the significance of gravity in the control of our normal physiology under terrestrial conditions. At this point in time it is possible only to offer some comment on probable relationships between

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gravity and physiology, including reference to problems encountered in space flight with the intention of stimulating controlled experimentation aloft.

Gravity and orientation

Man's orientation on Earth is controlled by the sensory receptors of vision, touch, proprioception, and the inner ear. Each of these plays an important part in the perception of our spatial alignment with respect to the normal upright position. In the weightless state vision is of paramount importance for determination of relative position, and space-flight experience in zero-G has shown this to be of prime significance since "up" and "down" become meaningless. This statement, however, is only partially correct in a hypo-G state, as shown during lunar exploration when locomotion and balance difficulties were experienced with sudden displacement (e.g., Apollo 17).

Although voluntary eye movements are apparently independent of gravity when the head is stationary under terrestrial conditions, head tilt can induce ocular counterrolling which is under otolithic control, and hence influenced by gravity, as shown by Miller and Graybiel [2]. Should an artificial gravity become incorporated as a component of future spacecraft, the threshold range for counterrolling responses could be determined. Such findings would also be invaluable in diagnostic procedures that could be used in clinical examination of vestibular disease. Reliable clinical tests of utricular and saccular integrity are lacking at present.

Under terrestrial conditions the vector representing the direction and magnitude of gravity is all important in determining the resultant stimulus characteristics when man is exposed to linear acceleration. Melvill Jones [3] has demonstrated the illusions that can be produced by aircraft acceleration reacting with terrestrial gravity. During straight and level flight sudden changes in velocity will produce a resultant force that is not in the direction of the Earth's gravitational vertical and hence gives a false impression of the pilot's spatial orientation. This accounts for the nose-down attitude which pilots report to have occurred as a result of appreciable decrease in linear velocity resulting from the application of air-brakes (and/or flaps). A sudden increase in speed, on the other hand, evokes the sensation of a nose-up attitude. Such sensations of spatial disorientation are undoubtedly the result of otolithic stimulation and can be of serious consequence should the pilot fail to rely on his instrument presentation.

Graybiel [4] introduced the term "oculogravic illusion" to describe the disorientation sensation when a subject exposed to a linear acceleration at an angle to gravity, perceives the direction of the resultant force of the imposed acceleration as that due to gravity. By the use of the slow rotating room located at the Naval Aerospace Medical Research Laboratory, Pensacola, Florida, many significant contributions to our knowledge of the physiology of the otoliths and of the semicircular canals have been made. The repetition of such tests in an orbiting space laboratory would offer an unparalleled opportunity for a better understanding of: (1) directional sensitivity, (2) the threshold of stimulation in normal subjects, and (3) pure uncontaminated otolithic responses.

Responses from the otoliths are difficult to distinguish from those of the semicircular canals and from other sensory inputs under terrestrial conditions. This is the result of interconnections within the central nervous system, together with the modifying control by higher centres in the cerebellum and cerebrum.

Interaction of response between the separate types of labyrinthine receptors has been noted but not fully understood. The classical experiments by Tait and McNally [5] with the frog as an experimental animal and using selective nerve-branch section, demonstrated that the ultricular receptors normally function in complement with the canals in response to rapid tilt. It can be concluded from those experiments that response in the normal animal to rapid tilt is the algebraic sum of the ultricular responses and activity of the canals. In other words, as stated by McNally and Stuart [6], "It may be concluded whereas the utricular maculae react quite slowly to occurring gravity changes, they also on the occasion of most of their responses need the quickly acting control of the four vertical canals." It is apparent, therefore, that animal experiments conducted in an orbiting laboratory, and designed to determine the physiological responses to otolith stimulation, should include animals whose afferent nerves from the semicircular canals have been inactivated. Findings from such experiments in a weightless state could well explain the locus of some specific signs and symptoms in patients suffering from vestibular disease as well as contribute fundamental knowledge of normal utricular and saccular function.

Any conclusions as to semicircular canal function, whether in weightlessness or under terrestrial conditions, must be carefully evaluated with respect to the control by the central nervous system. This must include both the higher and lower centres as well as otolith activity. When discussing semicircular canal activity, some authors have considered these motion receptors to be gravity independent. This inference can apply only insofar as motion of the cupula within the endolymphatic system is concerned. In the normal subject all of the above-mentioned relationships should be considered when attempting to understand the resultant responses.

Owada *et al.* [7] studied the results of ablating the nerves to the utricle and to the horizontal canals in the rabbit. They concluded that increased utricular activity would enhance any nystagmus to the same side while decreasing nystagmus toward the opposite side. Other findings have supported the conclusion that the utricle has an influence on nystagmus generated by the canals. Thus Bergstedt [8] found that positional nystagmus induced by alcohol or by caloric stimulation is enhanced with otolithic stimulation when G forces are applied by a centrifuge. He concluded that the otolith receptors actually generate the stimulus that results in positional nystagmus even if it occurs for pathological reasons or if the lesion be central or peripheral. It is significant to point out here that Nito *et al.* [9] found that positional alcohol nystagmus could be prevented by plugging the canals. Some current findings indicate that positional alcohol nystagmus actually results from change in specific gravity within the canals. This evidence comes from experiments by Money and Myles [10] involving the use of heavy water.

Further evidence that otolith activity reinforces canal responses has been demonstrated by Guedry [11]. While rotating human subjects about different axes, he noted more prolonged nystagmus when turning about a horizontal axis than when rotating about the vertical axis. He came to the conclusion that this prolonged response is dependent upon the continuous stimulation of otolithic receptors.

Although there is a considerable body of reliable evidence to indicate that nystagmus originates only from semicircular canal activity, some investigators claim that this response can also originate in the otolithic receptors during abnormal circumstances. Pathologic positional nystagmus, for example, has been claimed by Dix and Hallpike [12] to be the result of lesions in the utricle and induced by head position. Gernandt [13] reported nystagmus resulting from jets of air pressure applied directly to the utricle of squirrel monkeys, while Correia and Money [14] demonstrated nystagmus resulting from rotation about a horizontal axis even though the canals were blocked.

In any case, such divergency of opinion as to the possible sites of origin of vertigo and nystagmus could readily be resolved by controlled animal and human experiments in an orbiting space laboratory where the gravity component is absent.

Motion sickness

The advent of space flight has presented a hitherto unavailable opportunity to study interrelationships between the otolith gravity receptors and canal activity inasmuch as these can now be studied individually. Increased activity of the canals during weightlessness has been considered to be the probable cause of varying degrees of sickness in space as reported from the Apollo and the Skylab flights. The symptoms, ranging from mild gastric awareness to frank vomiting, are claimed to be the result of angular movements of the head, thereby implicating the canals which are considered to be more sensitive than usual while weightless, due to the absence of otolith influence [1].

It is proposed that another related factor in weightlessness which could alter canal sensitivity is the zero-G induced electrolyte imbalance. Of special interest in this regard is the marked potassium depletion that occurred in the Apollo crewmen [1]. This undoubtedly could cause cardiovascular dysfunction. The effects of potassium changes on canal sensitivity have been experimentally demonstrated by Dohlman and Johnson [15] in studies related to the etiology of Ménière's disease. This vestibular disorder is undoubtedly due to paroxysmal imbalance of the inner-ear activity, resulting from fluid electrolyte changes (endolymphatic hydrops). These changes can induce autonomic disturbances of the same types as are manifested during motion sickness. Those authors were able to induce related evidence of vestibular disturbance in squirrel monkeys. The experiments were prompted by the apparent possibility of a depolarizing influence on the vestibular nerves due to the escape of endolymph, which is relatively high in potassium concentration, into the perilymphatic spaces. Dohlman, while working with Fernández at the University of Chicago, was able to cause action-current decreases of the semicircular canal nerves by allowing endolymph to escape through an incision in the walls of the canal ampulla. He concluded that the resulting depolarization of the nerve fibres was due to the higher potassium concentration of the endolymph as compared to perilymph. The result was an increase in sensitivity at first, followed by complete lack of response to rotational stimulation. The normal sensitivity of the nerve could then be restored by application of either artificial perilymph or by flushing with isotonic potassium chloride solution. These laboratory findings correlate with apparent changes in vestibular sensitivity of the astronauts during early stages of the Apollo and Skylab flights when motion sickness was apparently induced by head movements. It would seem that further controlled experimentation should be carried out in order to compare changes in terrestrial vestibular sensitivity with those in the weightless state. Should potassium changes be established as a contributing factor to motion sickness in zero-G, this would greatly benefit treatment of some vestibular disorders in terrestrial clinical practice as well as in space flight.

A finding of considerable importance is that some of the signs and symptoms of vasovagal syncope (antidiuresis, nausea, pallor, and sweating) are seen in motion sickness whereas others (bradycardia and fall in arterial blood pressure) appear to be absent or at least inconsistent[16, 17]. Furthermore, peripheral vasodilation has recently been reported (McClure, personal communication) to occur early during the onset of motion sickness, as it also does during vasovagal syncope. The significance of such signs of extensive physiological changes as part of the motion sickness symptom complex has been demonstrated by Sunahara *et al.* [18] in experiments concerned with measurement of blood-distribution changes resulting from induced motion sickness. Healthy adult male subjects were exposed to strong vestibular stimulation produced by controlled cyclic nodding of the head while they were being rotated on a turntable at constant angular velocity. The subjects demonstrated wide variability in the amount of vestibular stimulation needed to cause nausea just short of emesis. Motion sickness, when unequivocal, was accompanied by increased blood flow as measured in the forearm. Resistant subjects, in whom motion sickness was either minimal or not apparent, showed no increase in forearm-blood flow. The magnitude of the change in this blood flow correlated with the severity of the symptoms, and it was often possible, by observing the blood-flow recordings, to predict when the subject would signal that he would vomit if stimulation was not discontinued. Simultaneous measurements have shown increases in blood flow in both forearms and legs during vestibular stimulation of susceptible subjects. It was concluded that such changes in blood flow occurred in all extremities and probably in most skeletal muscles. Computation of these blood-volume increases does indicate a large withdrawal of blood from the general systemic circulation, with consequent effects on the intracranial flow. Some of the subjects, in whom blood pressure was recorded continuously through a needle inserted into the brachial artery, showed no significant change in blood pressure or heart rate although these subjects were unequivocally nauseated.

As mentioned above, a marked antidiuretic response due to motion sickness has also been demonstrated[16]. Extensive studies, using both animals and humans as experimental subjects, conclusively demonstrated a highly significant correlation between antidiuresis and signs and symptoms of motion sickness.

Subjects who were not nauseated by the stimulus failed to exhibit an antidiuretic effect. The precise etiology of this effect has not yet been established although there is suggestive evidence. The findings are indicative of increased renal resorption, indicating that it results from a decreased glomerular filtration rate. Furthermore, evidence was found that the urine of motion sick subjects contained an antidiuretic substance, similar in its effect to that known to come from the neurohypophysis. It should be pointed out, however, that such an antidiuretic effect is not specific to motion sickness, since it also occurs with other stresses, such as fainting, pain, emotion, etc.

These findings involving antidiuresis and increased peripheral blood flow indicate a similarity between the signs and symptoms of vasovagal syncope and those of vestibular stimulation resulting in motion sickness. These changes indicate extensive and incapacitating physiological effects applicable to vestibular disturbances in space flight and under terrestrial conditions. Carefully controlled experiments aloft in orbiting laboratories may well contribute to a fuller understanding of the etiology, including a determination of the stimulus characteristics required to induce these changes.

Vestibular adaptation

As pointed out by McNally and Stuart[6], "It is generally known that repetitive vestibular stimulation, either rotatory or caloric, in both man and laboratory animals under certain special conditions, produces a response decline in all subjective and objective aspects of the reactions including nystagmus." This they called "habituation." The phenomenon is now generally considered to be a central process and not due to peripheral end-organ fatigue. The early state of knowledge concerning the physiology of this process was reviewed by McNally and Stuart[6]. Since the advent of the space age and the associated problems involving motion sickness, considerably more attention has been devoted to a study of vestibular adaptation, especially by Guedry and Graybiel[19] and by the Soviet scientists. For an outstanding treatise describing the latest findings on the subject of vestibular adaptation as applicable to man in space, the reader is referred to reference[20]. The need for a better understanding of how man adapts to his environment, whether under terrestrial conditions or in a hypogravic state, is emphasized by Graybiel who expressed the opinion that the vestibular organs have evolved to ensure proper orientation under the two-dimensional gravitoinertial force environment on Earth; hence, under the unique conditions in the weightless and especially in the rotating environment, not only may they furnish inadequate or inappropriate information, but also, under certain conditions, they may cause reflex vestibular disturbances and motion sickness.

Although chemotherapy has its value in suppressing some of the unpleasant and incapacitating effects of motion sickness in space flight, from the standpoint of long-lasting and more natural physiologic reactions, it would be more appropriate to apply carefully controlled head movement during early exposure to the weightless state. Now that we have the capability of conducting animal and human experimentation in orbital flight, we should gain a better understanding of the qualitative and quantitative aspects of the adaptive (habituation) process as it occurs in weightlessness and under terrestrial conditions. The stress profiles developed by Graybiel and his associates at Pensacola may well serve as guidelines for the planning of future research dealing with this challenging problem.

Conclusions

This presentation has emphasized the critical vestibular problems related to gravity. Although there are many gravity-related biological processes, extending from some intracellular processes to tissue and organ-system activity (including the highest parts of the central nervous system), it is not the objective of this limited presentation to evaluate all possible relationships. Other reviews with that broad objective have been published, such as the one entitled *Hypodynamics and Hypogravics* [21]. It should be pointed out that subgravity experiments hold the key to a better understanding of many of man's physiologic processes on Earth. Related research in orbit might be organized to show:

1. How bone mineralization and structure are related to gravity and muscle tone.
2. How endocrine activity is related to gravity, including differentiation between mechanical and emotional stress.
3. The normal tolerance range to stress with and without the resulting onset of pathologic changes.
4. How gravity controls specific processes in cellular physiology.
5. How gravity regulates metabolism.
6. The role of gravity in renal activity.
7. The role of gravity in the control of circulating blood volume and cardiovascular reflex activity.
8. The indirect effects of gravity on the central nervous system by comparison with reduced sensory input.

These among others constitute important problems that are applicable to man's newly developed capability of conducting animal and human experimentation in the weightless orbiting laboratory. Thus we are now offered an unparalleled opportunity to conduct research that undoubtedly will provide the key to a fuller understanding of the role of gravity in our terrestrial life processes, and this can be accomplished most efficiently by international cooperation.

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