PLASTICITY IN THE ADULT HUMAN VESTIBULO-OCULAR REFLEX

AN INVESTIGATION OF PLASTICITY IN THE HUMAN VESTIBULO-OCULAR REFLEX ARC

by

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ABSTRACT

This study is an investigation of long-term adaptation in the human vestibulo-ocular reflex (VOR). Repetition of prolonged unidirectional head rotation leads to progressive decline of the reflexly induced VOR. Yet such decline does not appear to occur during the natural movements of everyday life. The following experiments investigated the possibility that such changes only occur when they are functionally advantageous.

In the first major experiment, the VOR gain (eye angular velocity/head angular velocity) was measured in eight subjects, with eyes open in the dark, and exposed on 3 consecutive days to 1 hour of horizontal sinusoidal oscillation at 1/6 Hz and 60°/sec velocity amplitude. These values lie within the presumed range of velocity transduction in the human semicircular canal, and hence probably within the range of natural stimulation. The results showed no significant changes of VOR gain throughout the experiment.

The second experiment used the same subjects, with the same vestibular stimulus, but during rotation subjects attempted optokinetic tracking of a mirror-reversed image of the surround, therefore making the VOR oppose the visual fixation. The VOR gain now showed substantial (25%) and significant ($P \ll 0.001$) decline at the end of each 1 hour test period, and the pre-test control gain was significantly lower on 3rd than on the 1st day ($P \ll 0.001$).

The third experiment investigated the extent to which VOR could

be changed when given prolonged vision-reversal, here provided by the use of "dove" prism-goggles that reverse the horizontal, but not the vertical plane. They were worn continuously during all waking hours for up to 27 days. Results showed progressive decrease in VOR gain to almost zero in the first 7 days, and then an increasing but "reversed" response to about 50% of normal gain after 27 days. The "reversed" response at 1/6 Hz was about 50^{o} phase advanced relative to true reversal. Readaptation to normal was almost immediate for phase but lasted 3 weeks for VOR gain. No VOR change occurred in the sagittal plane, indicating high geometric specificity.

Tests of functional changes during the prolonged vision reversal showed that visual fixation was impaired even when the subject was permitted voluntary head oscillation. Postural equilibrium and visual perception were also shown to have changed as a consequence of whole-body adjustment, or optimisation, to the reversed visual environment.

RESUME

Cette étude a été entreprise pour étudier l'adaptation à long terme du réflexe vestibuloocculaire (R.V.O.). La répétition de mouvements prolongés de rotation unidirectionnelle de la tête entraîne une baisse progressive du R.V.O. induit. Toute fois une telle diminution ne semble pas survenir au cours des mouvements spontanés de la vie de tous les jours. Les expériences ont été entreprises pour tester la possibilité que ces changements ne surviennent que lorsqu' ils sont fonctionnellement avantageux.

Au cours de la première phase expérimentale le gain du R.V.O. (vitesse angulaire des yeux/vitesse angulaire de la tête) a été mesuré chez 8 sujets exposés les yeux ouverts dans l'obscurité pendant une heure, 3 jours consécutifs, à une oscillation sinusoïdale horizontale de fréquence égale à 1/6 herz et de vélocité égale à 60 degrés per second. Ces valeurs sont situées dans la zone présumée de rapidité de transmission dans le canal semicirculaire de l'homme et sont donc probablement dans less limites normales de stimulation naturelle.

Les résultats n'ont pas montré de changement significatif de gain du R.V.O. tout au long de l'éxpérimentation. La seconde série d'experiences a utilisé les mêmes sujets soumis au même stimulus vestibulaire. Au cours de la rotation les sujets ont essayé de suivre visuellement l'image de l'entourage inversée au moyen d'un mirroir, faisant ainsi s'opposer le R.V.O. et la fixation visuelle. Le gain du R.V.O. a montré dans ces conditions une baisse substantielle (25%)

et significative ($P \ll 0.001$) à la fin de chaque période d'une heure. De plus le gain mesuré avant le test s'est avéré significativement plus bas le 3^{e} jour que le prèmier ($P \ll 0.001$).

La 3^{e} série d'expériences a exploré les limites dans lesquelles le R.V.O. peut être modifié quand le sujet est exposé à une inversion visuelle prolongée. On a utilisé des lunettes (prismatiques) "dove" qui inversent le plan horizontal mais pas le plan vertical. Elles étaient portées pendant la totalité des heures ou les sujets étaient réveillés pendant une période pouvant aller jusqu' à 27 jours. Les résultats ont montré un déclin progressif du gain du R.V.O. pour aboutir à une valeur à peu près nulle vers le 7^{e} jour, puis une augmentation (inversee) de la réponse atteignant au bout de 27 jours une valeur normale. La réponse "inversée" à 1/6 Hz était à peu près en avance de phase de 50^{o} par rapport à l'inversion vraie. La réadaptation à la situation normale s'est avérée être presque immédiate pour le décalage de phase mais a nécessité 3 semaines pour le gain du R.V.O. Aucune modification du R.V.O. n'est apparue dans le plan sagittal, indiquant une grande spécificité géométrique.

Les tests effectués au cours de l'inversion visuelle prolongée ont montré que la fixation visuelle était altérée même lorsque le sujet effectuait des oscillations volontaires de la tête. L'équilibre postural et la perception visuelle se sont également avérés être modifiés, conséquence de l'ajustement de l'organisme à l'inversion visuelle de l'environnement.

DEDICATION

To my wife Anna

For her love, understanding, and patience

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TABLE OF CONTENTS

CHAPTER 1

GENERAL INTRODUCTION

1. DISARRANGEMENT STUDIES

(a) History

The basic phenomenon being studied in this thesis is "habituation", or long-term adaptation to an altered environment: in this particular case, a reversal of the visual surround on the retina. The concept of adaptation, whether of the whole organism or an individual cell, inherently implies that a change in the physiological or behavioral condition of the organism is possible. Put another way, as one climbs the phylogenetic level there is a movement from hereditarily built-in response, to environmentally controlled plasticity. Therefore, an animal very low on the phylogenetic scale may be said to be trapped in a straight-jacket of stereotyped motor patterns and behavioral responses. The early work in these fields, on lower phyla, can be found in a review by Bullock (1961), and a review of recent work in central patterning and neural control is covered well in the Neurosciences Research Program Bulletin on "Central Control of Movement" (1971). This latter review points out generally that in very low phyla such as the newt (Székely, Czéh and Vörös, 1969), the motor output is entirely central in origin and its automaticity is not effected by deafferentation. Higher up on the phylogenetic scale one can see centrally patterned movements triggered by the environment, as in the sound reflex of the Cicada (Hagiwara and Watanabe, 1956) which is mediated by two sound muscles, each innervated by a single

motoneurone. One external stimulus to the sensory nerve causes an alternating activation pattern of the two muscles.

Motor patterning in lower vertebrates and invertebrates seems to arise autonomously, irrespective of early experience. The motor coordination has been shown to be independent of practice. The same autonomy of central patterns that makes the low phyla immune to early sensory deprivation (Nottebohm and Nottebohm, 1971), as well as to deprivation of afferent input (Marler, 1964), also leaves them helpless when faced with abnormal changes in sensory input as after inversion of their visual fields (Sperry, 1950). Sperry (1950) showed that when the eyes of a fish are rotated 180°, it exhibits persistent circling behavior in a moving striped cylinder, and this movement will not adapt. The same behavior has been observed by von Holst and Mittelstaedt (1950) with fish and with the fly Eristalsis, whose head was turned 180° so that the two eyes were interchanged. When these insects begin to move in a striped cylinder or when the cylinder is moved, they spin rapidly to the left or to the right until exhausted.

Working with amphibians, Sperry (1943a) severed the optic nerves of a newt (Triturus Viridescens), and rotated the eyeball 180° about the optic axis. After recovery, visual perception was systematically reversed, optokinetic reactions were reversed, and there was erroneous spatial localization of small objects, with no later readjustment to normal. Similar results were obtained under identical circumstances using the more highly developed Anuran amphibians, such as frogs and

toads (1944), and in experiments with newts in which the eyeball was rotated with the nerve left intact (Sperry, 1943b). Cross-union of optic nerves, or contralateral transplantation of the eye (Sperry, 1945) also produced the same results, leading Sperry to the conclusion that reflex relations in the visual centers are apparently predetermined in an orderly manner by growth factors, regardless of the suitability of the functional effect for the animal.

In a more recent study on newts, Székely et al (1969) showed that a normal pattern of EMG activity during movement remained after complete deafferentation of one or both forelimbs. This included a high degree of co-contraction of antagonistic muscle groups. Székely's conclusion is that the coordination is controlled centrally, needing no afferent information from the limbs. Working with amphibians, Weiss (1950) exchanged adult salamander forelimbs so that the limbs pointed in the reverse direction. Although the limbs moved in a co-ordinated manner, the motion always remained reversed. This was the case even if the limb buds were reversed in the embryo. Deafferentation of frog tadpole legs (Weiss, 1941) also produced no impairment in the coordinated function of the legs. The conclusion is that in these phyla many of the coordinated mechanisms are built in, without need of sensory feedback. Therefore, if there is a reversed, or altered feedback, either by surgical procedure or external sensory change, the animal continues with the same set of predetermined mechanisms.

As one moves up the phylogenetic scale, the picture of built in patterned response becomes less clear. Newly hatched leghorn chicks (Hess, 1956) were fitted with rubber hoods containing binocular prisms that displace visual objects laterally by a few degrees. Their responses were correspondingly displaced. However, they constantly missed the target by a distance which matched exactly the visual displacement imposed by the prismatic spectacles. Chicks that are placed in complete dark isolation and fed artificially from a spoon for two weeks after hatching, and then returned to the light, never develop the pecking response (Padilla, 1935). The necessity for such a critical early time period for learning, makes it clear that practice, and therefore interaction with the environment, becomes more important in the higher phyla.

The ability of mammals to adapt their movements to some extent is typified by early experiments with Macaca Mulatta monkeys, where some adjustment of their movement was evidenced after wearing an inverting lens for eight days (Foley, 1940). Bossom and Hamilton (1963) similarly found that monkeys could adapt to a 13° lateral visual displacement after two days. After unilateral and bilateral forelimb deafferentation in monkeys, Taub and Berman (1968) noted that although large motor deficits occurred, there was adaptability in limb use during subsequent conditioning experiments. Held and Bauer (1967) combined a visual-motor coordination and restricted-rearing experiment, working with intact macaques monkeys. The animals were prevented from seeing their bodies for the first 34 days after birth. In the

post-restriction period the monkeys proceeded from an initial inability to coordinate visual-motor performance, to locomotor behavior indistinguishable from that of a normal monkey of comparable age after 2 to 3 months. Related studies on kittens by Hein and Held (1967) confirmed both the ability to adapt after restriction and the importance of visual-motor coordination. Bishop (1959), as well as others, have been able to show that cats can adapt to displaced vision. Various reviews of early experience and its effect on the behavior of animals may be found in Maier and Schneirla (1935), Beach and Jaynes (1954), and Melzack (1965).

(b) Adaptation in Man

Experiments concerned with inverted or displaced vision in man, have been carried out almost exclusively by psychologists, whose main concern has been the effect on perception and behavior. Since the latter changes are not the main emphasis of this thesis, only a brief summary of past work will be given, with special attention to the findings which have a bearing on the present work.

In fragmentary form, the work on human adaptation to optical distortion has a considerable historical background. Good reviews of this literature can be found in Harris (1965), and Howard and Templeton (1966). In general, the visual disarrangement studies are in two main groups. The first is concerned with displaced vision of a few degrees and its effect on perception and visual-motor coordination. The second group emphasizes adaptation to complete

inversion or reversal of the visual field. Since this thesis used a visual reversal technique, the second group will be emphasized.

(i) Adaptation to Displaced Vision

Work on displaced vision dates back to the late nineteen hundreds. Helmholtz (1867, 1962) reported adaptation to a displacement of the visual world, produced by looking through a wedge prism. He reported that in the initial stages, pointing to an object produces gross error in localization. Very quickly, however, the error is overcome, and the subject learns to point accurately. These experimental observations were not restudied for almost a century. Recent work by Harris (1965), Hamilton (1964) and Festinger, Burnham, Ono and Bamber (1967) have, in general, substantiated these results. It is now agreed that the most obvious consequence of wearing displacing prisms or spectacles, is the disturbance of visually-guided behavior, such as pointing. Movements towards objects will be directed to the position in space from where the displaced optical array would normally emanate. If the limb is in view, the initial mistakes are easily corrected, and the subject can guide his pointing limb to the target. Therefore, in an experiment in which the effects of distorting prisms are studied, the subject must not be allowed to see the moving part of his body until the movement is complete. Several authors have recently claimed that the adaptation results from a change in the felt position of parts of the body relative to each other, (Harris, 1963, 1965; Hamilton, 1964). They observed that the altered

reaching, apparent after reaching for displaced visual targets, is also evident for pointing at nonvisible targets such as sound sources (Harris, 1963). The indication that this generalization of shift is due to a change in proprioception which underlies the felt position of the reaching arm has been challenged by Efstathiou, Bauer, Greene and Held (1967). The theories accounting for this adaptation are still being argued.

An important aspect to much of this work has been the effect of voluntary movement as a sensory feedback to the adaptation process. Much of this work has emanated from the laboratory of Richard Held. In a 1963 experiment, Held and Hein placed two kittens in a circular apparatus containing vertical, black and white, alternating lines. The actively moving kitten was attached by a pulley arrangement to the passive kitten, whose vision was unobstructed but whose movement was confined to a box; the latter being pulled as the active kitten moved. The results showed that self-produced movement and the concurrent visual feedback are necessary for the development of visually-guided behavior. In human sensory rearrangement experiments (Held, 1955; Held and Hein, 1958; Held and Freedman, 1963), voluntary movements have also been shown to be essential for the achievement of complete adaptation to the new environment. Held and Bossom (1961), and more recently Held and Mikaelian (1964), used human subjects wearing wedge prisms which in one case displaced the visual field (1961), and in the second (1964) rotated the retinal image. One subject group was permitted "active" voluntary movement whereas the second "passive" group was moved about

in a wheel chair. The results of both these studies showed that in the "active" case, full and exact compensation occurred, whereas little or no adaptive changes were evident in the passive group. Although some of these results are still being debated (Howard and Templeton, 1966), it is agreed that "reafference" (von Holst, 1954), in the form of voluntary movement, is a powerful component of visual motor adaptation. This latter concept is covered in a later section of this introduction.

(ii) Adaptation to Reversed Vision

Another major line of inquiry, which has importance to this thesis dates back to Ardigo (1886), who reported that on wearing inverting and reversing lenses, objects were eventually seen as upright. When the optical devices were removed, objects at first appeared upside-down. More experiments were performed by Stratton (1897), who was concerned with whether or not one could re-invert an optically inverted visual world. For this purpose he wore a lens system which inverted and reversed the optical array in front of one eye (the other eye occluded), for eight days. His reports are all observations and thoughts on the visual-motor disturbances during that time. In his running account of day 1 he says: "Almost all movement performed under the direct guidance of sight were laborious and embarrassed... The wrong hand was constantly used to seize anything that lay to one side ... to write my notes, the formation of the letters and words had to be left to automatic muscular sequence..." (p. 344). Although there were still left-right, visual-motor coordination problems

on the fifth day, he did observe that: "the appropriate hand often came to the appropriate side of the visual field directly and without the thought that that visual side meant the other side in motor or older visual terms". (p. 355). Anticipating later work by Held and others on voluntary movement and adaptation, Stratton noted on day 5: "In rapid, complicated, yet practiced movements, the harmony of the localization by sight and that by touch or motor perception - the actual identity of the positions reported in these various ways - came out with much greater force than when I sat down and passively observed the scene". (p. 356). Stratton also noted that sound of objects out of sight - for instance of stones thrown out of sight - seemed to come from the opposite direction to where they had been seen to pass out of sight. However, when the source of sound was in sight, the sound seemed to originate in the visual object responsible for the sound. There was therefore a domination by vision. Furthermore, there is good evidence from Stratton (1897) and Ewert (1930), that after several days of continuous wearing of inverting glasses, subjects reported a stable scene when the head was moved. Stratton's reports are somewhat ambiguous, but one can reasonably infer that he gradually learned motor adjustments. However, Stratton's visual world, in the sense of visual perception, remained inverted.

Considerable space has been given to Stratton's experimental observations for several reasons. Firstly his introspective and behavioral approach led to a whole series of similar efforts by other authors (Ewert, 1930; Carr, 1935), whose conclusions were often

debates of Stratton's verbal observations, with few new concrete findings on the physiology, or psychology of visual-motor coordination. Stratton's work has added significance in that many of his observations were later incorporated into theoretical studies by authors such as Kohler, Held, and Harris, who attempt to explain the complicated adaptive mechanisms.

There were some similar studies done by Wundt (1894) and Ewert (1930), but it was the team of Erismann and Kohler who gave a new impetus to research on such problems. Kohler has published papers of their many studies (1951, 1953, 1956, 1962), in which they have done the most thorough work on the subject (see Kottenhoff, 1957a, b, for an English summary of this work). In their experiments the apparatus provided either right-left reversals of vision, or up down inversions, but not both simultaneously as in most earlier studies. They paid equal attention to motor readjustment, and to possible perceptual changes. An attempt was made to measure the course of both their maximum change, and the after-effects when the spectacles were removed after continuous wearing (for up to four months). Kohler's approach is phenomenological, relying on the introspective reports of his subjects, rather than on the application of controlled psychological and/or physiological tests.

From Kohler's reports, it is clear that motor readjustment precedes "perceptual" readjustment by days or weeks (Kohler, 1951). Furthermore, both motor and perceptual reorganization seem "easier"

with up-down than with right-left reversals. In his studies there are large individual differences in rate and extent of readjustment, as well as differences with age. The motor readjustment goes quite far. After two weeks or more subjects were able to execute smoothly, very complex movements such as skiing, climbing, cycling, fencing, and riding a bicycle in heavy traffic. In the context of this thesis it should be noted particularly that all these movements require high frequency head motion, which in turn requires a functioning vestibulo-ocular reflex to stabilize an image on the retina. Even at the end of the experimental period there still remained a tendency to make "false starts", and each new task had to be learned piecemeal; success at one skill not necessarily transferring to other skills. For the first few days, there is subjective motion of the visual scene, often accompanied by giddiness and nausea, the latter diminishing greatly after the initial periods.

In the perceptual sphere, adaptation is peculiar in that there seem to be piecemeal readjustments within the scene. With right-left reversing spectacles, subjects report at some stages that they "see" cars on the correct (actual) side of the street and hear the engine noises as emanating from the correct side, yet the cars bear licence plates in mirror writing. After many weeks, however, complete motor and perceptual adaptation occurs. Also important is that upon removal of the prism goggles subjects went through a readaptation process in the new reversed normal world, with the readjustment time course being of comparable length to the original adaptation.

Other work in recent years has substantiated Kohler's findings.

Snyder and Pronko (1952) used a control condition to investigate the effect of the constriction of the visual field which inverting spectacles necessarily impose. They found that constriction of the field to 20^{0} in their experiments did not appreciably influence the quantitative or qualitative results. They also noted, as did Peterson and Peterson (1938), that the visual-motor patterns learned during the adaptation period were retained when the subjects were again tested with the spectacles after a period of several months of normal visual experience. A startling report of adaptation was made by Taylor (1962). One of his subjects wore left-right reversing goggles for selected periods of the day, for several days. The remainder of each day was spent with normal vision. After only a few days this subject had developed a perfect conditional adaptation. While riding a bicycle he could put the goggles on and take them off without interference to the motor activity, and without altering his visual perception.

Needless to say, all this previous work is still being reviewed and argued (Rhule and Smith, 1959; Smith and Smith, 1962; Festinger et al, 1967), although it is agreed that the adaptability of man in both motor and perceptual spheres is enormous. The next section covers some of the main theories that have emerged from this work, and that have led to a clearer understanding of the possible underlying physiological processes.

(c) Reafference, Efference Copy, and Feedback Theories

In order to interpret all the previous findings in the disarrangement studies there was a need to formulate theories that could explain the perceptual changes and motor control. The theories on visual disarrangement would have to take into account the differences between movements on the retina produced by voluntary eye movement, and retinal change produced by movement in the physical world. It can be easily shown that if the eyeball is passively moved (by tapping on it) there is apparent movement of the visual field. If, however, the eye undergoes a normal voluntary movement, the visual field remains stationary. If the extra-ocular muscles are paralyzed, an intended movement of the eye (which does not in fact occur because of the paralysis), creates a subjective movement of the visual field in the direction of the intended movement.

Although there is a long history of psychological experiments and theories surrounding this and related problems, only those studies which have direct importance to this thesis will be covered here. After performing the experiment above, Helmholtz (1867, 1962), working with humans, proposed that centers in the brain are directly provided with information about the efferent output to the extra-ocular muscles in order to distinguish between voluntary eye movement and external movement in the visual surround. In the early 1950's papers by Sperry (1950), von Holst and Mittelstaedt (1950), Mittelstaedt and von Holst (1953) and von Holst (1954), put forward the theories of

"efference copy" and "corollary discharge" based on experiments on insects and fish already noted previously (p.3). von Holst (1954) proposed that the "efference" from higher centers leaves an image of itself in the CNS, to which "re-afference" from the effector movement compares itself. A superimposition would cancel the feeling of motion. The image of the efference from higher centers they called "efference copy". In the case of the insect with the rotated head, the re-afference would not nullify the efference copy, but would produce an error and generate continual movement, which in turn would generate improper re-afference, ad infinitum. It is noteworthy that at this phylogenetic level there is never an adaptation to the reversed visual condition. In an independent study, Sperry (1950), described results similar to those found by von Holst and Mittelstaedt (1950), and postulated that a stimulus from higher centers to the effectors (creating eye movement), would also send a "corollary discharge" to the visual centers to compensate for the retinal displacement when the eyes are rotated. Any anticipated adjustment would be wrong, and would accentuate rather than cancel the illusory outside movement. Similar observations, and theories are frequent in the more recent literature (Groen, 1957; Brindley and Merton, 1960; Hein and Held, 1962; Mackay, 1966) in which a variety of animals in the phylogenetic scale have been used.

Very recent neurophysiological experiments by Ito (1968, 1970, 1973) have produced a much closer link between these theoretical concepts and the available experimental evidence. Ito discusses

the concept of "feedforward" control, which hypothesises a direct link between the intended movement and the final selector stage. This "feedforward" would only roughly approximate the required movement, but would be backed-up by a "feedback" system for fine control. The importance of this concept is apparent in view of the experimental evidence obtained by Ito (1968) suggesting such a feedforward network in the vestibulo-cerebello-ocular system. The importance of Ito's findings, as well as other recent physiological studies on this topic, are covered in the discussion of Chapter 5.

2. VESTIBULAR HABITUATION STUDIES

The main object of this thesis surrounds the study of changes in vestibulo-ocular function, or "habituation", after repeated, vestibular stimulation. The phenomenon of habituation has been recognized for many years, and there is a considerable literature devoted to the study of its characteristics. In the following sections some of the causes and effects of habituation, as seen through the literature, will be discussed.

(a) Effect of Arousal

(i) History

The arousal phenomenon has long been recognized by psychologists as a response to new and unusual stimuli (Abels, 1906; Cannon, 1929; Duffy, 1951; Lindsley, 1951; Wendt, 1951; Guedry, 1965a). In daily

life, constant variations in stimulus conditions keep arousal at a high level. However, in a situation where a repetitive stimulus is delivered, and the subject is not required to produce any voluntary reactions to the stimulus, a loss of arousal with a concomitant decrease in reflex activity becomes apparent.

The general effects of arousal have been used to explain the phenomenon of nystagmus habituation due to repetitive vestibular stimulation. Abels (1906) mentioned that it was a possible cause of the decreases in response he observed. Wendt (1951) confirmed that habituation of nystagmus is a prime result of an uncontrolled altertness. In fact, he claimed that in the dark, habituation did not occur until a "reverie state" or loss of arousal was obtained. Earlier studies by Griffith (1920), Dodge, (1923), and others, showed response declines with repeated vestibular stimulation, but the lack of controlled alertness in their studies makes the results suspect. In recent years work on habituation and arousal has been intensive (Guedry, 1965a). In all cases the general conclusion obtained confirms that alertness is important in maintaining nystagmus under certain specified conditions.

Although there are some conflicting results due in part to interspecies differences or varying experimental conditions, the following conclusions are not in dispute. Alertness is a crucial variable for habituation, especially when other inputs such as vision are excluded (Collins, Crampton and Posner, 1961; Collins, 1963). Any extraneous change can immediately cause a return of nystagmus

(Guedry, Collins and Sheffey, 1961). The habituation, in cases of non-arousal for both men and monkeys, consists of a change from the normal vestibular nystagmus to a form of nonconjugate eye movements found in sleep (Wendt, 1936; Collins et al, 1961). Another common finding is a reduction of slow phase eye angular velocity (Collins et al, 1961). Collins and Guedry (1962) show further that arousal is important in maintaining the fast phase as well, with the fast phase undergoing the most variation.

(ii) Control of Arousal

Methods to control alertness have been studied extensively. Early work concentrated on methods which could reduce the variability of nystagmus caused by the changing subjective states. Wendt (1951) developed the concept of "environment-directed orientation", which would avoid the wandering, autogenous eye movements and the reduced nystagmus often seen in "inward-directed reverie states". He employed the method of having subjects imagine a ship on the horizon. This method is effective for some subjects. However, later studies (Collins, et al, 1961; Collins and Guedry, 1962) have shown that the important factor is the degree of mental activity, or alertness, and that whether the subject is "inward-directed" or not makes little difference, as long as his level of mental activity is high. Their results confirm Wendt's findings that at least for a short series of repetitive stimulations, nystagmus does vary with the type of mental activity. However, it is not necessary to have environmentally-

directed conditions. In fact, a mental arithmatic task seems to provide the least amount of trial-to-trial, intra-subject variability, as well as producing a vigorous nystagmus, and hence was used throughout this study for maintenance of arousal.

Many authors (Henriksson, Kohut, and Fernández, 1961 a,b; Crampton and Schwam, 1961; Collins, 1963; Brown, 1966) have studied arousal effects on cat nystagmic habituation. Crampton (1964), and more recently Brown and Marshall (1967), have made use of D-amphetamine to create a high arousal state. In all cases this drug was able to keep cats very aroused, although both Crampton and Brown (1965) conclude that habituation in the dark still takes place notwithstanding the amphetamine. Besides the inherent problems of drug administration in human experiments, the physiological effects of amphetamines are not fully understood. Therefore, the applicability of these studies to human habituation is still to be determined.

(iii) Habituation in the Dark; with Maintained Arousal

With a high degree of arousal maintained, the question has been raised above whether habituation will then take place, if vision is not present. A review of the relevant literature can be found in Chapter 3.

(b) Effect of Vision

The importance of vision as a factor in vestibular habituation has long been recognized. Dodge (1923) showed that vision had an important control over vestibular input. Griffith (1920), using human subjects who were permitted visual fixation, found a dramatic decrease of about 80% in both frequency and duration of nystagmus. It became apparent, therefore, in these early studies, that allowance for visual fixation was necessary if marked vestibular habituation was to occur. However, even the early studies were not in agreement as to the effect of vision on nystagmic habituation. Wendt (1936) performed 12 trials in which there was alteration between fixation and no-fixation during the rotation, and vision allowance at the termination of each trial. He saw no evidence of habituation. Note that in the latter experiment vision during rotation gave an optokinetic stimulus synergistic with vestibular nystagmus whereas the optokinetic stimulus during the post-rotation was antagonistic to the vestibularly-induced nystagmus. This latter phenomenon has been used in our own study and is discussed below.

Recent studies have been able to approach the problem of visual factors more effectively. Since arousal-level has been recognized as a probable cause of the habituation found in the early studies, it is now controlled much more accurately, permitting a closer examination of habituation due to visual fixation. Wendt (1951) put forward the view that in an experiment where arousal is controlled and vision permitted, nystagmus due to the vestibular input does not

occur to a significant degree. Rather, the habituation seen is due to an increasing visual control. The conclusion is that a learning process is probably taking place and the visual factors are dominating. .Such a response would occur during cases involving vision in a post-rotatory situation where the vestibular nystagmus produces movement across the retina, in turn creating an antagonistic optokinetic nystagmus. This condition is encountered by such people as ballet dances, pilots, and skaters who encounter unnatural stimulation in their daily occupations.

Mowrer (1934), who tested ballet dancers and skaters, noted that if inspection was made of their eye movements when eyes were opened immediately after a turn, very little or no post-rotational nystagmus was observed. Similar results have been obtained by McCabe (1960) and Collins (1966, 1968). Collins showed, in addition, that brisk nystagmus did occur when fixation was not permitted after a spin, concluding that nystagmus decline observed when fixation is permitted does not transfer to the former condition. In commenting on these results, Guedry (1965a) stresses the importance of voluntary action in suppressing nystagmus and apparent motion effects. He contrasts it with the introduction of vision in human and animal experiments in which the test subject is passively rotated. Even in the latter case experiments by Guedry (1965a) confirm that vision is an important factor in habituation of vestibular nystagmus in man..

There is a large literature concerned with other forms of habituation. Crampton (1962b) has pointed out that in "discussing response decrements, it is necessary to indicate the stimulus parameters,

the experimental animal, and the response; ocular nystagmus, oculogyral illusion, or subjective judgements of velocity." Reduced vestibular responses are studied with reference to both visual and arousal habituation, as well as caloric habituation and sensory adaptation. Guedry (1965a) has included another very important stimulus condition: habituation involving coriolis acceleration. The latter form brings in two more factors; conditioned compensatory factor and a conditioned general suppression of vestibular response. These two factors are discussed in the next section of the chapter. Finally, transfer and retention of habituation have not been dealt with in this review. Four extensive reviews (Wendt, 1951; Collins, 1964a; Guedry, 1965a; Guedry, 1974) in the literature are available for further reference to the areas not covered in this study.

(c) The Conditioned Opposing Response

Arousal has already been discussed in a previous section. To date it appears that although arousal loss is a definite component mechanism of habituation, overall the latter is due to several mechanisms of which reduction of alertness is only one type (Crampton, 1962a; Crampton and Schwam, 1961).

For example, simple loss of arousal could not account for the results of long-term habituation studies performed by Guedry, Graybiel, and others, in the 1960's. These authors have begun to consider the similarities between vestibular habituation and learning.

The "sea legs" phenomenon has often been described as a case of conditioning of opposing response tendencies, and Groen (1960) has even spoken of a central "pattern center" which stores the memory of repeated sensory inputs; in this case inputs of vestibular origin. This center, when set up, anticipates and compensates for movements in the unusual environment. This is very close to the "efference" principle of von Holst and Mittelstaedt (1950), which has already been covered. Both Dodge (1923) and Wendt (1936) have suggested that one may suppress vestibular responses by conditioning opposing responses. In fact, these authors have been instituting the mechanism of learning which is itself not understood well physiologically.

In the 1960's Graybiel and his co-workers started a series of experiments on complex vestibular stimulation in a slow rotating room, or SRR (Graybiel, Clark and Zarriello, 1960), in these cases vestibular reactions are produced by voluntary head movement during whole body rotation. As pointed out by Guedry (1965a), during this rotation there is much more than a simple conflict of visual and vestibular sensory inputs. During head tilt relative to the axis of rotation, the stimulus creates a conflict between messages sent to the CNS by the semicircular canals, otoliths, proprioceptive, and visual elements. A good review on the SRR work may be found in Guedry (1965a). However, due to the importance of this work to the present study a brief resumé will now be included.

It is interesting to note, in view of the present experiments, the literature review on disarrangement studies (Kohler, 1951), and

related theories on reafference (von Holst, 1954; Held, 1961), that Guedry (1965a) sees the SSR experiments as a new form of the sensory "rearrangement" experiments, producing systematic alteration of vestibular sensory input attending movement of the head body. Held (1961) has spoken of the importance of active versus passive movement for the production of proper reafference as well as a-typical relations between movement and contingent reafferent stimulation, so that progressive shifts in coordination compensate for the errors induced by the atypical conditions.

In the SRR experiments, where a complex interaction of canal, otolith, proprioceptive, and visual stimulation takes place moment to moment, the "atypical conditions" that Held sees necessary for adaptation are definitely present.

In these experiments, subjects were rotated for various time periods (hours to 12 days) and at various speeds (5.4 to 10 rpm). Subjects were allowed voluntary whole body movement in most cases, although during several experiments only certain restricted movements was permitted (Guedry, Collins and Graybiel, 1964). When permitted freedom of voluntary movement, and vision, a striking effect was observed during post-rotation tests. Namely, tilting tests produced nystagmus that was opposite in direction to that produced by the same movements during the rotation tests. This "compensatory nystagmus" could persist for several hours (Guedry and Graybiel, 1962), and did not occur when, in other experiments, subjects were restricted in their freedom of movement (Guedry, 1964). In the most extensive

run, consisting of continuous 12 day rotation at 10 rpm (Guedry, 1965b), rotation tests before and after the 12 day period showed that rotations in the same direction as that of the 12 day period produced almost no nystagmus. This contrasted with tests in the unaccustomed direction, where nystagmus showed increased intensity from that obtained in tests prior to the 12 days rotation. In addition, even when the compensatory reactions disappeared, there remained a depressed nystagmus in both the practiced and unpracticed directions of test rotations.

Guedry attributes the response changes observed to a conditioning of the otolith and visual systems, neck kinesthetic receptors, and the intention involved in head movement, that together signal a particular pattern of discordant influx from the semicircular canals, and eventually release what he calls a "competing response". In light of the experiments on visual-vestibular interaction to be described in the present study, Guedry's observations bear considerable interest, in that they serve as a bridge between the psychological observations and the more recent neurophysiological research. The latter is reviewed in detail in Chapter 5.

3. CELLULAR HABITUATION

As a correlate to studies of the behavioral component of habituation, there has been an increasing amount of attention focused on habituation as it applies to the individual neurone in the CNS. Recently a number of researchers have described CNS neurones which exhibit properties very similar to those of behavioral habituation

(Bruner and Tauc, 1966; Kandel and Tauc, 1965; Kandel, Castellucci, Pinsker and Kupfermann, 1970). In short-term studies it is found that the units respond to the first stimulus presentation, but their responses decrease or cease entirely if the stimulus is presented for intervals of seconds to minutes. The response decrement is more or less specific for the stimulus, since after habituation a change in the stimulus parameter can re-excite the neurone. Recovery can take seconds in mammalian neurones, or hours in the case of invertebrates. A combined behavioral and neurophysiological approach has been applied to the marine mollusc Aplysia by Kandel and his co-workers (Kupfermann and Kandel, 1969; Pinsker, Castellucci, Kupfermann and Kandel, 1970).

If weak or moderate tactile stimuli are applied to the siphon of Aplysia there is a gill withdrawal reflex. This response is controlled by five motoneurones in the abdominal ganglia, which receive direct input from mechano-receptor sensory neurons and inputs from adjacent interneurones. Kupfermann and Kandel (1969), in intracellular studies of these motoneurones, have shown that reflex withdrawal to tactile stimulation results from direct excitatory input on the motoneurones from the mechano-receptors. Spontaneous withdrawal response can occur, however, from both excitatory and inhibitory input from interneurones, allowing for quite variable response, and for adaptation. The intact animal, in behavioral response to tactial stimulation, gradually habituates to a stimulus repeated 10 to 50 times, with the recovery lasting up to 2 hours (Pinsker et al, 1970). Intracellular recording

of identified motoneurones controlling the gill movements showed that the behavioral habituation paralleled a decrease in amplitude of the EPSP in the motoneurones (Kupfermann, Pinsker, Castellucci and Kandel, 1970), Kandel (1971), concludes that habituation involves a marked change in the synaptic effectiveness of the excitatory synapses between sensory and motor neurones. The importance of new protein synthesis is discarded since the changes occurred unaltered after 97% of protein synthesis had been inhibited for several hours. Long-term habituation has been examined behaviorally in these animals (Carew, Pinsker and Kandel, 1971), and it is found that habituation builds up gradually across days in a 5 day experiment, with 10 trials per day. This habituation remains unchanged for at least a week. Furthermore, spaced training (10 trials per day for 4 days) gave significantly more habituation on days 5 and 12 than massed trainings (40 trials per day on day 4). Since the neural components of these reflexes are well understood, these authors feel that they now have the possibility of studying the neural mechanism of long-term habituation.

It seems clear, therefore, that with experiments on phyla containing relatively simple neural systems, there may be an opportunity to study the changes in the CNS during adaptation and habituation situations.

More precisely, in the case of the present study on human habituation one sees marked and retained reflex changes which would most probably call for changes at a cellular level. The fact that the latter is now being shown to exhibit large scale changes during habituation conditions lays a strong foundation for the larger scale

CNS changes observed in the present study. A definitive review of the cellular habituation field may be obtained in the two volume series, "Habituation", (Peeke and Herz, 1973 a, b).

4. THE VESTIBULAR NUCLEI AND THEIR CONNECTIONS

Neurophysiological experiments currently in progress, that are attempting to determine the possible sites and mechanisms responsible for changes in vestibulo-ocular response similar to the those seen in the present experiments (see discussion in Chapter 5), have centered on the cerebellum and vestibular nuclei as likely candidates. The present section is a brief review of the anatomy and physiology of the vestibular nuclei, with particular emphasis on some of its numerous connections in the central nervous system.

(a) Anatomy

The first major synaptic center reached by the bipolar vestibular sensory neurone, coming from the vestibular end organ, is the vestibular nuclei. Since these nuclei represent a preliminary stage for signal modification and message spread, they are an important determinant of the final response to vestibular input. Before discussing relevant neurophysiological findings, recent work on the anatomical connections will be summarized.

The vestibular nuclei are classically composed of 4 main areas: the lateral (Deiters), the superior (Bechterew's), the medial (triangular, or nucleus of Schwalbe), and the descending (spinal) nucleus. Work on the cat has shown that there are other small cell groups of

lesser importance such as group x lateral to the descending nucleus, the interstitial nucleus of Cajal, and a group of large cells in the caudoventral portion of the descending nucleus (Brodal and Pompeiano, 1957).

A very comprehensive review on the connections and synaptic organization may be found in Brodal, Pompeiano and Walberg (1962), Brodal (1967), and Brodal and Pompeiano (1972).

(i) Afferent Connections to the Vestibular Nuclei

The largest afferent input comes from the receptor organ by way of the vestibular sensory bipolar neurones in the vestibular portion of the eighth cranial nerve. Lorente de No (1933) studied the distribution of specific labyrinthine fibers to the vestibular nuclei. Canal afferents entered all 4 major nuclei, while macular afferents went mainly to the lateral and descending vestibular nuclei. With destruction of one vestibular nerve, Walberg, Bowsher and Brodal (1958) showed that degeneration did not involve all portions of the nuclei but rather that termination was principally confined to the rostroventral part of Deiters nucleus, with termination on small and medium sized cells. No primary fiber degeneration was found in the contralateral vestibular complex. These results have recently been confirmed by Mugnaini, Walberg and Brodal (1967), who showed that termination occurs not only on small and medium sized cells, but also on some giant neurones. A very recent comprehensive study of receptor end organ connections to the vestibular nuclei may be found in

Gacek (1969).

Spinovestibular fibers have their chief termination in the dorsocaudal portion of the lateral vestibular nucleus with some connections to the caudalmost parts of the descending and medial nuclei (Pompeiano and Brodal, 1957). Interestingly, these latter discrete portions are devoid of primary vestibular endings. Furthermore, the spinovestibular fibers end on the giant cells.

Pompeiano and Walberg (1957) have found termination from higher levels of the brain onto the medial vestibular nucleus, mostly caudally and dorsomedially. The fibers seem to eminate mostly from the ipsilateral interstitial nucleus of Cajal.

A great many afferent as well as efferent fibers connect the cerebellum and vestibular nuclei. Direct cerebellar corticofugal fibers to the vestibular nuclei were first noted by Allen (1924). The fibers are in two main groups; those coming from the cerebellar cortex, and the ones from the cerebellar nuclei. Jansen and Brodal (1942) traced fibers from the vermis of the anterior lobe, the pyramus, and the uvula, to the homolateral lateral vestibular nucleus, as well as the superior nucleus. There are in addition many direct fibers from the flocculus ending on the superior and lateral nuclei (Dow, 1936). Other recent findings suggest a somatotopical pattern in many projections from the cerebellar cortex, as well as termination mostly on the giant cells. The latter are avoided by receptor primary afferents, as well as by the cerebellar nuclear projections. A detailed account of direct cerebellar projections is covered in Jansen and Brodal (1958). Recently

Walberg and Jansen (1961, 1964), and Angaut and Brodal (1967), have shown evidence of direct ipsilateral termination of Purkinje cell axons from the vermis onto cells in the dorsal portion of lateral vestibular (Deiters) nucleus, with some endings in the dorsal portion of the superior and descending nuclei. All vestibular nuclei except the lateral (Deiters) nucleus are also covered by Purkinje cell axons from the flocculus, nodulus, uvula, and paraflocculus. Interestingly, the ventral part of Deiters nucleus receives very few direct cerebellar corticofugal projections. The degenerating synaptic terminals seem to be situated mostly on the giant cells and particularly on the larger dendrites. Less degeneration was observed immediately next to the cell bodies themselves. The functional significance of these findings are still not clear.

Many direct cerebello-vestibular fibers pass through the rostral third of the fastigial nucleus (Walberg, Pompeiano, Brodal and Jansen, 1962). This nucleus itself supplies the entire vestibular nuclear complex (Brodal, 1960). However, it avoids many of the areas of termination of the direct cerebellar fibers and ends mostly on the small and medium sized cells. In general the rostral third of the fastigial nuclei has direct cerebellar corticofugal fibers, and projects to all parts of the vestibular nuclei, while the caudal third passes by way of Hook's bundle to areas not served by the direct fibers. Also, the caudal third fibers are homolateral. For comprehensive information on the connections and functional correlates see Brodal et al (1962). Finally, a comment by Brodal (1960) has importance to all these findings,

as well as to this thesis.

"It is characteristic that those regions, which receive few or no primary vestibular fibers, are supplied by afferent from other sources.... It seems a reasonable assumption that an integration between vestibular impulses and impulses entering the vestibular nuclei from the spinal cord or descending in the medial longitudinal fasciculus will to a large extent not be immediate... Only with regard to the cerebellar afferents the situation appears to be different, since all parts of the lateral, medial and descending vestibular nuclei receive cerebellofugal fibers." (p. 242). The importance of these cerebellar connections will be emphasized in later parts of this chapter as well as in Chapter 5.

(ii) Efferent Connections from the Vestibular Nuclei

Efferent Projection to the Labyrinth

Leidler (1916) was the first to show efferent fibers running along the vestibular nerve to the receptor cells. In 1955, Petroff found that the fine fibers in the vestibular rami disappeared following midline cuts in the floor of the fourth ventricle or eighth nerve section. Wersäll (1956), Rasmussen and Gacek (1958), and Dohlman, Farkashidy and Solonna (1958), showed the existence of degenerated endings on receptor cells possessing properties of efferent fibers found elsewhere.

Wersäll (1956) pointed out the existence of nerve endings on Type II receptor cells in the crista, containing a dense accumulation

of vesicles. Similar vesiculated endings contact the nerve chalices of Type I cells (Wersäll, 1960). Engstrom (1958) showed efferent fibers to both the cochlear and vestibular cells. He compared the structure of the vesiculated nerve endings with presynaptic endings in the central nervous system and suggested that all the vesiculated nerve endings were the terminals of efferent fibers.

Dohlman (1960), Brodal (1960), and Rossi and Cortesina (1963), showed the existence of acetylcholinesterase in the vestibular sensory epithelia. Localization of the acetylcholinesterase was studied by Hilding and Wersäll (1962), and it was demonstrated to be localized at the granulated nerve endings. Gacek (1960) was able to show the existence of efferent nerve fibers reaching from the vestibular nuclei to all the vestibular sensory epithelia.

Combined with physiological data (Sala, 1965), it seems clear that efferent fibers from the vestibular nuclei to the receptor endings do exist and that their effect seems to be an inhibitory one (Llinás and Precht, 1969). Recent reviews of anatomical evidence for central connections may be found in Gacek (1967), Rossi (1967), and Lindeman (1969).

Vestibulocerebellar Connections

It is well known that the oldest portion of the cerebellum (Archicerebellum) is the primary projection area for vestibular fibers (Larsell and Dow, 1935). The interrelationship between the flocculonodular lobe and the vestibular system is extensively covered

in publications by Jansen and Brodal (1954), Dow and Moruzzi (1958), and Brodal et al (1962).

Primary vestibulo-cerebellar connections have been traced to the flocculus, nodulus, uvula, and fastigial nucleus, in many species, and according to Dow (1936) these fibers are all homolateral. Carpenter (1960) notes, however, that the fibers are distributed bilaterally to the nodulus, uvula, lingular and fastigial nuclei, and ipsilaterally to the flocculus. He also found no primary vestibular fibers entering directly into the medial longitudinal fasciculus. The primary fibers were first identified by Cajal (1909), and have recently been found to terminate synaptically on Purkinje cells in the frog (Llinás, Precht and Kitai, 1967). Their importance in cerebellar modification of vestibulo-ocular function is discussed in Chapter 5.

Secondary vestibulo-cerebellar fibers (vestibular primary afferents to vestibular nuclei, to cerebellum), have also been traced to the nodulus, flocculus, uvula, and fastigial nucleus (Larsell, 1936; Dow, 1936).

In some of the most extensive work to date, Brodal and Torvik (1957), after lesioning the nodulus, uvula, flocculus, and roof nuclei, found that the vestibulo-cerebellar fibers are derived from the ventrolateral part of the medial vestibular nucleus, while most of them are from the ventrolateral regions of the descending nucleus. Carpenter (1960) did extensive studies on projections to the fastigial

nucleus and found that they receive mostly uncrossed and some crossed secondary vestibular nuclei. In Brodal and Torvik's studies, termination of the secondary fibers also occurred bilaterally in the uvula, nodulus and fastigial nucleus while those to the flocculus were homolateral.

Vestibular Projection to Other Centers

Unlike the secondary vestibulo-cerebellar fibers, those ascending in the brain stem are derived from all vestibular nuclei subdivisions. Brodal and Pompeiano (1957) lesioned the brain stem above the vestibular nuclei and found retrograde cellular changes in all four vestibular nuclei. Many of these fibers pass beyond the oculomotor nucleus (Brodal, 1960). Fibers have been traced to the interstitial nucleus of Cajal (Ferraro, Pacella and Barrera, 1940), the colliculi, medial geniculate body, red nucleus, nuclei in the thalamus (Carpenter, 1957; Carpenter and Strominger, 1965), and even into the hypothalamus. Possible vestibulo-cortical projections may exist (Tunturi, 1950; Andersson and Gernandt, 1954), but these pathways are not well understood. Vestibulo-spinal connections have been reviewed by Brodal et al (1962). Fibers descending mostly from the medial (Pompeiano and Brodal, 1957; Nyberg-Hansen, 1964), and possibly from the descending vestibular nuclei, are in the medial longitudinal fasciculus. Nyberg-Hansen (1964) has shown that these medial vestibulo-spinal tract fibers are confined to the upper half of the cord. Although

there are bilateral projections, most fibers are ipsilateral. These medial fibers are smaller in diameter and less abundant than the fibers in the second and most important tract; the lateral vestibulo-spinal tract. The fibers from the lateral (Deiters) nucleus go by way of the lateral vestibulo-spinal tract (Pompeiano and Brodal, 1957). All cell sizes in the nuclei send fibers to the cord, and at least in the lateral vestibulo-spinal tract there seems to be a somatotopical organization throughout the cord (Pompeiano and Brodal, 1957), and only ipsilateral innervation.

Both pathways have fiber termination on laminae VII and VIII of the spinal gray matter, mostly on interneurones. It is interesting that the utricular macula is the main input to the lateral nucleus, while the medial nucleus obtains primary vestibular input from the canals (Brodal et al, 1962; Shimazu and Precht, 1965). This presents a functional difference when applied to innervation at the cord level. A review of recent anatomical and physiological functional aspects of vestibulo-spinal pathways may be found in Nyberg-Hansen (1968).

(b) Physiology

It is clear, from the previous section that vestibular nuclei have an extremely complex anatomical organization. Information on the related physiology, that has recently been accumulating, is confirming much of the anatomical information, as well as adding a

further dimension to our understanding of the functional organization of this important nuclear center.

(i) Lateral Vestibular Nucleus

Ito, Yoshida, Okada and Obata (1964) were able to obtain a monosynaptic EPSP on the ventral Deiters neurones after stimulation of the vestibular nerve. Wilson, Kato, Peterson and Wylie (1967), in substantiating this result, note that this monosynaptic excitation is found almost exclusively in the ventral portion of Deiters nucleus. It seems clear that this part of the nucleus receives direct input mostly from utricular receptors of the labyrinth (Peterson, 1967).

Most of the Deiters neurones, however, respond with relatively small EPSP's, IPSP's following the monosynaptic EPSP (Ito, Hongo, and Okada, 1969). It therefore seems that an inhibitory pathway exists, containing one interneurone most probably in the surrounding descending and/or superior nuclei. Wilson, Wylie and Marco (1968) have also shown evidence of polysynaptic input to the ventral Deiters nucleus.

The spinovestibular input creates short-latency excitatory post-synaptic potentials in the caudal portion of the lateral (Deiters) nucleus (Wilson, Kato, Thomas and Peterson, 1966), but the effect is not very important in this portion of the nucleus. It is interesting, in this connection, that input from deep somatosensory receptors such as joint receptors in the pericapsular space, have been demonstrated to have influence on all vestibular nuclei (Fredrickson, Schwartz,

and Kornhuber, 1966), with this information being an important on-going feedback for postural adjustment. There was no indication in this study as to which nucleus is most important in this regard. Stimulation of ipsilateral and contralateral forelimb and hindlimb nerves often produces facilitatory influences on the same Deiters neurone, inferring a great deal of convergence (Wilson et al, 1967). Cutaneous nerves also create excitatory effects. It is noteworthy that stimulation of the spinal afferents also produces inhibitory influences, due to impulses reaching Purkinje cells of the cerebellar cortex, with subsequent direct inhibition of dorsal Deiters neurones (Ito and Yoshida, 1966).

Convergence of stimulation of the vestibular nuclei, in particular Deiters nucleus, can become quite complicated. Primary vestibular fibers go directly to the flocculus and nodulus (Brodal et al, 1962), and, as will be discussed later, resulting Purkinje firing produces inhibition of dorsal Deiters neurones. These primary fibers can be considered axon collaterals. Monosynaptic EPSP's can be induced in Deiters neurones by stimulating extracerebellar centers which send afferents to the cerebellum, and axon collaterals to Deiters. These include the ventral and lateral funicule of the cervical spinal cord (Ito, Yoshida, Okada and Obata, 1964), and the inferior olive (Ito, Obata and Ochi, 1966). This latter center produces monosynaptic EPSP's in Deiters neurones in advance of the IPSP's created by the fibers in the olivocerebello-vestibular loop. Stimulation of the medial longitudinal fasciculus in the midbrain produces strong EPSP's monosynaptically in Deiters

neurones (Eccles , Ito and Szentagothai, 1967, p. 293).

Electrical stimulation of Deiters neurones results in facilitation, both monosynaptic and polysynaptic, of extensor motoneurones in all cord levels (Wilson and Yoshida, 1968), although not with as clear a somatotopical arrangement physiologically (Wilson et al, 1967), as anatomically (Brodal, 1967).

In general, however, neurophysiological experiments support the view that the dorsal Deiters nucleus can be considered as a way station in a cerebello-vestibulo-spinal pathway (Brodal, 1967), whereas the ventral Deiters nucleus acts as part of a labyrinthine-spinal pathway.

(ii) Medial Vestibular Nucleus

The medial vestibular nucleus receives chief innervation, in the form of monosynaptic EPSP's, from the ipsilateral labyrinth (Precht and Shimazu, 1965; Shimazu and Precht, 1965). Most of this input comes from the horizontal semicircular canals, with the cells being of two main categories: Type I cells, excited by ipsilateral and inhibited by contralateral acceleration, and the Type II cells, inhibited by ipsilateral and excited by contralateral acceleration (Shimazu and Precht, 1965; Wilson, 1968). The medial cells are also connected to the contralateral labyrinth (Shimazu and Precht, 1965). These cells can be excited and inhibited by contralateral labyrinth stimulation, the pathway being most probably through the commissural vestibular fibers (Ladpli and Brodal, 1968). The latency of the

inhibition is as short as 1.6 msec (Wilson et al, 1968) and, it seems that some of the commissural fibers are inhibitory (Shimazu and Precht, 1966), consisting in the simplest form of an inhibitory commissural cell, activated monosynaptically by vestibular afferents (Mano, Oshima and Shimazu, 1968). Other pathways consist of an excitatory commissural cell exciting an inhibitory interneurone on the contralateral side, near the medial nucleus cell to be inhibited (Precht, Grippo and Wagner, 1967).

The medial nucleus receives inputs from all three canals as well as from utricular afferents (Stein and Carpenter, 1967). Recent experiments by Shimazu and Precht (1965) indicate that cells in the medial nucleus can be excited or inhibited by natural stimulation in the form of horizontal acceleration. In an intercollicular decerebrate cat preparation, Melvill Jones and Milsum (1970) has shown that single specifically horizontal canal-dependent neural units in the medial nucleus respond in phase with stimulus angular velocity in a frequency range from about 0.1 to 5 Hz. These authors conclude that the similarity between the theoretical end organ response and the message from the medial vestibular nucleus is very close. The relationship of medial nucleus response to the total vestibulo-ocular reflex arc has been covered very recently by Melvill Jones (1971).

(iii) The Vestibulo-Ocular Reflex Arc

There is a clear correlation between stimulation of the various semicircular canals and movements of the eyes in particular directions

(Lowenstein and Sand, 1940; Szentágothai, 1952). The connections from the vestibular nuclei to the oculomotor nuclei have been studied quite extensively. Early experiments, Lorente de Nó (1933) and Szentágothai (1950) produced both physiological and anatomical details of the basic three-neurone vestibulo-ocular reflex arc. In Lorente de Nó's experiments (1933) on the rabbit, the stimulus was caloric stimulation to individual canals of the labyrinth. Lesions were made in many areas of the midbrain, reticular formation, and vestibular nuclei, and the effect on recorded extraocular muscle movement was observed. His results show that a basic vestibulo-ocular reflex exists, involving both crossed and uncrossed fibers, mostly in the medial longitudinal fasciculus. Szentágothai (1943) performed gross unilateral lesions of the vestibular nuclei and found synaptic degeneration in subdivisions of the oculomotor, trochlear, and abducens nuclei. He correlated the termination with maps of individual extraocular muscles in these nuclei (Bender and Weinstein, 1943), and concluded that ascending fibers from the vestibular nuclei on one side terminate in regions supplying the homolateral medial rectus, inferior oblique, and superior rectus muscles, and the contralateral inferior oblique, inferior rectus, and lateral rectus muscles. In essence, these results implied that there must be a three-neurone arc connection between each crista and two extraocular muscles. From more recent physiological studies by Szentágothai (1950) on cats and dogs, in which individual canals were stimulated by artificial endolymph currents, the results

above were substantiated, in that it appears that the crista of the superior semicircular duct has predominant connection with the ipsilateral superior rectus and the contralateral inferior oblique; the crista of the posterior duct with ipsilateral superior oblique and the contralateral inferior rectus, and the horizontal duct with the ipsilateral medial rectus and the contralateral lateral rectus. In effect, he found short latency responses for each canal stimulation, in only one muscle of each eye. Transection of the medial longitudinal fasciculus abolished these short latency responses. Recently, McMasters, Weiss and Carpenter (1966) have shown secondary neurone synapses directly on corresponding III, IV and VI cranial nerves.

Very recent neurophysiological investigation, using electrical stimulation, has shown that primary afferent vestibular discharge crosses the secondary vestibular neurones, to produce either EPSP's or IPSP's, with disynaptic latencies, in the oculomotor nuclei (Baker, Mano and Shimazu, 1969; Precht and Baker, 1972). Using long single pulses of 3-5 msec duration, Ito, Nisimaru and Yamamoto (1973a) stimulated afferent fibers from individual canals in the rabbit, and revealed that in the case of all 12 extra-ocular muscles, stimulation of one canal produces a reflex excitation in one extra-ocular muscle one each side. Each canal excites a different pair of muscles, with no overlap between the pairs for different canals. This is exactly the same relationship found previously in the cat (Cohen, Suzuki and Bender, 1964).

Specifically, reflexes from horizontal canals relay by way of the medial vestibular nucleus, to excite the ipsilateral ("i") medial rectus and the contralateral ("c") lateral rectus. Excitation from the anterior canal to the "i" superior rectus and "c" inferior rectus is mediated by the y group projecting through the brachium conjuctivum.. The posterior canal relays excitation by way of the medial vestibular nucleus to the "i" superior oblique and 'c' inferior oblique.

In addition there exists a vestibulo-ocular inhibition, such that stimulation of a canal produces inhibition in the muscles whose antagonist muscles receive excitation from that same canal. (Ito, Nisimaru and Yamamoto, 1973b).

Besides this basic three-neurone reflex arc, there seem to be other complex reflex mechanisms superimposed.. Lorente de No (1933), after lesioning the MLF, found that all the labyrinthine reflexes of the ocular muscles could still be elicited. If the MLF was left intact, but the reticular formation and pons lesioned instead, the canal reflexes were abolished. Szentagothai (1950) could not produce the short latency contractive muscle action of the reflex, after cutting the MLF. However, the reciprocal inhibition to the muscles was less affected or not affected at all. Often a normally contractive response was changed to an inhibitory one. If only the MLF was left intact, normal contractive responses remained, but reciprocal inhibition of the antagonist disappeared. Certain contractile responses were abolished by transection of the brain stem, with the exception of the fasciculus,

and often unchanged after transection of the fasciculus. Szentagothai surmizes that there exist numerous intermediate chains in the reticular formation which are important in reciprocal inhibition of all the extra-ocular muscles, as well as in connecting functionally any one crista with any one of the extra-ocular muscles. Recent information on reticular formation involvement in vestibulo-ocular response may be found in Chapter 5 of this thesis.

(iv) Monosynaptic Inhibitory Action of the Cerebellum on the Vestibulo-Ocular Reflex

The specific inhibitory action of cerebellar Purkinje cells was discovered by Ito and Yoshida (1964). During stimulation of the ipsilateral cerebellar anterior lobe, IPSP's appeared with monosynaptic latencies on the target neurones in the dorsal Deiters nucleus. This monosynaptic inhibitory area comprises most of the vermal cortex of the anterior lobe and some of the posterior lobe (Ito, Kawai, Udo and Sato, 1968). The distribution of this inhibitory area conforms closely to the anatomical evidence of Purkinje cell corticovestibular projection (Walberg and Jansen, 1964).

Similarly, monosynaptic inhibitory action occurs on superior vestibular nucleus neurones when the ipsilateral flocculus is stimulated (Ito, 1968), and this conforms to histological evidence (Dow, 1938; Angaut and Brodal, 1967). Also in good accord with the histological findings is the fact that monosynaptic inhibition is not present in neurones of the ventral Deiters nucleus, which is known not to receive

termination of Purkinje cell axons from the anterior and posterior lobes (Walberg and Jansen, 1961).

In relation to the vestibulo-ocular reflex, experiments on the rabbit's secondary vestibular neurones have shown that stimulating the flocculus produces inhibition that counteracts the monosynaptic excitation coming from the ipsilateral primary afferent fibers (Ito, Highstein, and Fukuda, 1970). Furthermore, intracellular recording in the third nucleus shows that stimulating the flocculus will depress either the EPSP's or IPSP's produced during primary afferent firing. Similar results have been obtained from the cat's fourth nucleus (Baker, Precht, and Llinas, 1973).

Very recently Ito, Nisimaru and Yamamoto (1973c), have tested the effect of this floccular inhibition upon each of the 12 main pathways from the secondary vestibular nuclei. Inhibition was found for one half of the pathways of vestibulo-ocular excitation and inhibition. Specifically, there was bilateral inhibition of the inhibitory and excitatory paths connected with the anterior canal, and only ipsilateral inhibition of the inhibitory and excitatory paths related to the horizontal canals. Therefore the flocculus can effect any of the 12 muscles by inhibiting either its excitatory or inhibitory input.

(v) Monosynaptic Inhibitory Action of Cerebellar Purkinje Cells on Neurones of Intracerebellar Nuclei

Just as with vestibular nuclei, the intracerebellar nuclei

neurones receive monosynaptic inhibition from Purkinje cell axons, those in the interpositus nucleus from the anterior lobe cells, and those in the fastigial nucleus from the vermal cortex. With the cerebellar nuclei inserted, the connection from Purkinje cell to vestibular nuclei neurones becomes disynaptic. However, the cerebellar nuclei have terminations with all parts of vestibular nuclei, therefore extending the inhibitory projection area of Purkinje cells. Furthermore, the cerebellar nuclei make direct connections with the thalamic, red, and reticular nuclei, which in turn project to motoneurones all through the CNS. The Purkinje cell effect can therefore be very widespread. It is noteworthy that the fastigial axons have excitatory action upon vestibular neurones. Purkinje cell inhibition of the cerebellar nuclei cells therefore withdraws this excitation (Eccles et al, 1967). An important point here is that in the dorsal Deiters and superior nuclei, the fastigial influence parallels direct cortical inhibition, while in ventral Deiters the fastigial pathway is the only cerebellar control.

(vi) Axon Reflex-Collaterals of Cerebellar Afferents

Although cerebellar efferent stimulation produces IPSP's in subcortical neurones, it has also been shown to evoke monosynaptic EPSP's as in the case of the superior vestibular nucleus (Ito and Yoshida, 1966), the ventral Deiters nucleus, and dorsal Deiters nucleus (Ito, 1968). Ito (1968) shows evidence that this EPSP response is caused by cerebellar efferents which make contact with the subcortical

nuclei via their collaterals. One of these sources is the primary vestibular nerve. It is known anatomically that primary vestibular fibers go to part of the lateral (Deiters) as well as superior nuclei, and also to the flocculus and nodulus of the cerebellar cortex (Brodal et al, 1962). It is suggested that both the cortical and nuclear structures are innervated commonly by axon collaterals of the same afferent fibers. This idea is exemplified by experiments in which stimulation of the ipsilateral flocculus produces EPSP's in the superior vestibular nucleus. Concomitant stimulation of primary vestibular fibers and resulting occlusions due to impulse collision and refractoriness, makes it clear that the primary nerve has sent branches both to the vestibular nucleus and the flocculus (Ito, 1968).

In summary, two types of synaptic organization exist in the cerebello-vestibular complex. One type is represented by ventral Deiters neurones, which receive inputs directly from primary vestibular and medullary afferents but no direct cerebellar cortex input. In a second organization, exemplified by the superior and dorsal Deiters neurones, primary inputs go to these cells as well as to the cerebellum, which in turn sends Purkinje cell inhibition to interact post-synaptically with original primary excitatory input. In a later stage of this thesis there will be a discussion of the possible importance of these pathways to the adaptability of the vestibulo-ocular response.

PROBLEM FORMULATION

The purposes behind the present study, both as a whole or in component parts, are probably best understood when viewed in light of their historic development.

The concern of this thesis was at all times the phenomenon of long-term adaptation in the human vestibulo-ocular reflex arc. The impetus came from earlier experiments which showed that under conditions of repetitive vestibular stimulation, changes occur in relevant output, such as a reduction in magnitude of physiological response, or "habituation". More specifically, in laboratory tests on human (Collins, 1964a; Guedry, 1965a) and animal subjects (Collins and Updegraff, 1966; Komatsuzaki, Harris, Alpert and Cohen, 1969), in which prolonged and repetitive rotational stimulation was given, results consistently showed a progressive and retained decline in vestibulo-ocular response. In addition, this decline occurred in the absence of vision, leading one to believe that the attenuations observed might well be due to repetitive stimulation of the semicircular canals per se.

A closer look at these experiments revealed that, almost exclusively, the prolonged rotational stimulus used was of a unidirectional nature, and therefore most probably unnatural, when considered relative to the movements experienced in everyday life.

The first major question posed in this thesis was, therefore, whether similar changes of response would arise during natural movement (Chapter 3). To simulate a natural stimulus compatible with

experimental feasibility, the stimulus chosen was a sinusoidal oscillation of 1/6 Hz frequency and 60°/sec velocity amplitude, well within the normal dynamic response range of the human semicircular canals (Jones and Milsum, 1965). To assure that any changes observed would be due solely to the vestibular stimulus, the test runs were conducted in the dark. Slow phase angular velocity of compensatory nystagmus was used as the measured response, with DC electro-oculography (EOG) as the method of recording the eye movement. However, changes occur in the corneo-retinal potential of the eye when the level of ambient illumination is altered, the latter seriously affecting EOG records. The initial experiment (Chapter 2) was therefore undertaken to define the time course of the transition effects in a changing light environment, in order to assure that any changes in the vestibulo-ocular response were due to the vestibular stimulus and not corneo-retinal potential changes.

The repetitive sinusoidal oscillations in the dark, without the aid of vision, did not produce habituation. This raised the second major question of the thesis (Chapter 4). Is it possible that the habituation is not produced by a prolonged vestibular stimulation per se, but rather by a situation in which the induced response is inappropriately matched to other sensory inputs? In experimental terms, could habituation now be produced using the same stimulus, by creating an environment in which the previously non-habituating stimulus would be made inappropriate? Such a situation was produced by superimposing a mirror-reversed visual tracking task on the non-

habituating sinusoidal vestibular stimulus. Under these conditions the two main inputs to the oculomotor system, the vestibular and visual tracking systems, become antagonistic, with the vestibulo-ocular reflex rendered inappropriate. The results showed clearly that in such a situation habituation in the form of an attenuated vestibulo-ocular reflex, does indeed occur.

But was simple attenuation of the reflex an appropriate response to this reversed visual environment? The common feature of most previous experimental results was attenuation of the vestibulo-ocular reflex. However, the visual action was most often fixation during a post-rotational stimulus, which would indeed call for vestibulo-ocular attenuation to zero as the most appropriate vestibular response. In the present situation attenuation to zero would be helpful. But for proper image stabilization during head movement the vestibulo-ocular reflex (VOR) would have to become reversed. This latter observation raised the final major question, leading to the most extensive experiments of the study. Namely, would prolonged continuation of vision-reversal during rotational head movement lead merely to suppression of the VOR to zero, or to an overt reversal of that response? Put another way, could one conceive of attenuation of response as being only a part of a more general central nervous system capability to systematically remodel the relevant neurological elements, so as to optimise its response in relation to the new environment?

Furthermore, would optimisation of the VOR response lead to any functional impairments or readjustments in the subject's visual

fixation capability, postural equilibrium, and perception? Finally, should such radical changes in central nervous function occur, what possible neural mechanisms would be at play?

In summary, the major questions posed in this study of adaptability in the human vestibulo-ocular reflex are the following: (1) Can one habituate the vestibulo-ocular reflex during "natural" stimulation in the dark? (2) If not, can habituation be produced by creating antagonism of the two relevant stimuli; that is, a normal vestibular, and reversed optokinetic input? (3) To what extent will a prolonged vision reversal lead to readjustment of the vestibulo-ocular reflex so as to optimise its response to the radical change in environment? (4) What functional impairment and readjustments are consequent to the changes incurred.

In preparing this thesis, I have taken advantage of the option as outlined in section 4.2.7(h) of the thesis regulations of McGill University Faculty of Graduate Studies and Research (February, 1972), which makes it permissible to produce a doctoral thesis in the form of original papers suitable for publication. However, in order to aid the reader of this thesis, references from all the papers have been placed in alphabetical order at the end of the thesis (Bibliography).

CHAPTER 2

EFFECT OF CHANGES IN ILLUMINATION LEVEL ON ELECTRO-OCULOGRAPHY (EOG)

SUMMARY

1. This investigation is concerned with the changes that occur in the corneo-retinal potential of the eye when the level of ambient illumination is altered. These changes can seriously affect electro-oculographic (EOG) records, a technique frequently used for measuring nystagmus.

2. EOG calibrations were done on seven human subject for periods during which the illumination was varied between normal room light, red light, and total darkness.

3. The time dependence of the observed variations was established and seen to be reasonably consistent between all subjects. For purposes of EOG calibration, no difference was found between a red light environment and total darkness.

4. When experiments are to be performed in the dark, or with eyes closed, it is strongly recommended that subjects be dark adapted for at least 50 minutes prior to calibrating and recording eye position.

INTRODUCTION

Electro-oculography (EOG) is frequently used as a method for recording eye movement since it is both quick to set up and convenient to use. However, a serious problem of calibration may be associated with transition from one level of illumination to another (Arden and Kelsey, 1962; Homer, 1967; Homer and Kolder, 1966; Homer, Kolder and Benson Jr., 1967; Miles, 1940; Kris, 1958).

The effect is especially evident when changing between normal room lighting and total darkness. But since this manoeuvre is often used in vestibular experiments, as when calibrating in room light and experimenting with eyes closed, it can jeopardize results unless care is taken to overcome the effect. The present article describes experiments which define the time course of transition effects in these circumstances and suggests a practical measure for avoiding them.

METHODS

Seven human subjects were employed, all of whom were free from apparent oculomotor or visual defects other than simple errors of refraction. Eye position was recorded with bio-potential skin electrodes (Beckman Instruments Inc., Spinco Division, Palo Alto, California, U.S.A.),

applied one to the center of the forehead (ground) and one at each outer canthus of the eye, as close to the eyeball as practical. The differential output from the latter two was DC amplified and fed into a pen recorder.

Subjects were seated, with their heads held in place by means of a fixed dental bite. They faced three targets, situated 5 ft. in front of them. One center target was flanked on either side by two similar ones symmetrically placed along a horizontal line and each subtending 25^{o} with the center line at the bridge of the subject's nose. Each target was a 3/8 inch black disc in the middle of which was a pin-hole dimly illuminated from behind.

At 2-minute intervals subjects looked at the middle of the center spot, with both eyes open, then at one of the side spots, back to center, to the other side, and back to center again. They were told to stare at each target spot until a satisfactory record was obtained. After changing the lighting conditions, the above calibration manoeuvre was repeated once per minute, until transient changes had diminished, whereupon the regular 2-minute sequence was resumed.

Each run started with 20 minutes in normal room light (overhead fluorescent tubes). Once a base-line had been established, the fluorescent lights were extinguished, and the room (about 10 ft. by

10 ft with moderately reflective walls, floor and ceiling) was illuminated by two Westinghouse 40 watt red incandescent bulbs, in diagonally opposite corners. This condition was maintained until the calibration had resumed a steady level (usually 40-50 minutes). Extinguishing the red lights created a condition of total darkness, the only things visible being the dim pin-holes in the targets. Following this, the red lights were turned on again, and this condition was maintained for another fifteen minutes, with readings taken every two minutes. The normal room lights were then turned on, and readings taken every minute until the transient effects settled down and the calibrations once more became stabilized (usually after 40-50 minutes).

A plot was then made of the pen deflections produced by each excursion of the eyes from the center position, as a function of time. A small, consistent asymmetry in potential changes to left and right was obtained in all cases. This was found to depend on the relative placement of the two active electrodes, and with proper care could be kept to a minimum.

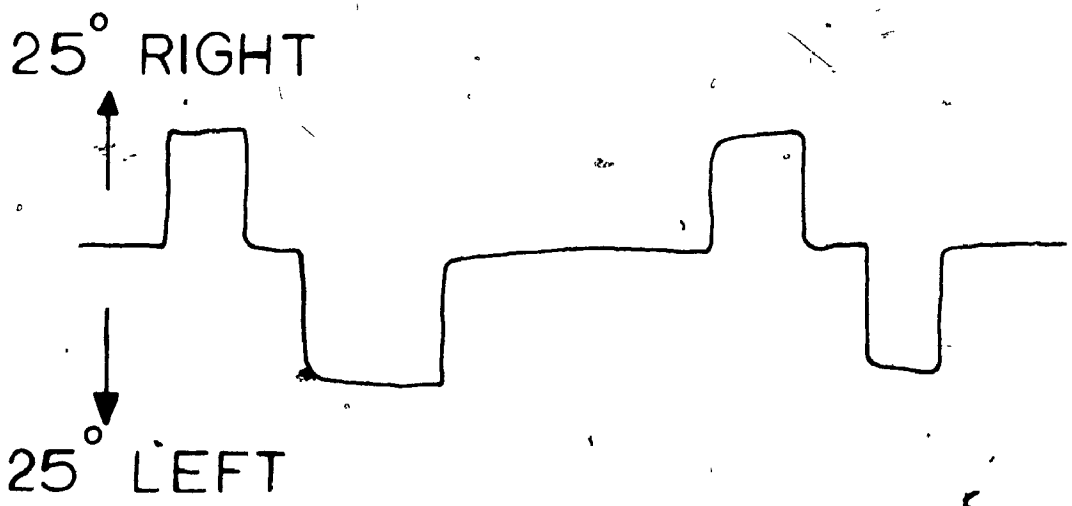
RESULTS

Figure 1 shows an extract from an original record obtained during an experimental run. Figure 2 shows graphically the collected

(Fig. 1 near here)

Fig. 1.

EOG records of eye movement calibration obtained during an experimental run.


25° RIGHT
25° LEFT

results obtained from one subject. The ordinate gives calibration in microvolts (μV) resulting from 25° of eye movement from center, and the abscissa gives time in minutes after commencing the experiment. The points on the graph give mean values obtained from one eye excursion to each side. During the initial 20 minutes in normal light, 25° eye movement produced approximately 270 μV (11 mm pen deflections). On changing to red light the response progressively decreased to a minimum during the first 10 minutes and then returned to its original value over a similar time course. Thus a total of approximately 20 minutes in red light conditions was necessary for restabilization, with the particular feature that the new (red light) stabilized response was of similar magnitude to that obtained in normal light conditions.

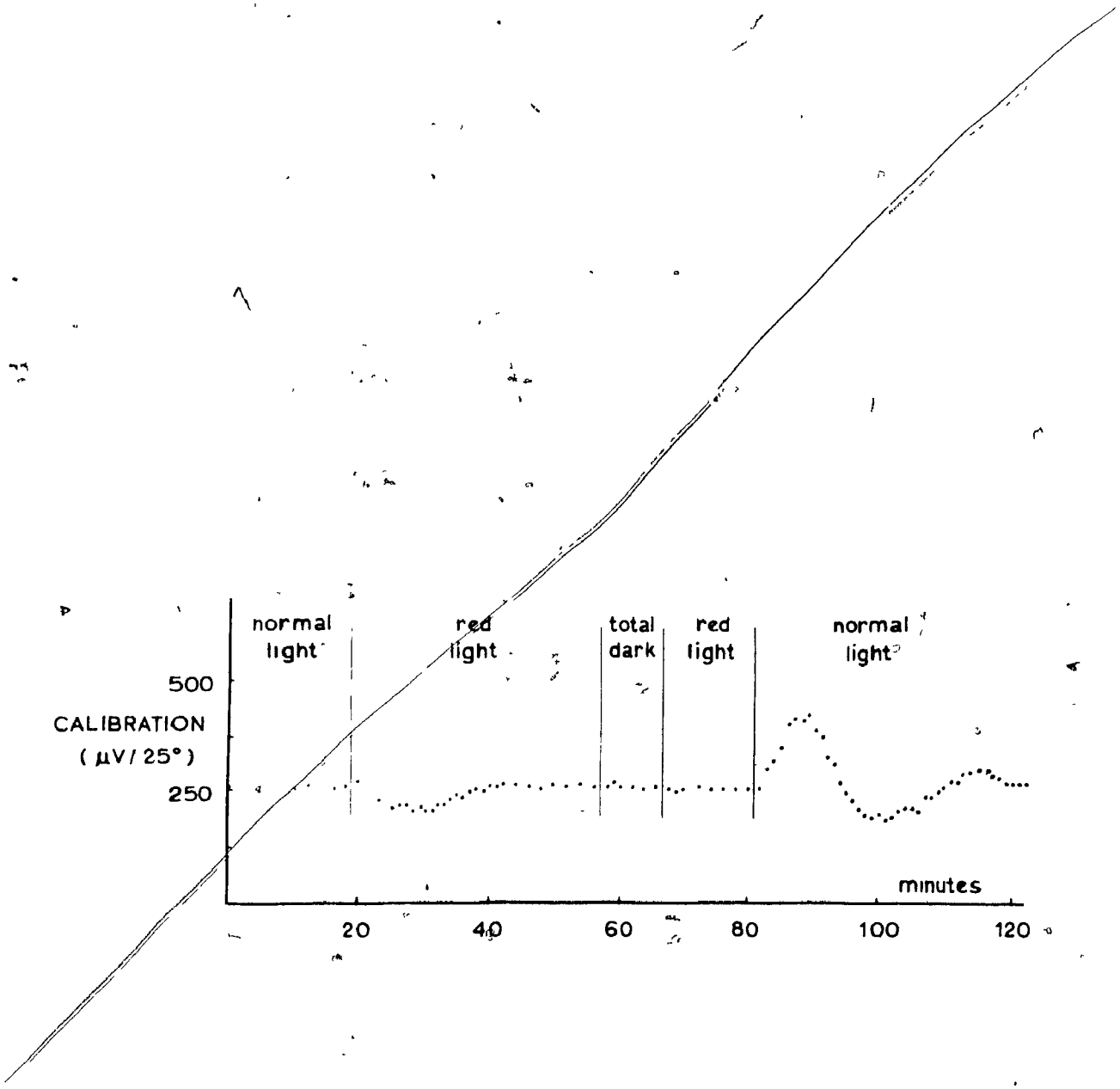
(Fig. 2 near here)

Transition from the stabilized red light condition to total darkness and back again to red light did not bring about any further change. But transition from red light to normal room light produced a striking sequence of changes. During the initial 10 minutes, there was a rapid increase in EOG response per 25° eye movement, reaching a maximum value which was about 60% higher than the steady state one. Thereafter, the response typically followed the course of a damped oscillation, so that a new steady condition was established after a total of about 40 minutes.

Table 1 gives the maximum percentage change of EOG voltage per

Fig. 2.

Collected results obtained from one subject over an entire dark-adaptation experiment. Ordinate gives calibration in $\mu V/25^{o}$ of eye movement from center and the abscissa gives time in minutes after commencement of the experiment. Each point gives the mean value obtained from one eye excursion to each side of center.


normal light
red light
total dark
red light
normal light
500
CALIBRATION
(µV / 25°)
250
minutes
20
40
60
80
100
120

25^{o} eye movement after changing lighting conditions for all subjects. The two striking results here are, first the negligible changes associated with transition from red light (R.L.) to total darkness (T.D.) and vice versa, and secondly the relatively large changes associated with transition from normal light (N.L.) to red light, and especially from red light to normal light again.

(Table 1 near here)

Although the overall pattern of response was consistent for all subjects, the time course of the above-mentioned events varied considerably. To evaluate this variation, the times required for each subject to return to within 10% of his baseline was measured. Going from normal light to red light required an average of 35 minutes with a maximum of 51 minutes and a minimum of 17 minutes. Going from red light to normal light required an average of 34 minutes with a maximum of 52 minutes and a minimum of 29 minutes to stabilize.

DISCUSSION

The example shown in Figure 2 is representative of the response from all subjects. Qualitatively it appears that the response to a transient represents a damped sinusoidal oscillation. However, it has previously been found (Homer, 1967; Homer and Kolder, 1966; Homer et al, 1967) that the response is non-linear and can be approximated by a four-component model, with nine parameters.

TABLE 1. MAXIMUM PERCENTAGE CHANGE OF EOG VOLTAGE PER 25^{o} EYE MOVEMENT AFTER CHANGING LIGHTING CONDITION

Subject	N.L.-R.L.	R.L.-T.D.	T.D.-R.L.	R.L.-N.L.
C.M.(1)	-30	0	0	+ 56
A.G.	-15	-9	+ 5	+ 43
A.F.	-21	0	-2	+ 35
B.D.	-30	+ 7	0	+ 64
C.M.(2)	-23	0	0	+ 68
F.T.	-22	0	-3	+ 62
A.C.	-33	-	0	+ 67
Mean	-24.9	-1	0	+ 56.4

N.L. = Normal Light; R.L. = Red Light; T.D. = Total Darkness

Of particular interest is the large transient apparent within the first fifteen minutes after entering or leaving normal lighting conditions. These transients can be up to 50-60% of the baseline values. Thus, errors of at least this magnitude can be expected in an experimental protocol where calibrations are done in normal room lighting, followed by a 10-minute experiment in total darkness, with recalibration in normal light. Under such conditions, one could expect calibrations which erred by a factor of two from what was happening in the dark. However, the far more common case would be calibrating eye displacement in a normal light environment, going to total darkness, and commencing the experiment after some 15 minutes. Even under these conditions, one could expect to find the calibrations to differ from the conditions during the experiment by at least 30%. Presumably, measurements of angular velocity during nystagmus will err by a similar amount.

The insidious aspect to this lies in the fact that the changes occur very smoothly, and could be wrongly interpreted as a slow change in the response to a prolonged ongoing stimulus rather than the change in illumination.

From these results, it is concluded that when using an electro-oculographic method to measure eye movement, the subject should be dark adapted for approximately 30 minutes before attempting to calibrate and measure eye position. A red light environment for these purposes has the same effect as total darkness, and may prove to be far more practical.

This chapter has been published under joint authorship with Dr. R. Malcolm. (Gonshor, A. & Malcolm, R. (1971), see Bibliography).

CHAPTER 3

HABITUATION OF THE HUMAN VESTIBULO-OCULAR REFLEX-ARC BY ROTATIONAL STIMULATION WITHIN THE RANGE OF NATURAL MOVEMENT

SUMMARY

1. Repeated rotational stimulation of the semicircular canals leads to a response decline known as "habituation".

2. This investigation concerned the study of habituation in man during rotation within the frequency (1/6 Hz) and velocity amplitude (60^{0}/sec) range of the human semicircular canals.

3. Seven subjects had the stimulus imposed for 3 consecutive days, daily exposure being ten 2-minute runs with a 3-minute rest between runs.

4. Over this time period there was no consistent change in the ratio of slow phase eye angular velocity to turntable velocity (vestibulo-ocular gain).

5. Vestibulo-ocular gain, with eyes open in the dark, was consistently less than one.

6. Natural patterns of rotational movement do not induce progressive changes of the kind to be expected from previous habituation studies.

7. The stimulus used in this experiment may be useful for studying vestibular functions without interference by habituation.

INTRODUCTION

It has frequently been shown experimentally that repeated rotational stimulation of the semicircular canals has led to decline in response to this stimulus. Early researchers such as Abels (1906), noted a decline in nystagmic response to repetitive vestibular stimulation; an observation later confirmed by numerous authors (Griffith, 1920; Dodge, 1923). Wendt (1951) negated the usefulness of many of the previous results by noting that the decline in response was probably due to "reverie states", or the loss of arousal; a parameter they did not normally control. He noted that any change in the arousal level could bring about a return of the nystagmus. This assertion was plausible in view of the then recent discovery of an arousal process centered in the brain stem (Moruzzi and Magoun, 1949). Arousal effects on several sensory systems have been noted more recently by Hernández-Peón (1955, 1959), and by Sharpless and Jasper (1956) for the auditory system.

More recent investigations have centered on the question of changes in response to rotational, as well as caloric stimulation, during tests with or without vision. It is generally accepted that vision is an important factor in the habituation of vestibular nystagmus in man (Guedry, 1965a, 1974; Collins, 1968, 1974; Dix and Hood, 1969). With repeated unidirectional rotational stimulation of rabbits, and with vision permitted, Hood and Pflatz (1954) were able to show marked declines in both duration of nystagmus and number of nystagmic beats. No such decline was found with repeated caloric stimuli of comparable

intensity. Recently Henriksson et al (1961a, b) have shown sharp declines in slow phase eye velocity during repetitive caloric stimulation of cats who where permitted vision, whilst caloric stimulation in humans (Fluur and Mendel, 1962a, b) produced marked decreases in nystagmus duration.

However, the presence of vision is apparently not a necessary condition. Thus, with arousal controlled, many investigators have shown changes in vestibular response to unidirectional stimulation in the dark. Collins (1964a), working with human subjects, observed a reduction in slow phase nystagmus response of 30% from the pre to post-test situations, after 200 unidirectional accelerations. Other authors have found substantial decrement in slow phase output to unidirectional rotation in cats (Crampton, 1962a; Collins and Updegraff, 1966) and dogs (Collins and Updegraff, 1966). Similar findings by Brown and Marshall (1967), while using D-amphetamine as an arousal method and comparing it to nembutal and a placebo, led to the statement that, "although large differences in total slow phase nystagmic output were found between groups, the habituation patterns across trials were essentially unaffected". Their conclusion was that in the dark the habituation seen is due to more than mere lack of arousal. Unilateral caloric stimulation in the dark, both in the cat (Mertens and Collins, 1967) and the monkey (Komatsuzaki, Harris, Alpert and Cohen, 1969), have produced changes very similar to those seen with the unilateral rotation stimulations, leading one to believe that the attenuation observed in the dark is not merely

an arousal phenomenon, but a decrease in response to repetitive stimulation of the semicircular canals per se.

The question arises as to whether similar changes of response will result during natural movement? Almost all the previous studies have in fact been dealing with unnatural stimuli produced by prolonged unidirectional stimulation. For this reason a controlled natural stimulus was used in this experiment. It consisted of a sinusoidal stimulus well within the frequency and velocity amplitude range of the human semicircular canals.

METHODS

One male and six females, between the ages of 20 and 26, were rotated sinusoidally in a horizontal plane at a frequency of 1/6 Hz and angular velocity amplitude of 60^{o}/sec. The head was fixed to the platform by means of a dental bite with the horizontal semicircular canals in the plane of rotation. This particular stimulus was chosen in order to provide a means of long-term bidirectional vestibular stimulation within the frequency and amplitude range of natural head movement. Thus 1/6 Hz lies within the natural velocity transducing range of the human semicircular canals (Jones and Milsum, 1965), and Hallpike and Hood (1953) have shown velocities of natural head movement in the order of 700^{o}/sec. The stimulus was imposed for three consecutive days, the daily exposure being ten 2-minute runs with a 3-minute rest

between runs (Fig. 1).

(Fig. 1 near here)

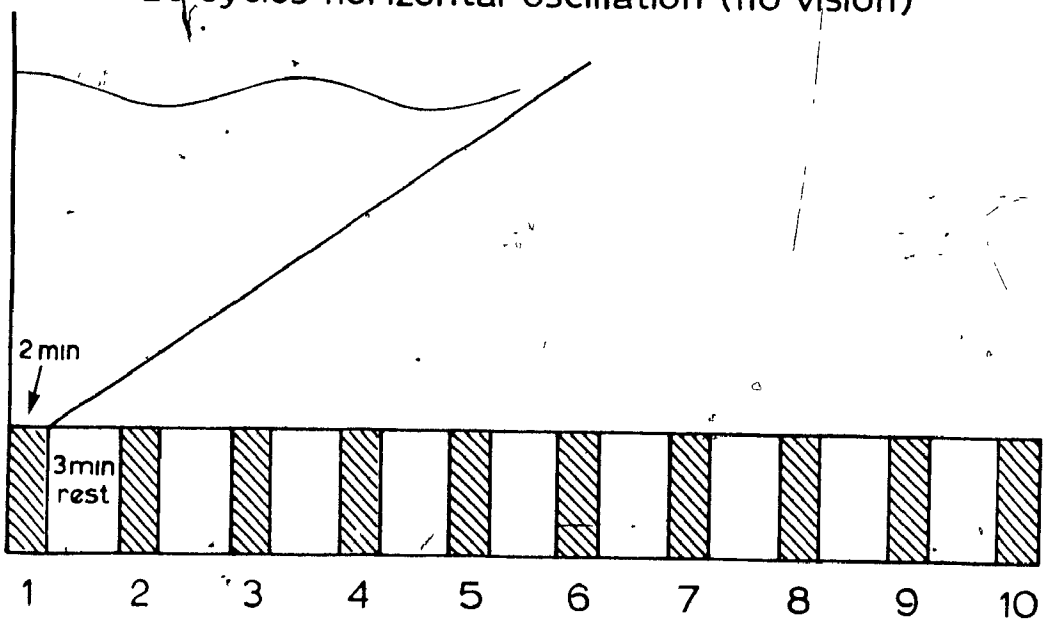
The oculomotor response to this vestibular stimulation was recorded as horizontal eye rotation using D.C. electro-oculography (EOG). Static calibrations, at 25° either side of center, were performed before and after each 2-minute run. Shackel (1960) has shown that using these methods of recording and calibration, angular eye movements relative to the skull can be measured over a range of $\pm 30^{\circ}$, to an accuracy of $\pm 1.35^{\circ}$. Linearity and reliability were periodically checked by dynamic calibrations obtained from records of eye movement induced by fixation on the outside world during the standard oscillation described above. In the present experiments, all measured eye movements extended over a much smaller range than $\pm 30^{\circ}$. Possible changes in EOG gain occurring with changes in light environment were minimized by a preliminary 50 minute period of dark adaptation, and thereafter maintaining a red light environment (Gonshor and Malcolm, 1971).

The magnitude of response relative to stimulus was determined as a ratio of eye angular velocity relative to head angular velocity (gain) from simultaneous pen records of EOG and turntable angular velocity in a manner described in Results. The need for control of arousal (Collins, Crampton and Posner, 1961; Collins, 1962) was met by having the subjects do arithmetic problems for a competitive

Fig. 1.

Block diagram of the experimental method. The stimulus was imposed for 3 consecutive days, the daily exposure being ten 2-minute test runs (no vision), interspersed with 3-minute rest periods in red light. The 2-minute run consisted of 20 cycles of sinusoidal oscillation about the vertical axis, at 1/6 Hz and 60°/sec velocity amplitude. Static calibrations were performed before and after each test run.

TEST = 20 cycles horizontal oscillation (no vision)



monetary reward. During the test runs the subjects were in total darkness with eyes open behind black-out goggles, and during the rest periods were allowed vision only under the red light conditions. External auditory cues were effectively excluded by high attenuation ear defenders.

RESULTS

Figure 2 shows one cycle of original records of eye position and turntable (head) angular velocity taken from a standard 2-minute run consisting of 20 cycles. The top trace shows the nystagmoid patterns of eye movement produced in the absence of vision as a reflex response to rotational stimulation of the semicircular canals. This trace is composed of two main components of eye movement: the smooth pursuit or slow phase compensatory motion, and the saccadic or fast phase repositioning flicks seen here between the pairs of dashed lines. The bottom traces shows the standard angular velocity stimulus. The middle trace of "cumulative eye position" (Meiry, 1965) is composed of the sequential compensatory slow phase eye movements in the cycle with the saccades omitted. This trace describes the overall change in eye position which would have occurred if the eye were capable of unrestricted rotation in the orbit. The peak-to-peak displacement so obtained was used to calculate the angular velocity amplitude of compensatory eye movement according to the relation;

$$\dot{\theta}_{e\,max} = \dot{\theta}_{e\,max} \cdot 2\pi \cdot F \quad \ldots\ldots\ldots (1)$$

where $\dot{\theta}_{e\,max}$ = maximum eye angular velocity relative to head

$\theta_{e\,max}$ = amplitude of cumulative eye displacement

F = frequency of sinusoidal motion expressed in Hz.

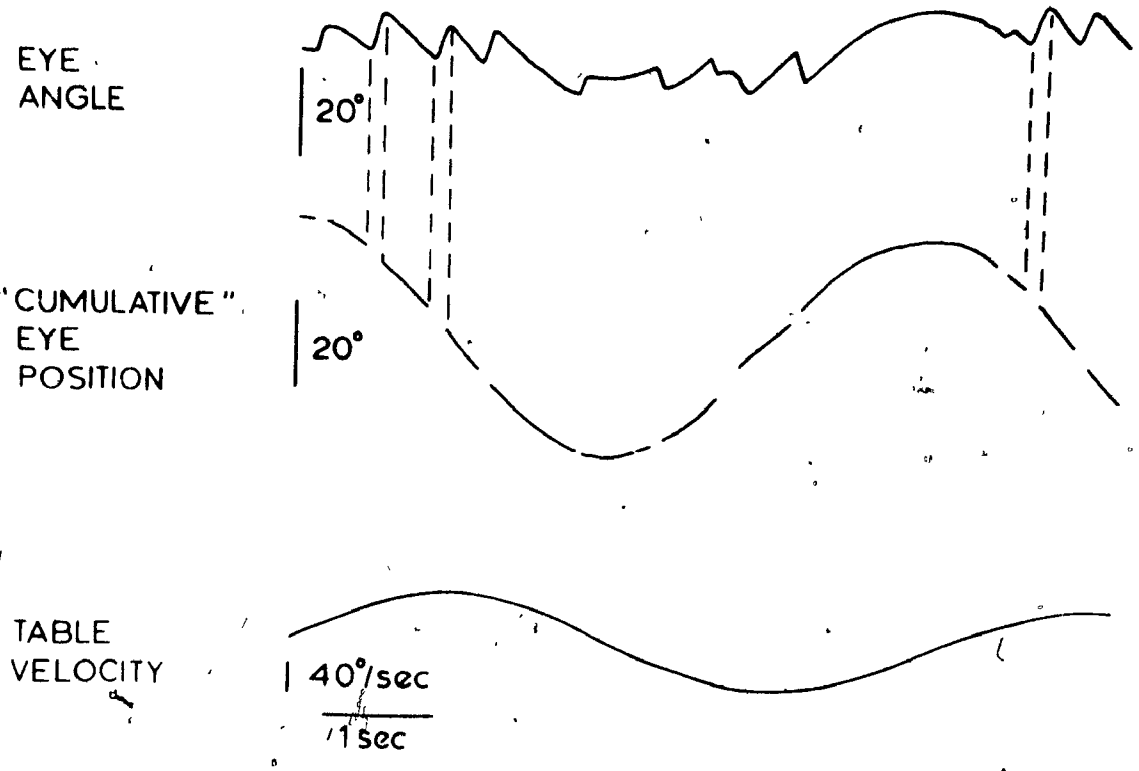
The ratio of the maximum eye angular velocity ($\dot{\theta}_{e\,max}$) to the corresponding angular velocity amplitude of the head ($\dot{\theta}_{h\,max}$) provided the measure of vestibulo-ocular gain used in this experiment. It is noteworthy that the correct compensatory eye-movement (response) is necessarily 180° out of phase with the corresponding head movement. Bearing this in mind it may be seen that in the bottom trace the peaks of turntable velocity are approximately 90° phase advanced with respect to the peaks of the response. In practice, this phase advancement was consistently 85°, and this small difference from the ideal conforms to the view that we were using a stimulus within the functionally effective range of the normal human vestibulo-ocular system.

(Fig. 2 near here)

The results were examined for changes occurring over the three time scales of a 2-minute run, the 1 hour daily test period composed of 10 runs, and the complete 3 day sequence. Figure 3 shows the collected data for all subjects in one run. The results in this figure are expressed as mean maximum eye angular velocity, in degrees/sec (left-hand ordinate) as a function of sequential cycle numbers in the run. The upper dashed line gives the maximum turntable angular velocity

Fig. 2.

Extracts from original records of eye position relative to the head (top trace) and turntable (head) angular velocity (bottom trace). The middle trace of "Cumulative eye position" (Meiry, 1965) is composed of the sequential compensatory slow phase eye movements in the cycle with saccades (between dashed lines) omitted. In all traces upward displacement = right-going movement.


EYE ANGLE
20°
"CUMULATIVE" EYE POSITION
20°
TABLE VELOCITY
40°/sec
1 sec

of 60^{0}/sec attained in each cycle of the standard sinusoidal stimulus. The right-hand ordinate shows the vestibulo-ocular gain ($\dot{^{0}}e$ max/$\dot{^{0}}h$ max).

(Fig. 3 near here)

Each point shows the mean value for one cycle of run 5 in all 3 days, and for all subjects, and therefore is a mean of 21 individual values. The calculated linear regression line through these points showed no significant slope, from which it may be concluded that there was insignificant change in gain within the 2-minute period of continuous stimulation. Of additional interest is the observation that at the frequency and amplitude of this stimulus, the mean gain obtained from the data in Figure 3 is 0.7, with a standard deviation of the mean (S.E.) of 0.23 (n = 420). This value was obtained with eyes open in the dark. However, during dynamic calibration with eyes open and fixating on the outside world, the gain always reverted to a value indistinguishable from 1, which substantiates the validity of dynamic calibration as described in Methods above.

(Fig. 4 near here)

Changes within the 1 hour daily test periods of 10 runs are shown in Figure 4, in which the ordinates are as in Figure 3. The abscissa shows the 3-day experimental sequence, divided into the separate, daily 1 hour test periods of ten runs each. Thus, each point in Figure 4 represents a mean value of data calculated from

Fig. 3.

Changes occurring over a 2-minute run. The left-hand ordinate shows the mean maximum eye angular velocity ($\dot{\theta}_{e\ max}$ in °/sec), as a function of the 20 cycles within a 2-minute run. The right-hand ordinate gives the vestibulo-ocular gain ($\dot{\theta}_{e\ max}/\dot{\theta}_{h\ max}$). Each point is the mean for 1 cycle of run 5 in all 3 days and for all 7 subjects (n = 21).

The upper dashed line gives the maximum turntable angular velocity of 60°/sec attained in each cycle of the standard sinusoidal stimulus. Note the break in both ordinates.

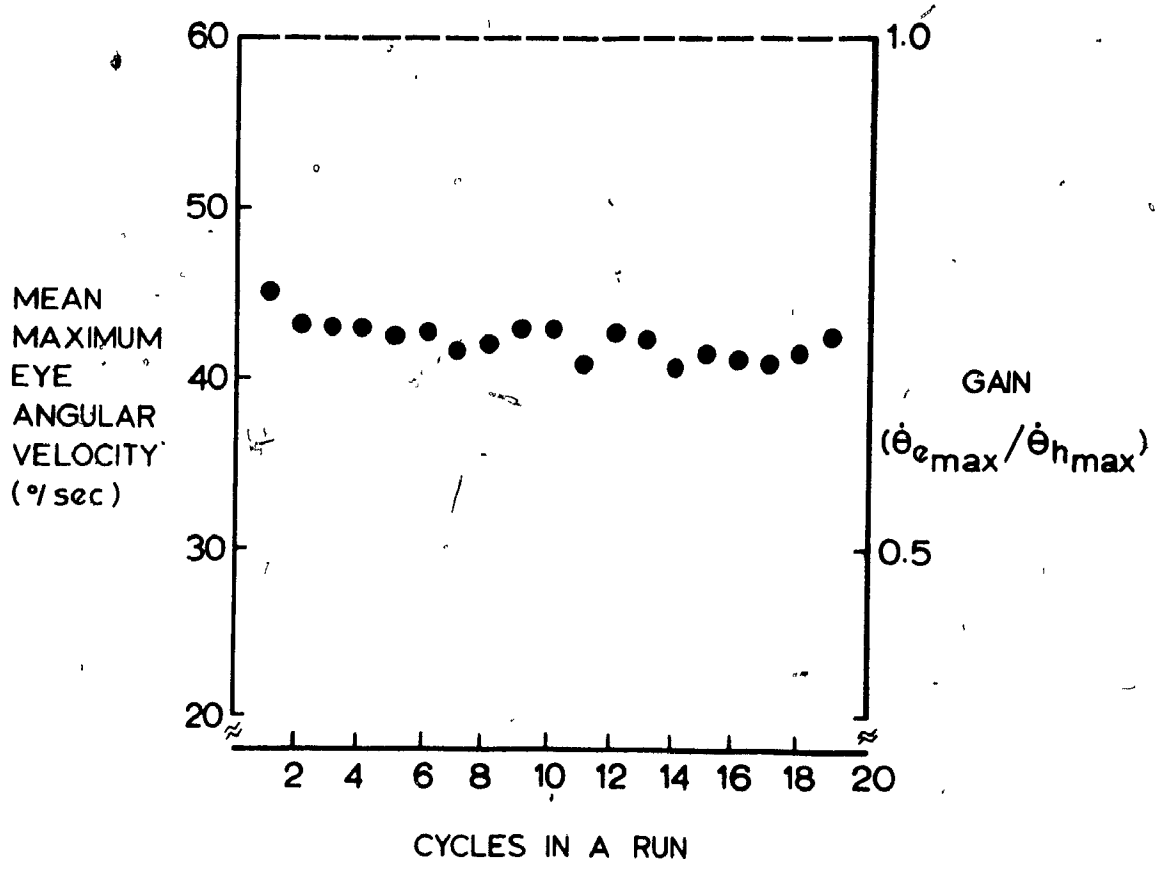
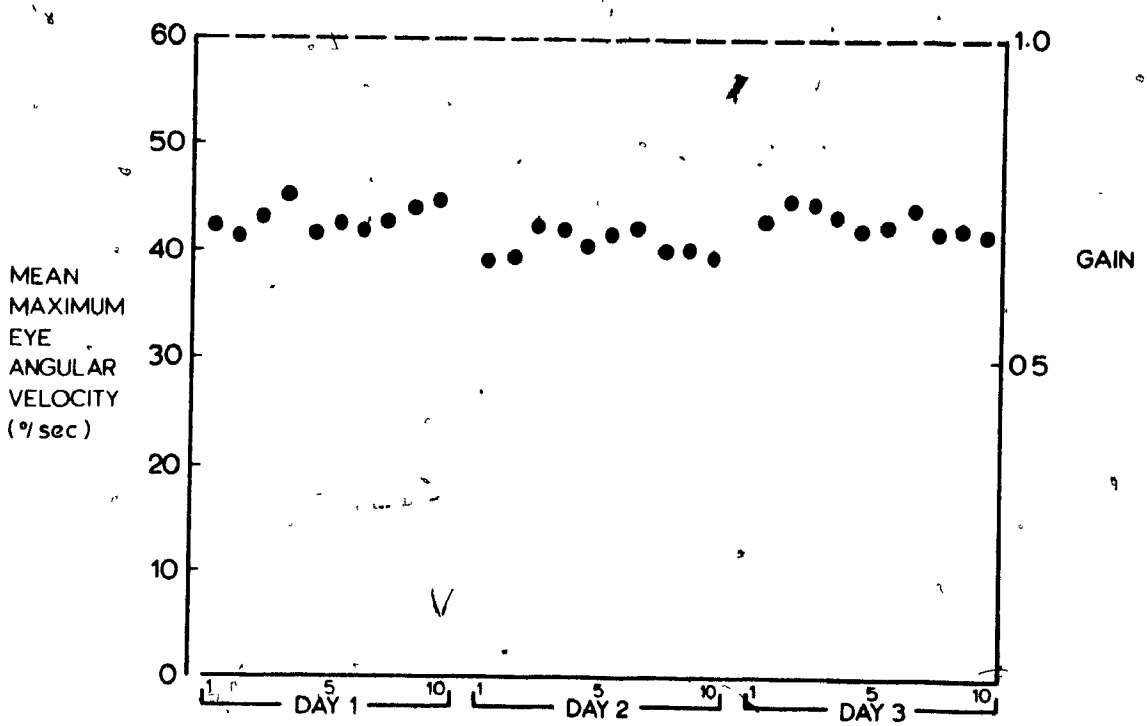

60
50
40
30
20
1.0
0.5
MEAN MAXIMUM EYE ANGULAR VELOCITY (°/sec)
GAIN
$(\dot{\theta}_{e_{max}}/\dot{\theta}_{h_{max}})$
2 4 6 8 10 12 14 16 18 20
CYCLES IN A RUN

Fig. 4.

Changes occurring over the time scales of 1 day and 3 day experiment. Ordinates and dashed line as in Figure 3. The dashed line represents the peak angular velocity of the turntable during its sinuspidal movement in one cycle. Each point is the mean value from four centrally located cycles in a 2-minute run for all 7 subjects (n = 28).


60
50
40
30
20
10
0
1.0
0.5
MEAN MAXIMUM EYE ANGULAR VELOCITY (°/sec)
GAIN
1
5
10
DAY 1
DAY 2
DAY 3

4 centrally located cycles within each 2-minute run for all subjects. Evidently, there was little or no change in vestibulo-ocular gain during any of the 1 hour test periods. This was confirmed by the fact that the slope of the calculated regression line for all the points associated with the 1 hour test period, irrespective of the day number, was statistically indistinguishable from zero ($P > 0.1$). With regard to the complete 3 day sequence, the results in Figure 4 indicate that there were minimal changes between days. Table 1 gives the mean values of $\dot{\theta}_{e\ max}$ obtained from each subject on each of the 3 days, together with the overall means and their S.E.s for each day. These data show that the difference between the mean values on the first and last day is statistically insignificant ($P < 0.2$), although it is interesting to note that the mean on day 2 was slightly, but significantly ($P < 0.01$), less than those on the first and last days.

(Table 1 near here)

Figure 5 shows the phase advancement of compensatory eye movement relative to head movement over the two time scales of the daily 1 hour test period and the 3 day experiment. There are no statistically significant changes over these two time scales, nor over the time scale of a 2-minute run. The overall mean value was $5^{o} \pm 0.6^{o}$. This value conforms closely with that to be expected from a frequency response analysis of the human vestibulo-ocular reflex system performed by Niven, Hixson and Correia (1965).

TABLE 1.

Individual and overall means of maximum eye angular velocity ($\dot{\theta}_{e\ max}$ in ^{o}/sec) for all 7 subjects and all days.

Subjects	Day 1	Day 2	Day 3
A.C.	32.7	31.2	44.2
A.F.	59.7	52.6	48.8
S.T.	44.1	37.2	40.1
J.B.	36.3	33.2	38.0
D.P.	46.3	43.4	40.7
C.M.	39.3	41.3	42.3
D.M.	45.5	43.2	46.5
OVERALL MEAN	41.8 (S.E.±0.27)	39.2 (S.E.±0.27)	41.3 (S.E.±0.18)

(Fig. 5 near here).

In view of the possible significance of changes in saccadic frequency (Collins, 1964b), it is of interest to note that visual inspection of original records during detailed analysis of gain and phase showed no obvious changes in this parameter over the three time scales.

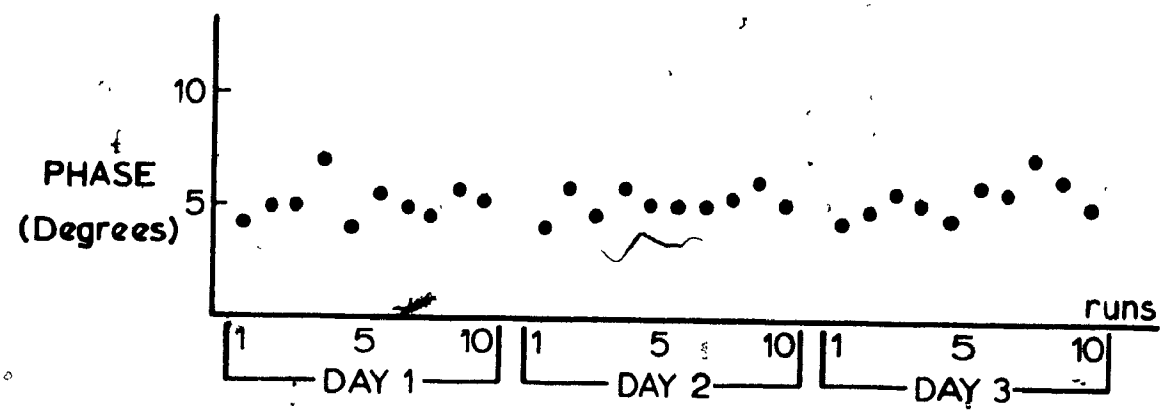
DISCUSSION

The main outcome of these experiments is that no consistent changes, which could be described as habituation, were observed over any of the three time scales of a 2-minute run, the daily 1 hour test period of 10 runs, or the 3 day experiment. Incidently, the lack of any consistent attenuation of response with time itself indicates that a consistent level of arousal was maintained by the arithmetic task imposed for this purpose. The question arises, how to reconcile the lack of habituation seen in these experiments with the many previous observations demonstrating almost invariable habituation of vestibulo-ocular response with repetitive rotational (Hallpike and Hood, 1953; Collins and Updegraff, 1966) or caloric (Fluur and Mendel, 1962 a, b; Hood and Pfaltz, 1954; Mertens and Collins, 1967) stimulation of the canals in the presence of adequate arousal?

A common feature of the latter experiments was the unidirectional nature of the imposed vestibular stimulation, which presumably placed them outside the range of natural experience. Specifically,

Fig. 5.

The Phase advancement (degrees) of compensatory eye movement relative to head movement as a function of the same time scales as in Figure 4. Each point is the mean phase from 4 cycles in a 2-minute run for all 7 subjects (n = 28).


10
5
PHASE
(Degrees)
runs
1
5
10
DAY 1
1
5
10
DAY 2
1
5
10
DAY 3

it seems fairly certain that the natural mode of semicircular canal transduction is that of angular velocity. Indeed, it has been implied on the basis of good objective evidence (Jones and Spells, 1963; Mayne, 1965; Melvill Jones, 1974) that, "there has been strong evolutionary pressure for selection of canal parameters specifically yielding an angular velocity signal over the frequency range appropriate to each species." (Melvill Jones and Milsum, 1970). It has been shown that in man good velocity transduction in the semicircular canals may be expected to extend at least over the frequency range of 0.1 to 5.0 Hz. The low frequency components of the unidirectional stimuli, referred to above, usually lie well outside this range. For example, with a step change in angular velocity there is an initial appropriate canal response that subsequently decays due to elastic restoration of the deflected cupula.

In these circumstances therefore the canal response to an unidirectional stimulus rapidly becomes at variance with the real movement, thereby becoming discrepant with other sensory inputs. On the other hand, our sinusoidal stimulus of 0.17 Hz was specifically chosen to be well within the velocity transducing range of the human canal and hence presumably such discrepancy did not arise.

The present results would thus appear to be consistent with the view that habituation may not be induced by sustained vestibular stimulation per se, but rather by a situation in which the response induced is inappropriately matched to other sensory inputs. This view is supported by the results obtained from a further series of

experiments in which a reversed visual trading task imposed during oscillatory head rotation served to render the vestibulo-ocular reflex inappropriate for visual fixation.

CHAPTER 4

HABITUATION OF THE HUMAN VESTIBULO-OCULAR REFLEX INDUCED BY REVERSAL OF THE RETINAL IMAGE DURING SINUSOIDAL ROTATION OF THE HEAD

SUMMARY

1. Previous experiments showed that repeated exposure to rotational stimulation within the range of natural experience, without the aid of vision, did not produce habituation.

2. In the present investigation the aim was to induce habituation by creating antagonism between the vestibular and optokinetic drives to the oculomotor system while using the same stimulus (frequency 1/6 Hz and velocity amplitude, 60^{o}/sec) as in a previous experiment.

3. The stimulus was imposed on seven subjects for 3 consecutive days, daily exposure being ten 2-minute runs with a 3-minute rest between runs.

4. A mirror fixed at a 45^{o} angle from the subject's frontal plane reversed the optokinetic input to the eyes. The 2-minute rotation periods in the dark at the start (V_1), middle (V_2), and end (V_3) of each day were interspersed with the mirror (habituating) trials.

5. In contrast to the previous experiment, substantial (25%) and significant ($P \ll 0.001$) vestibulo-ocular reflex decline was found at the end of each 1 hour test period, and pre-test control gain was significantly lower on day 3 than day 1 ($P < 0.001$).

6. Habituation was induced not by maintained vestibular stimulation per se, but by making that stimulation actively oppose the eye movement required for retinal image stabilization.

INTRODUCTION

In a previous article, it was determined that prolonged sinusoidal rotation of the semicircular canals within the presumed range of natural head movement, and in the absence of vision, did not lead to habituation of the vestibulo-ocular reflex (Gonshor and Melvill Jones, 1974a). However, many unhatural forms of prolonged canal stimulation, known to generate misleading sensory information, do produce such habituation (Guedry, 1965a). This raises the possibility that the habituation is not produced by prolonged vestibular stimulation per se, but rather by a situation in which the induced response is inappropriately matched to other sensory inputs.

The present experiments examine this possibility by superimposing a reversed visual tracking task on the non-habituating sinusoidal vestibular stimulation employed in the previous experiments. Specifically, the inertially driven vestibulo-ocular reflex was rendered inappropriate for visual tracking, by mirror-reversal of the direction of relative movement of the surrounding visual scene during sinusoidal rotation of the head. The results show that in this antagonistic situation, marked habituation does indeed occur in the vestibulo-ocular reflex.

METHODS

The experimental procedure was almost identical to the one used in the previous experiment (Gonshor and Melvill Jones, 1974a). Briefly, using the same seven subjects as before, each subject was

rotated sinusoidally in a horizontal plane at a frequency of 1/6 Hz and angular velocity amplitude of 60°/sec. The stimulus was imposed for three consecutive days, the daily exposure being eleven 2-minute runs with a 3-minute rest between runs. Static calibrations of electro-oculographic records of eye movement were made before and after each run. The whole experimental procedure was conducted in red light as detailed in a previous article (Gonshor and Malcolm, 1971).

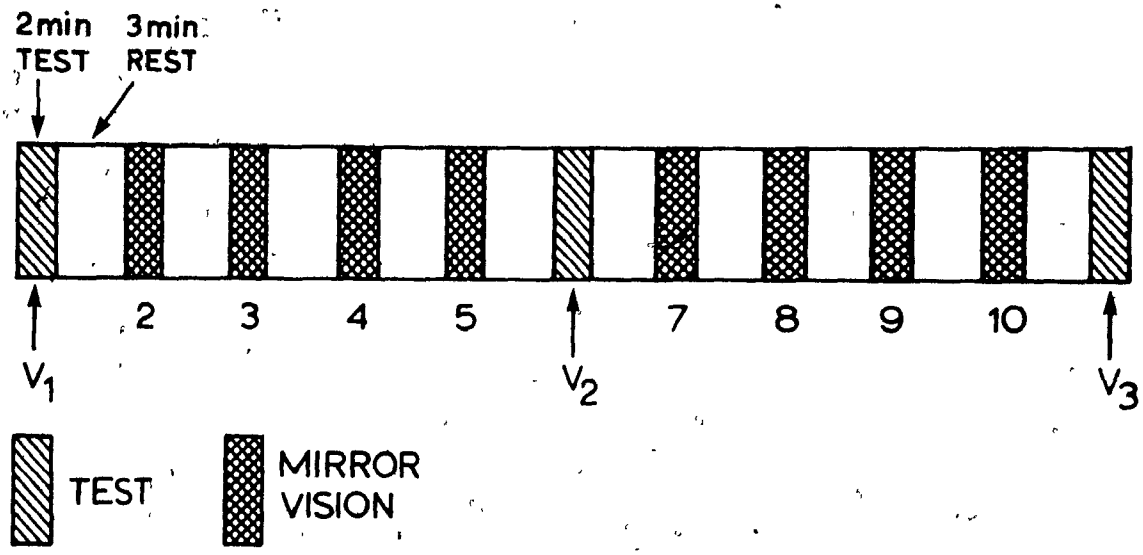
(Fig. 1 near here)

The only significant modification was that whereas in the previous experiment all runs were performed without vision, in this experiment runs 2 to 5 and 7 to 10 inclusive (habituating trials) were performed with the subject trying to fixate on a mirror-image of the visual surround. Suitable screening constrained vision solely to the mirror-reversed scene. The three runs, 1, 6 and 11 (termed respectively, V_1, V_2, V_3), were performed without vision (behind black-out goggles) to impose purely vestibular stimuli before, during, and after the habituating trials. Habituation was assessed during the test runs V_1, V_2 and V_3, as changes in vestibulo-ocular gain (eye angular velocity/head angular velocity) measured from continuous records of head and eye movement.

(Fig. 2 near here)

Fig. 1:

Block diagram of the experimental method, showing one day of the 3 day experiment. Daily exposure consists of the 3 test runs performed without vision (black-out goggles), before (V_1), during (V_2), and after (V_3) the habituating trials 2 to 5 and 7 to 10 inclusive (mirror vision). Each run consists of 2-minute sinusoidal oscillation in the horizontal plane at 1/6 Hz frequency and 60°/sec velocity amplitude, interspered with 3-minute rest periods in red light.


2min
TEST
3min
REST
2
3
4
5
7
8
9
10
V1
V2
V3
TEST
MIRROR
VISION

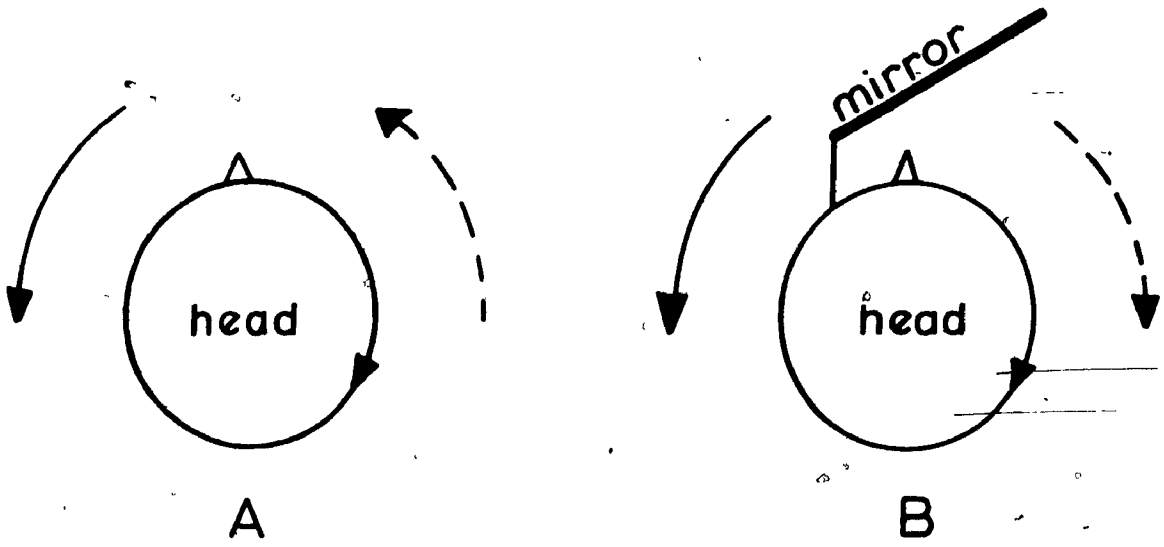
The significance of visually tracking the mirror-reversed image becomes apparent in Figure 2. In Figure 2A, where the head is shown turning to the right, both the vestibulo-ocular reflex (seen as ◄——) and the visual tracking response (seen as◄ – –) act to drive the eyes in a compensatory direction to the left, relative to the skull. Figure 2B shows the changes made in this experiment to produce the habituating stimulus. Here, the mirror is placed in front of the subject's eye at 45° to the sagittal plane of the skull, and attached to the dental bite holding the subject's head to the turntable. Whereas normally (Fig. 2A) an angular movement of the head to the right would produce a relative motion of the scene to the left, the mirror has the effect of reversing the direction of this relative movement. Now, rotation of the head to the right generates a right-moving visual surround relative to the subject, without changing the magnitude of the relative velocity. The optokinetic input, (– – ► in Fig. 2B) now provides a right-going drive to the oculomotor system during a head movement to the right, and this becomes antagonistic to the inertially driven vestibulo-ocular reflex (◄—— in Fig. 2B) which still provides a left-going drive.

During test periods subjects wore black-out goggles, and during calibrations the head was fixed to the dental bite to insure that no head movement would take place whilst normal (non-mirror) vision was permitted.

Fig. 2.

(A) Normal Situation. During head rotation to the right with eyes open, both vestibular (◄———) and visual (◄ – – —) influences act synergistically to produce compensatory eye movement to the left.

(B) Habituating Situation. Due to mirror vision the visual influence is reversed and this produces antagonism between the visual and vestibular drives to the oculomotor system.


head
A
mirror
head
B

RESULTS

(Fig. 3 near here)

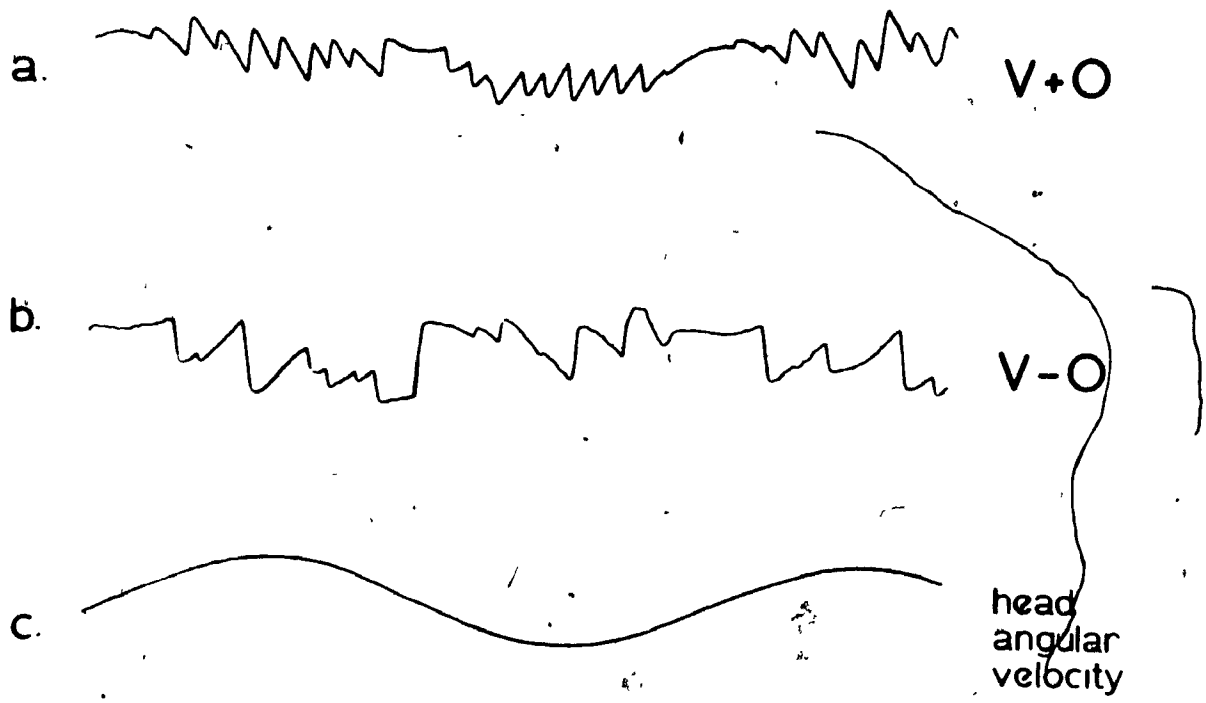
In response to sinusoidal stimulation of the semicircular canals, the oculomotor system reflexly produces a nystagmoid pattern of eye movement composed of smooth pursuit compensatory motion alternating with saccadic repositioning flicks. Normally this compensatory nystagmus is enhanced by a synergistic optokinetic drive as in Figure 2A. Figure 3A illustrates an extract from an original nystagmoid record obtained under these circumstances, when vestibular (V) and optokinetic (O) influences complement one another (V+O) to produce a compensatory response operating close to unity gain (compensatory eye angular velocity/head angular velocity). Figure 3B is a record of nystagmus produced as a result of the antagonism set up, as in Figure 2B, between vestibular and optokinetic (V-O) drives to the oculomotor system. In these particular circumstances ((V-O) in Figure 3) the nystagmus is seen to be reversed with respect to the normal pattern of compensatory response (V+O), indicating that the mirror-reversed optokinetic stimulus was overriding the vestibular one, but the resulting eye velocity was by no means sufficient for successful visual fixation. This necessarily implies a considerable rate of image slip on the retina, numerically equal to the difference between the eye and (reversed) target angular velocities. Presumably this difference

Fig. 3.

Extracts from original records of eye position relative to turntable (head) angular velocity.

a. Compensatory nystagmus resulting from complementary vestibular (V) and optokinetic (O) stimuli (V+O).

b. Nystagmus resulting from antagonistic vestibular and optokinetic stimuli (V-O). The mirror-reversed optokinetic stimulus in b. overrides the vestibular one, but not sufficiently for successful visual fixation. c. The angular velocity stimulus has a 6 sec period and 60^{o}/sec velocity amplitude (peak-to-peak 120^{o}/sec). In all traces upward movement = right.


a.
V+O
b.
V-O
c.
head
angular
velocity

constitutes the essential stimulus responsible for generating the habituation which was found to occur in these experiments.

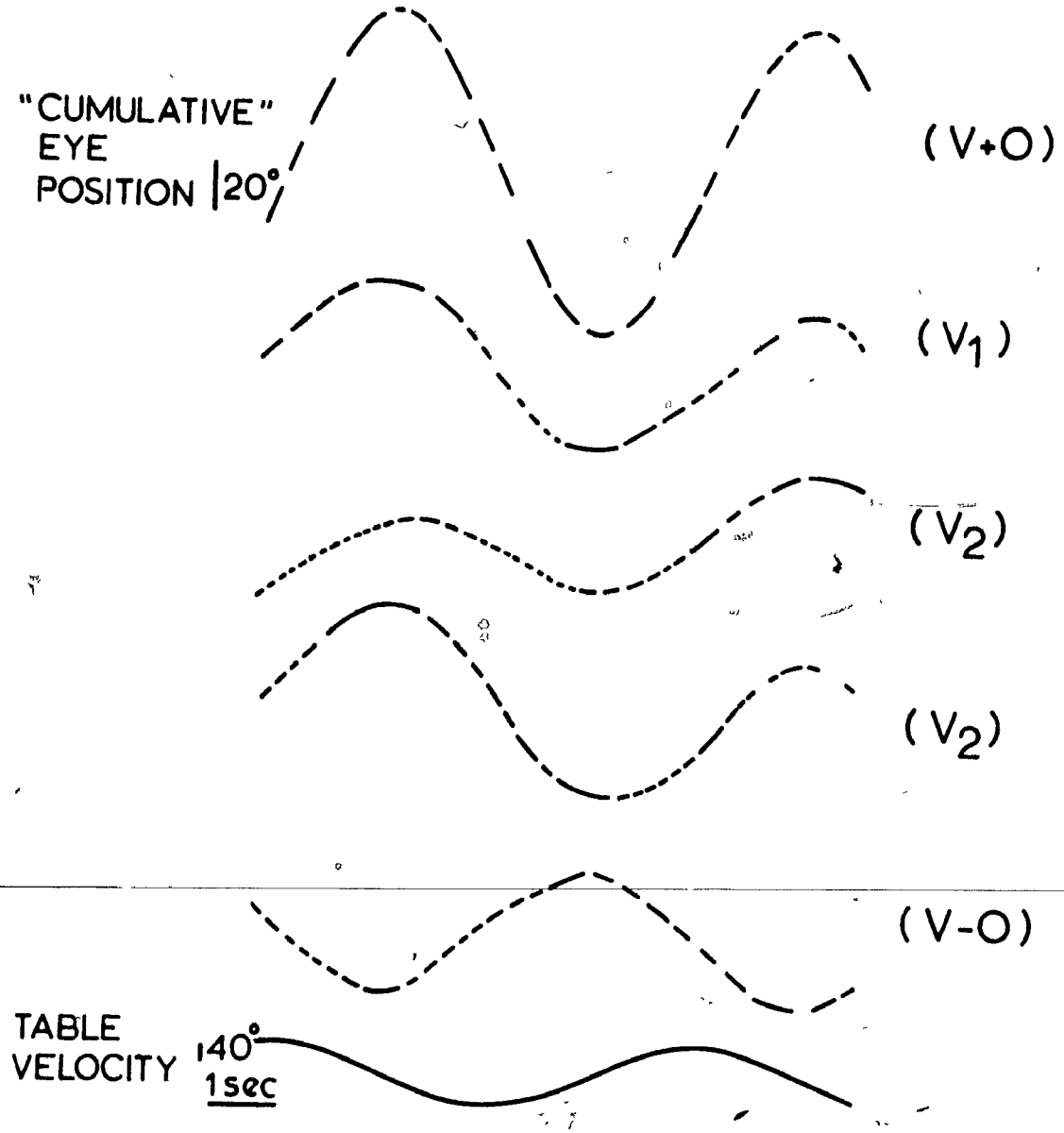
(Fig. 4 near here)

Using the method described previously, the records in Figure 3 can conveniently be turned into corresponding records of "cumulative eye position" (Meiry, 1965) similar to the first (V+0) and fifth (V-0) traces in Figure 4, by constructing continuous curves of slow phase eye movements with the saccades omitted. As in the previous article, the peak-to-peak amplitude of such curves was used to determine peak eye angular velocity, which in turn was used to determine the gain of response. In this article no further consideration is given to the records of (V-0).

The top trace (V+0) of Figure 4 shows the "cumulative eye position" through just over one cycle of a pre-habituation test run where normal visual tracking (without mirror) was permitted. It may be seen that the amplitude of this response is much larger than that of the remaining traces. The next trace (V_1) is taken from a pre-habituation run without vision. Here the substantially decreased amplitude of response is due to the absence of the complementary optokinetic stimulus. It is noteworthy that this trace is comparable in every way to those obtained from the same subject in the previous set of experiments, and therefore provides a convenient reference by which to compare the two sets of experiments.

Fig. 4.

Records of "Cumulative" Eye Position and table (head) angular velocity. (V+0) indicates the normal eye response to sinusoidal rotation with eyes open (no mirror), in which vestibular and optokinetic influences complement one another. (V_1) is derived from a pre-habituation test run in the dark where only the vestibular input is operational. Both the (V_2) traces are derived from the mid-test run after the first four habituation runs, and show both the initial decreased amplitude and eventual recovery within the 2-minute test run. (V-0) is an example of the reversed nystagmus during an habituating run in which the vestibular and optokinetic inputs act antagonistically.


"CUMULATIVE" EYE POSITION
20°
(V+O)
(V1)
(V2)
(V2)
(V-O)
TABLE VELOCITY
140°
1sec

The two traces marked V_2 are cycle 2 (upper trace), and cycle 10 of a 2-minute test run in the dark (20 cycles) following the first four habituation runs (see Fig. 1). Two important features are seen in these two traces. First, the initial V_2 trace, coming at the beginning of this test run, is of considerably lower amplitude than V_1, taken from the pre-habituation control. The change of vestibulo-ocular gain between V_1 and V_2 constitutes habituation as defined in this article. Secondly, the gain of the lower V_2 trace, located in the middle of the same 2-minute test run, shows marked recovery. Both these changes represent general trends found in the collected data.

(Fig. 5 near here)

The collected results for one subject during day 1 of the 3 day experiment are presented in Figure 5. The maximum eye angular velocity, in degrees/sec (left-hand ordinate) is expressed as a function of the sequential cycle number in runs V_1 (●), V_2 (◆), and V_3 (✕) of day 1. The upper dashed line gives the maximum head angular velocity of 60°/sec produced during each cycle of the standard sinusoidal rotation, and the right-hand ordinate describes the vestibulo-ocular gain ($\dot{\theta}_{e\ max}/\dot{\theta}_{h\ max}$). Each point represents the maximum eye angular velocity attained during one cycle. Runs V_2 and V_3, both coming after a series of habituation trials with the reversing mirror, show initial cycles with highly decreased gain of response. However, within the 2-minute (20 cycle) period of each test run the gain rose to

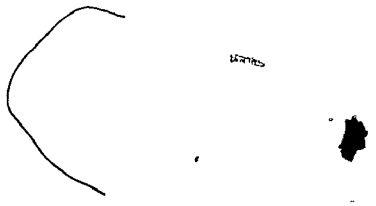
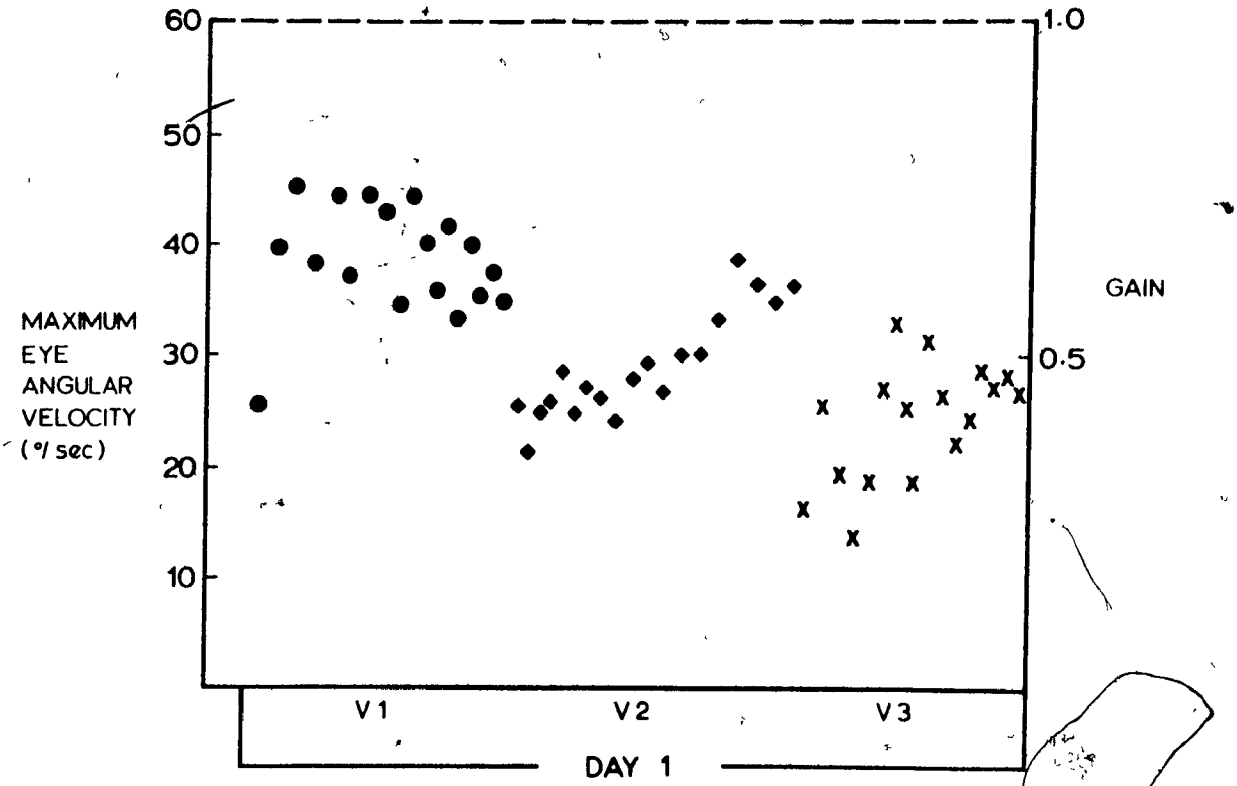


Fig. 5.

The collected results for one subject during day 1 of the 3 day experiment. The ordinate shows the maximum eye angular velocity in ^{o}/sec. The abscissa gives the three test runs V_1, V_2, and V_3 (2 minutes each) separated by the habituating runs which are not shown. Each point represents the maximum eye angular velocity attained during <u>one</u> cycle. The dashed line gives the maximum sinusoidal head angular velocity of each cycle. Gain = $\dot{\theta}_{e\ max}/\dot{\theta}_{h\ max}$ in this and all subsequent figures.


60
50
40
30
20
10
1·0
0·5
GAIN
MAXIMUM
EYE
ANGULAR
VELOCITY
(°/sec)
V1
V2
V3
DAY 1

approach the pre-habituation level (V_1). Visual inspection of the figure as a whole suggests in addition a cumulative habituation from beginning to end of the one hour experiment on day 1.

(Fig. 6 near here)

Mean changes within a run are shown in Figure 6, in which the mean maximum eye angular velocity in degrees/sec (left-hand ordinate) is expressed as a function of the 20 cycles making up a 2-minute run. Each point of V_1 (●), V_2 (◆), and V_3 (X) represents the mean maximum eye velocity attained in one cycle for all subjects and all days (n = 21). Also included for comparison (faint plotted lines) are collected data for all subjects and days from runs 5 and 10 of the previous experiment (Gonshor and Melvill Jones, 1974a). In that experiment the vestibular stimulation produced during an identical sinusoidal rotation profile did not induce habituation over similar time periods. Runs 5 and 10 were specifically chosen for this comparison since they correspond most closely to V_2 and V_3 of the present experiment, although all runs in the previous experiment gave the same result.

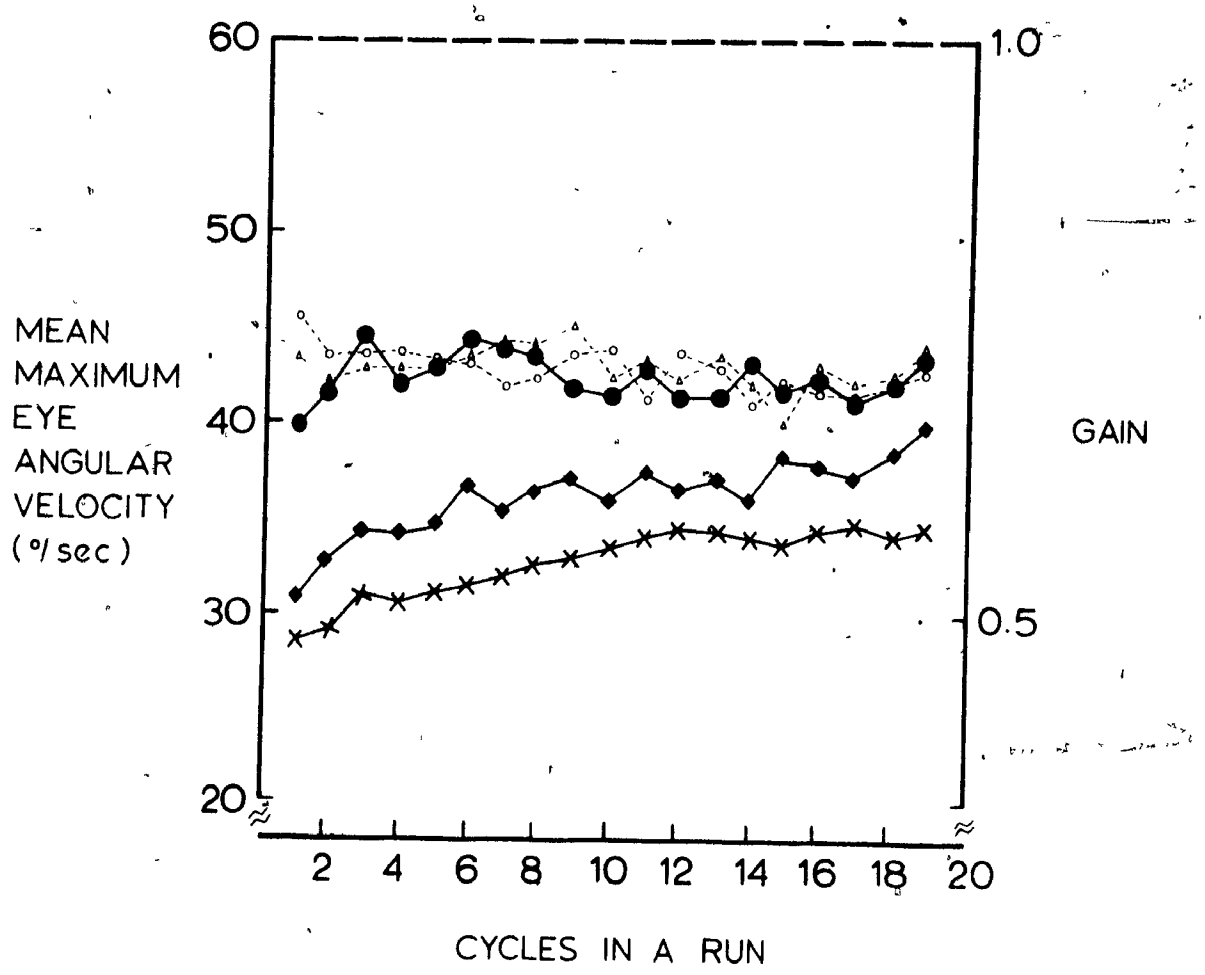
The calculated regression line through the V_1 results in Figure 6 is statistically indistinguishable from those through each of the data sets of runs 5 and 10 of the previous experiment (faint lines). This provides good assurance that there has been no change in the response characteristics of the subjects between the previous

Fig. 6.

Changes within test runs V_1, V_2, and V_3, for all subjects and all days. Each point of V_1 (●), V_2 (◆), and V_3 (X) represent 21 individual cycles.

Stage 1: Each point of run 5 (O) and run 10 (Δ) represents 210 individual cycles. These points are included to show the indistinguishability of V_1 - Stage 2 and any of the Stage 1 runs.

Please note the breaks in both ordinates.


60
50
40
30
20
1.0
0.5
GAIN
MEAN
MAXIMUM
EYE
ANGULAR
VELOCITY
(°/sec)
2
4
6
8
10
12
14
16
18
20
CYCLES IN A RUN

and present experiments (6 months). Furthermore, this consistency establishes the V_1 results of the present experiment as reliable control data.

The V_2 and V_3 test runs shown in Figure 6 were performed respectively after 8 minutes and a further 8 minutes of the habituating stimulus (Fig. 2B). These collected data confirm the main features seen in the previous figure. First, the initial V_2 cycle shows approximately 30% decrease in vestibulo-ocular gain relative to the mean V_1 control level. Secondly, however, this decrease progressively diminishes during the 20 cycles of this 2-minute test run in the dark, reaching a final gain in the 20th cycle just below the control level. Thirdly, the V_3 test run results show the same features as those of V_2 except that the whole curve is consistently a further 7% depressed with respect to the V_1 control level. The mean values

(Table 1 near here)

of the V_1, V_2, and V_3 results for each day, and for the overall 3 day experiment are shown in Table 1. It is noteworthy that these means underestimate the initial suppressions of gain in both the V_2 and V_3 test runs.

(Fig. 7 near here)

Figure 7 separates these mean values into those obtained from

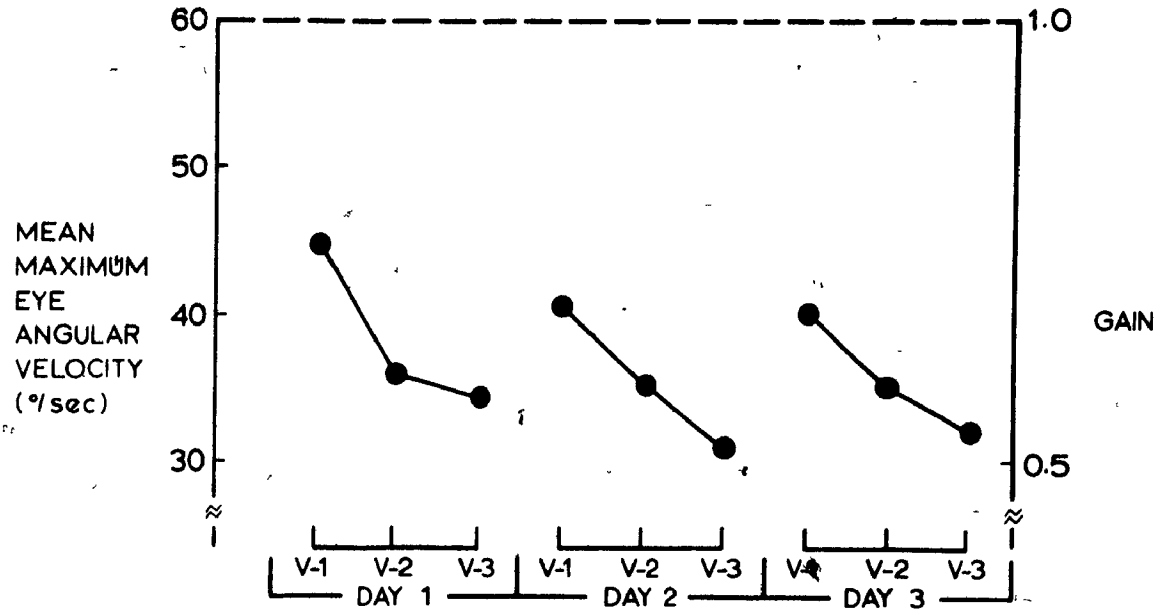
TABLE 1.

Mean values of maximum eye angular velocity (^{o}/sec) for runs V_1, V_2 and V_3 in each day of the 3 day experiment, with overall means for V_1, V_2, and V_3 in the right-hand column.

Test Runs	Day 1 Mean S.E.	Day 2 Mean S.E.	Day 3 Mean S.E.	Overall Mean S.E.
V_1	44.57±0.64	40.48±0.78	40.20±0.72	41.75±0.72
V_2	35.78±0.84	35.02±0.65	35.09±0.66	35.30±0.75
V_3	34.30±0.93	30.86±0.65	32.07±0.62	32.41±0.78

Fig. 7.

Combined results for all subjects and all experiments over the 3 day experimental period. The ordinate gives the mean maximum eye angular velocity in °/sec. The abscissa gives the 3 day experiment with the three test runs in the dark each day. Each point on this expanded scale represents the mean maximum eye angular velocity for seven subjects.


60
50
40
30
1.0
0.5
GAIN
MEAN MAXIMUM EYE ANGULAR VELOCITY (°/sec)
V-1
V-2
V-3
V-1
V-2
V-3
V-1
V-2
V-3
DAY 1
DAY 2
DAY 3

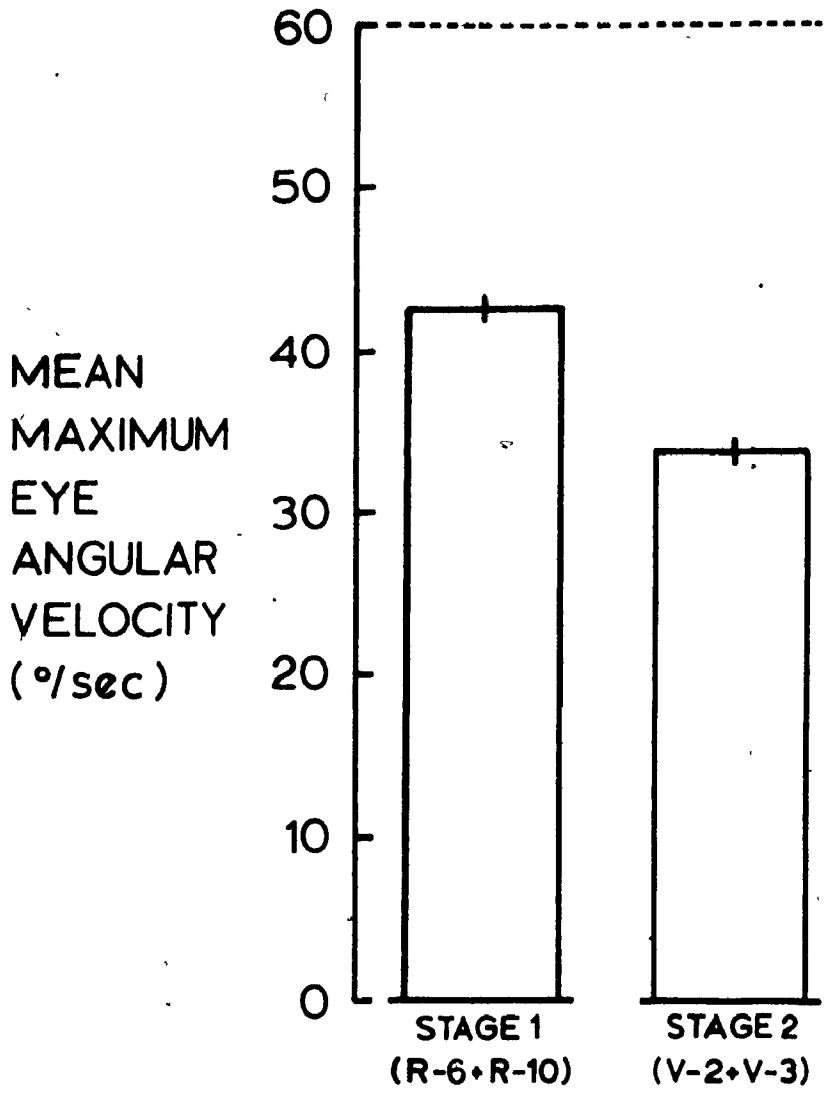
days 1, 2 and 3 of the 3 day experiment. With exception of the V_2-V_3 comparison in day 1 ($P > 0.1$) all the decreases within a day are highly significant ($P \ll 0.001$). Secondly, between days there was almost full recovery of gain, although V_1 on both days 2 and 3 was still very significantly lower than the day 1 pre-habituation V_1 control ($P < 0.01$ and 0.001 respectively).

(Fig. 8 near here)

Figure 8 shows a comparison of test runs after periods of habituation in this experiment with corresponding non-habituating runs on the same subjects in the previous experiment. (Gonshor and Melvill Jones, 1974a). In detail we see a comparison of the lumped means of runs 5 and 10 of the previous experiment (faint lines in Figure 6) with those of V_2 (run 6) and V_3 (run 11) in the present experiment. The actual means are 42.6^{o}/sec (S.E.±0.26) and 33.8^{o}/sec (S.E.± 0.30) respectively, the vertical bars in the figure representing two standard errors either side of the mean. Because the protocols in the previous and present experiments were virtually identical, this comparison affords a ready means of isolating those changes due purely to the habituating influence of mirror-reversal of the visual scene.

Fig. 8.

A comparison of the lumped means of runs 5 and 10 in Stage 1 and runs V_2 (run 6) and V_3 (run 11) in Stage 2. The ordinate is mean maximum eye angular velocity in ^{o}/sec. Without inclusion of V_1 - Stage 2 in the lumped mean, the result shows the effect of the habituating stimulus in Stage 2 on V_2 and V_3. Bars represent two S.E.s.


MEAN
MAXIMUM
EYE
ANGULAR
VELOCITY
(°/sec)
60
50
40
30
20
10
0
STAGE 1
(R-6+R-10)
STAGE 2
(V-2+V-3)

DISCUSSION

Results from the previous experiment showed that no consistent changes in vestibulo-ocular gain occurred during a sequence of repeated sinusoidal vestibular stimulation. For reasons adduced in the previous article (Gonshor and Melvill Jones, 1974a) it was inferred that the commonly reported habituation due to repetitive vestibular stimulation may not be induced by sustained vestibular stimulation per se, but rather by a situation in which the response is inappropriately matched to other sensory inputs. The main objective of the present experiment was to examine this possibility by making the vestibulo-ocular reflex directly opposed to a reversed optokinetic stimulus, whilst retaining the original protocol of vestibular stimulation. The fact that substantial and systematic decrease of vestibulo-ocular gain resulted from the procedure is consistent with the above inference, and strongly implicates the reversed optokinetic stimulus as the cause of the observed habituation.

Other authors have shown the effects of vestibular-visual interaction in humans. Guedry (1965a) exposed human subjects to long durations of continued unidirectional rotation followed by sudden cessation of rotation. In these circumstances normal subjects experience a violent reversed canal stimulus often referred to as post-rotational stimulation, whilst they themselves are stationary. The resulting vestibulo-ocular reflex generates involuntary nystagmus, so that any attempted visual fixation would lead to antagonism between optokinetic and vestibular

stimuli, usually producing retinal image slip. Without vision the repeated post-rotational stimulation led to sizeable habituation of the vestibulo-ocular response. However, over and above this, when subjects attempted visual fixation on the stationary surround during the post-rotational stimulus, a roughly twofold increase of habituation was observed.

Collins (1966, 1968) has done a series of studies on professional skaters in which he showed that during the violent post-rotational vestibular stimulation associated with cessation of a spin in a practiced direction, subjects will suppress the vestibulo-ocular reflex almost completely following visual fixation. Collins' experiments, as well as previous work on skaters by McCabe (1960), serve to show the importance of <u>voluntary</u> visual action in opposing vestibularly-induced nystagmus. This is probably quite a different interaction from that produced when vision is introduced to either humans or animals during passive rotation. This is especially true in animals where inconsistent findings may be due to the reaction to restraint (Guedry, 1965 a).

Two alternative interpretations of these results would seem to be reasonable. On the one hand superposition of an optokinetic stimulus upon a vestibular one could merely enhance an on-going habituation in the vestibulo-ocular reflex arc which is inherently caused by the repeated vestibular afferent input itself. On the other hand the added habituation introduced by the optokinetic stimulation could be due to a quite independent ability of retinal

afferent signals generated by the resulting image slip to modify the characteristics of response in the vestibulo-ocular system. Whereas in all the above quoted experiments the vestibular stimulus employed was of a nature known to produce habituation on its own, a particular feature of the vestibular stimulus employed in the present experiments was that it did not of itself produce habituation of the vestibulo-ocular reflex. Hence such changes as were incurred in our experiments must presumably have been introduced solely by the independent action of retinal afferent signals originating from image slip during attempted visual fixation.

A common feature of all experimental results has been attenuation of the vestibulo-ocular response. In those experiments involving visual fixation on a stationary world during a post-rotational vestibular stimulus, the most functionally appropriate end-point of habituation would be attenuation of the vestibulo-ocular response to zero. In our experiments the ultimate goal would be not merely attenuation to zero but complete reversal of the vestibulo-ocular reflex response. This raises a fundamental question of whether habituation merely serves to attenuate the response to a repetitive stimulus, or to systematically remodel the relevant neurological elements in an attempt to meet new optimization criteria no matter how radical the change. The results of a further series of experiments designed to examine this question strongly favour the latter possibility (Gonshor and Melvill Jones, 1974c).

It is of additional interest to note that the form of habituation

demonstrated in these experiments is not common to all species. Thus when Sperry (1950) surgically rotated the eyes of fish, the reversed optokinetic stimulus produced by the animal's own movement generated a perpetual circling with no sign of habituation. In similar experiments, where von Holst and Mittelstaedt (1950) rotated the head of the insect Eristalis 180° so that the two eyes were reversed, any self-induced motion resulted in rapid whirling in the direction of initial movement to the point of exhaustion. Apparently gross habituation of the kind seen in the mammalian experiments described above do not occur throughout the phylogenetic scale.

CHAPTER 5

PLASTICITY IN THE VESTIBULO-OCULAR REFLEX ARC REVEALED BY LONG-TERM PRISM-REVERSAL OF VISION DURING NATURAL HEAD MOVEMENT

SUMMARY

1. The present experiments were designed to examine habituation or change in the vestibulo-ocular reflex (VOR) consequent to long-term prism-reversal of vision.

2. Four normal adults (aged 20 to 50 years) were subjected to experiments conducted over periods of 4,17,25, and 49 days, with vision reversal during all the waking hours of 2,6,7, and 27 days. A reversal of the horizontal plane was obtained with the use of "dove prisms". Daily tests in the dark, and in both the horizontal and sagittal planes, consisted of sinusoidal oscillation through 20 cycles at a 1/6 Hz frequency and 60°/sec velocity amplitude.

3. Results from horizontal plane oscillation showed complex changes in gain and phase, falling into 5 recognizable stages. First, a rapid and significant decrease of VOR gain to 30 or 40% pre-vision reversal levels, with no marked phase change. In the second stage (days 3 to 14), almost exclusively large and continuously varying phase. In the third stage (days 14 to 28), a plateau of gain and phase to 40% pre-stimulus gain and 125° phase lag. The fourth stage, occurring immediately after prism removal, was a rapid return of phase to normal, with a slight drop in gain. The fifth and final stage was a slow return, over 3 to 4 weeks, to normal gain.

4. High geometric specificity occurs, since response change was confined strictly to the plane of vision reversal.

5. It is proposed that habituation may represent an attempt by the

organism to restructure its neurological characteristics so as to optimize for a clearly defined physiological goal, here being minimization of retinal image slip. The cerebellum is put forward as a prime candidate responsible for this capability.

INTRODUCTION

In a previous study it was found that prolonged sinusoidal rotational stimulation of the human semicircular canals, performed in the absence of vision and in the range of natural head movement, did not cause any change in the associated vestibulo-ocular reflex response (VOR), measured as the ratio of compensatory eye angular velocity to head angular velocity ($\dot{\Theta}e/\dot{\Theta}h$) (Gonshor and Melvill Jones, 1974a). However, when an antagonistic visual (optokinetic) tracking task was superimposed on this non-habituating vestibular stimulus by means of mirror-reversal of the visual image, marked and sustained attenuation of the VOR, measured in the absence of vision, systematically occurred in all subjects (Gonshor and Melvill Jones, 1974b). VOR attenuation has been observed by others (Brown and Guedry, 1951; Collins, 1968; Mertens and Collins, 1967) in situation calling for an ultimate suppression of the vestibulo-ocular response to zero: for example, attempted visual fixation on a stationary surround during post-rotational vestibular stimulation. However reversal of optokinetic stimulation during head rotation ultimately calls for reversal of the VOR, rather than mere attenuation to zero.

This raises the question which led to the present study; namely, would prolonged continuation of vision-reversal during rotational head movement lead merely to suppression of the VOR towards zero, or to overt reversal of that response?

The previous method of stimulation, where subjects were seated

on an oscillating turntable whilst looking at a mirror-reversed surround, was obviously not amenable to continuous stimulation lasting many days or weeks. It was therefore decided to replace the mirror of the previous experiment with "dove" prism goggles mounted on the head, which established not only the required visual-reversal, but also allowed continued free body and head movement. The turntable was used as before to test intermittently the vestibulo-ocular response in the absence of vision.

A preliminary account of this work has been reported briefly (Gonshor and Melvill Jones, 1973).

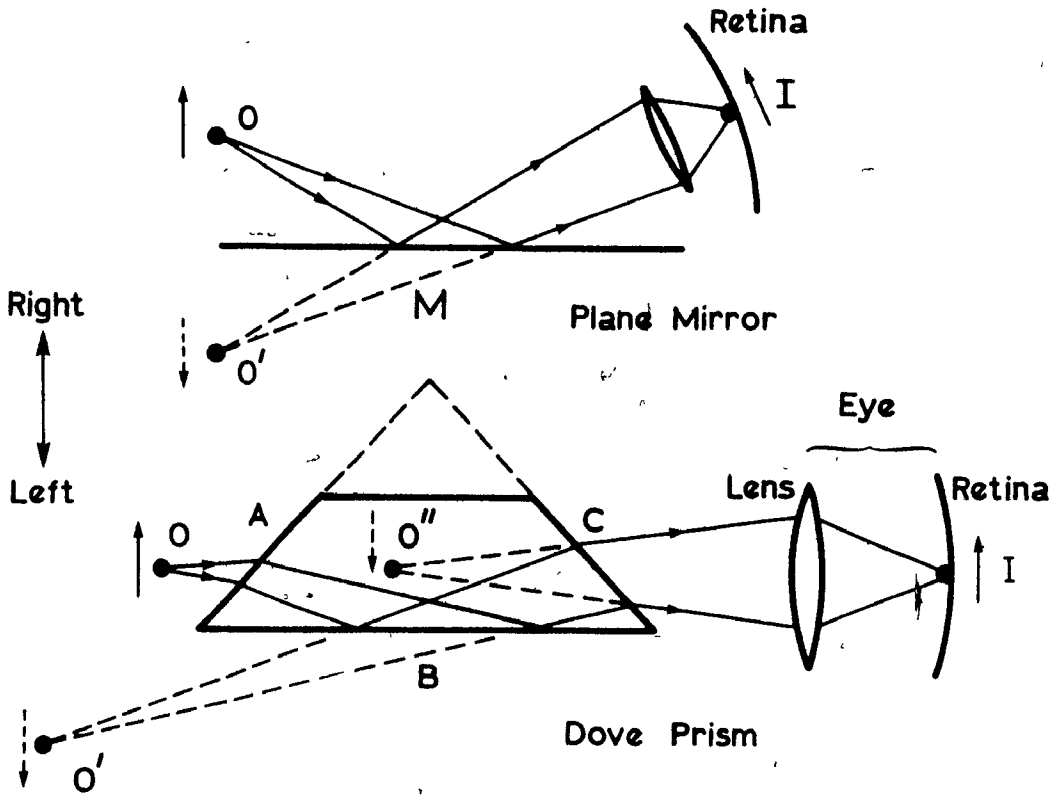
METHODS

Prism Reversal of Vision. The method of image reversal by means of the "dove" prism is outlined in Figure 1. The upper section of this figure illustrates how a plane mirror causes reversal of image movement seen by the eye. The real object, O, generates a real image, I, on the retina after reflection at the mirror surface, M. Then movement of the object, O, say from left to right (solid arrow), is associated with movement of a virtual object, O', in the reversed direction, namely from right to left (broken arrow). Consequently the resulting movement of the real image, I, across the retina is perceived as a reversed movement of the object; i.e. as though from right to left.

(Fig. 1 near here)

Fig. 1.

Image reversal on the retina by means of a plane mirror and a "dove" prism. In the upper diagram the real object (O) generates a real image (I) on the retina after reflection at the mirror surface (M). Movement (↑) of the real object (O) is associated with movement of a virtual object (O') in the reversed direction (↓), and a resultant movement of the real image (I) across the retina (↑), perceived as reversed movement of the object. The lower diagram depicts a similar situation obtained with a "dove" prism, when the eye and prism are stationary relative to one another. Rays from the real object (O) are refracted at the prism surfaces A and C and totally internally reflected at surface B. Therefore a movement of the real object (O) to the right causes a reversed movement to the left of the virtual object (O'), and perception of reversed movement of the image (I) on the retina. (O") represents the seen virtual object which, due to the prism, is in direct line of vision.


Retina
I
O
M
Plane Mirror
O′
Right
Left
Eye
Lens
Retina
A
O″
C
O
I
B
Dove Prism
O′

A similar situation obtains with the "dove" prism illustrated in the lower section of Figure 1. With eye and prism stationary relative to one another, movement of O from left to right leads to reversed movement of the virtual object, O', due to total internal reflection at surface B. As before, the resulting movement of the retinal image, I, leads to perception of a reversed movement of the object from right to left. The main advantage of the prism mode of image reversal is that refraction at surfaces A and C brings the seen virtual object, O", into the direct line of vision. A pair of such prisms can thus readily be mounted in goggles which permit forward vision of a mirror-reversed external world (Kohler, 1962), although with somewhat restricted visual field of approximately 60^{o} solid angle. Since prism and skull then remain stationary with respect to one another, any head rotation in a horizontal plane, say to the left, will be associated with apparent relative movement of the outside world to the left, rather than to the right as would normally be the case. In addition, the goggle-mounted prisms can be tolerated for prolonged periods of "normal" activity.

It is important to note that "dove" prism reversal takes place in one plane only, which in these experiments was arranged to be horizontal with head erect. Consequently there was no reversal in the sagittal plane, which conveniently allowed movement in this (i.e. sagittal) plane to be employed for control purposes.

Experimental Procedures. The main objective of these experiments

was to expose human subjects to long periods of natural head movement with horizontal prism-reversal of vision and periodically examine the effect of this experience upon the corresponding compensatory VOR to horizontal rotational stimulation, measured in the dark. As will be described in detail below, such effect was measured in terms of gain and, in the longest experiment described below, phase of ocular response relative to head rotation. Any consistently retained change in either of these parameters from their control values will hereafter be referred to as Habituation.

Four adult subjects (three male and one female), ranging in age from 20 to 50 years, and free from vestibular and oculomotor disorders, were employed. The experiments were performed with the full understanding and consent of each subject. Initial trials lasting up to 4 hours established acceptable conditions for the much more prolonged main experiments. Four main experiments were then conducted over periods of 4, 17, 25 and 49 days, with the durations of prism-reversal of vision extending over the waking hours of 2, 6, 7 and 27 days respectively.

Each subject was first matched with a second individual whose duty was to monitor the subject's moment-to-moment activity from beginning to end of the whole experiment, in order to serve the interests of personal safety. On day 1 (D_1) both individuals were introduced to the experimental program and the subject fitted with the prism-goggles to test their comfort, exclusion of non-reversed vision, and acceptable binocular fusion. To avoid unintended habituation, the

subject's head was at this stage held still during fitting. Heavy stress was laid on the importance of rigorous continuity in wearing the goggles throughout the subject's waking hours until their planned removal. Two standard test sequences detailed below were run to obtain morning and afternoon control data. The prisms were not worn during head movement on D_1.

On D_2 a third standard control test sequence was run in the morning. The subject then donned the prism-goggles and immediately engaged in locomotor exercises consisting of simple, aided, walking in and out of laboratory rooms and corridors. The preliminary trials mentioned above showed that rapid and severe nausea and/or vomiting may occur under these conditions. Consequently, to avoid unacceptable discomfort, 15 minute periods of such activity were alternated with 30 minute periods of complete rest (supine, with head still) during the first 3-4 hours of the first day. On D_2, standard test sequences were performed 1, 3 and 6 hours after the prisms had been donned.

From D_3 on subjects underwent the full test sequence at least once daily, except on occasions during the longest experiment when the subject was sometimes allowed home for a week-end, after careful briefing of his wife and family to ensure continuity of prism-reversal of vision. On several days selected components of the test sequence were repeated several hours after the first test series for reasons such as the detection of response inconsistencies, laboratory equipment failure, or the presence of particularly rapid rates of change in response characteristics.

Between laboratory test sequences subjects were allowed complete freedom of movement within the scope of their capability, but always with the second individual in close attendance. It cannot be too strongly emphasised that without consciencious, moment-to-moment, personal attendance, the risk of serious personal injury to a subject wearing the prisms is high; particularly, for example, when negotiating stairways and when more freedom becomes possible - road traffic. Initially, movement was limited to the laboratory environment. Later, the subject would be encouraged to range progressively more freely until by D_{4-6} he would venture outdoors for extended periods. During these periods he would take walks in both country and city environments. Indeed, active participation in normal city life was further encouraged by providing funds for purchase of theatre tickets, quality restaurant meals, and petty cash for limited shopping in down-town stores. Thus, although between test sequences there were few formal exercises, the subjects did engage in a wide range of ordinary motor activity whilst wearing the reversing prisms.

On the final day of prism-reversed vision the subject wore his goggles until after the standard morning test sequence. The prisms were then removed and the subject required to engage in normal locomotor activity again. Test sequences were performed for about the same number of days as the prisms were worn, the actual period of testing depending upon each subject's time course of return towards his control response conditions.

The Standard Test Sequence. Three main series of experimental tests were performed during each formal test sequence. These were designed to examine (1) the dynamic characteristics of the VOR in the absence of vision; (2) functional impairment of visual fixation due to habituation of the VOR, measured during head rotation without vision reversal (Gonshor, 1974a); (3) functional impairment of postural control (Gonshor, 1974b). Additional observations were made on optokinetic tracking ability with head still, and the characteristics of saccadic eye movements. The present account is confined to the outcome of the first of these test procedures which primarily comprised measurement of the gain of VOR in the absence of vision. In the longest experiment measurements of phase as well as gain were made.

The rotational test stimulus, and the equipment employed have been fully described elsewhere (Gonshor and Melvill Jones, 1974a, b). Briefly, subjects were rotationally oscillated through 20 cycles of sinusoidal movement at a frequency of 1/6 Hz and an angular velocity amplitude of 60^{o}/sec. During rotational stimulation the subject's head was fixed to the turntable by means of a dental bite board so arranged as to bring the horizontal canals into an earth horizontal plane, thus ensuring that only one pair of canals would be stimulated by the imposed rotation. The resulting eye movements were recorded by DC electro-oculography (EOG). All such recordings were made in the absence of vision; in practice with eyes open behind blackout goggles. Arousal was maintained by mental arithmetic (Collins, Crampton and Posner, 1961) and particular care was taken to avoid

significant changes of EOG gain due to transient changes in levels of retinal illumination (Kris, 1958; Gonshor and Malcolm, 1971). In the present experiments this was ensured by restricting recording in the dark to less than 3 minutes, which was shown by supplementary quantitative experiments to be too short to interfere with reliable recordings of VOR gain. As an added precaution EOG calibration was always conducted immediately before and after each period of 20 cycles rotational oscillation. Simultaneous records of table and eye movement were made as shown in subsequent figures. The above oscillatory rotational stimulus was chosen because earlier experiments had shown that this pattern of vestibular stimulation did not of itself lead to habituation in the VOR (Gonshor and Melvill Jones, 1974a).

Some 15-20 minutes after oscillatory rotation in the plane of the horizontal semicircular canals subjects underwent a similar series of 20 cycles oscillatory rotation with the sagittal plane of the skull brought into the true horizontal. Similar EOG recording of vertical eye movement, obtained in the absence of vision and employing precautions described previously (Barry and Melvill Jones, 1965), allowed comparison of responses in orthogonal degrees of freedom, one in the plane of prism-reversal (horizontal), the other in a plane which was not associated with vision reversal (sagittal).

RESULTS

Figure 2 reproduces an extract from records of head (i.e. turntable) and eye movement obtained from one subject during a control test

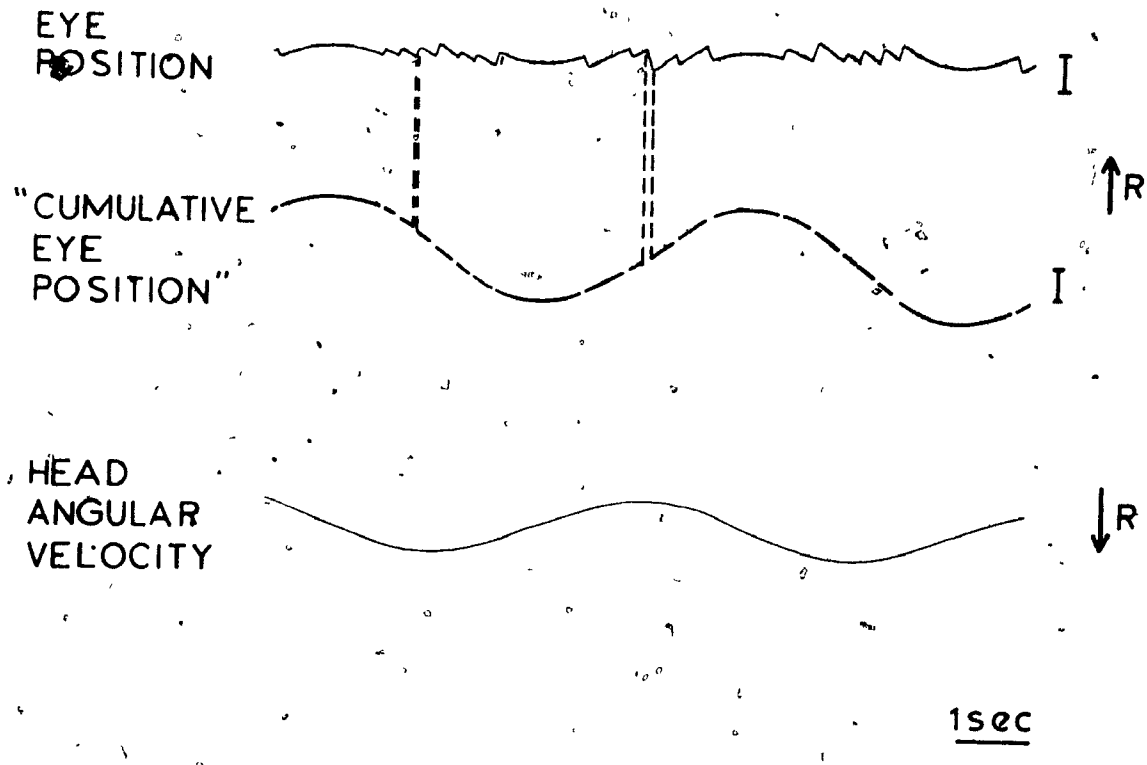
prior to donning the reversing prisms. The bottom record gives head angular velocity during sinusoidal oscillation of the man-carrying turntable at 1/6 Hz and 60°/sec angular velocity amplitude (peak-to-peak 120°/sec), obtained from a tachometer on the turntable. The top record shows the reflexly induced compensatory nystagmoid eye movement obtained in a horizontal plane, with eyes open behind blackout goggles. Bearing in mind that the upper record is of eye position relative to the skull, whilst the lower one is head angular velocity relative to space, it can be seen that the response obtained was almost exactly compensatory in phase. Thus the maxima and minima of eye position lie midway between peaks of head angular velocity, as should be the case if compensatory eye movement is properly phase related to the head movement. For example, the eyes were maximally displaced left in the skull at the moment when the head was maximally displaced right; i.e. when the head came to a halt after a period of turning with angular velocity to the right. Between peak displacement of the eyes to right and left, compensatory movements are normally interspersed with quick phase repositioning eye movements, thus generating the normal nystagmoid pattern of compensation seen in the figure.

(Fig. 2 near here)

The relationship between these two traces was measured as described in detail previously (Gonshor and Melvill Jones, 1974a). Briefly, curves of Cumulative Eye Position (CEP) were constructed

Fig. 2.

Extracts from original records of eye position relative to the head (top trace) and head angular velocity (bottom trace). The middle trace of "Cumulative eye position" (Meiry, 1965) consists of the sequential compensatory slow phase eye movements in the cycle with saccades (between dashed lines) omitted. In this figure, as in all subsequent figures, the stimulus is a sinusoidal oscillation at 1/6 Hz frequency and 60^{o}/sec velocity amplitude (peak-to-peak, 120^{o}/sec). The eye calibrations, unless stated otherwise, always denote 20^{o} displacement, symmetrical about the mid gaze position. "R" is right going movement.


EYE
POSITION
I
"CUMULATIVE
EYE
POSITION"
R
I
HEAD
ANGULAR
VELOCITY
R
1sec

as in the middle trace of the figure by extraction of quick phase eye movements (Meiry, 1965). From such CEP curves the gain, G, of the VOR was estimated, cycle by cycle, by calculating the ratio of peak eye angular velocity ($\dot{\theta}_{e\ max}$) to peak head angular velocity ($\dot{\theta}_{h\ max}$), so that

$$G = \dot{\theta}_{e\ max} / \dot{\theta}_{h\ max} \quad \text{.....(1)}$$

Mean values of these ratios were then obtained over each test run to yield the measured gain for the run. The mean gain obtained in this way from the control run in Figure 2 was 0.58, standard error of the mean (S.E.$\pm$0.017; n = 18).

In the long-term experiment the phase of response was measured at each half cycle by the cyclical degrees of phase shift between peaks of compensatory eye position and velocity nodes in the trace of head movement. The convention has been adopted throughout that the phase of eye movement is zero when its peak is exactly in phase with the required response for perfect ocular compensation. At 1/6 Hz the human compensatory response defined in this way would be expected to be 5-7 degrees phase advanced due to normal semi-circular canal and oculomotor dynamics (Hixson and Niven, 1962). The mean phase obtained from the control run represented in Figure 2 was $+7.2^{o}$ (S.E.$\pm$0.36; n = 18).

The objective was to obtain measured results from at least 10 cycles near the middle bracket of the standard 20 cycle test

run. However, as described below, some records obtained during transitional periods of rapid habituation yielded less than 10 useable cycles. When less than five measurable cycles were available no mean was recorded (see intermittent portion of the curve in Figure 7).

MEDIUM-TERM EXPERIMENTS

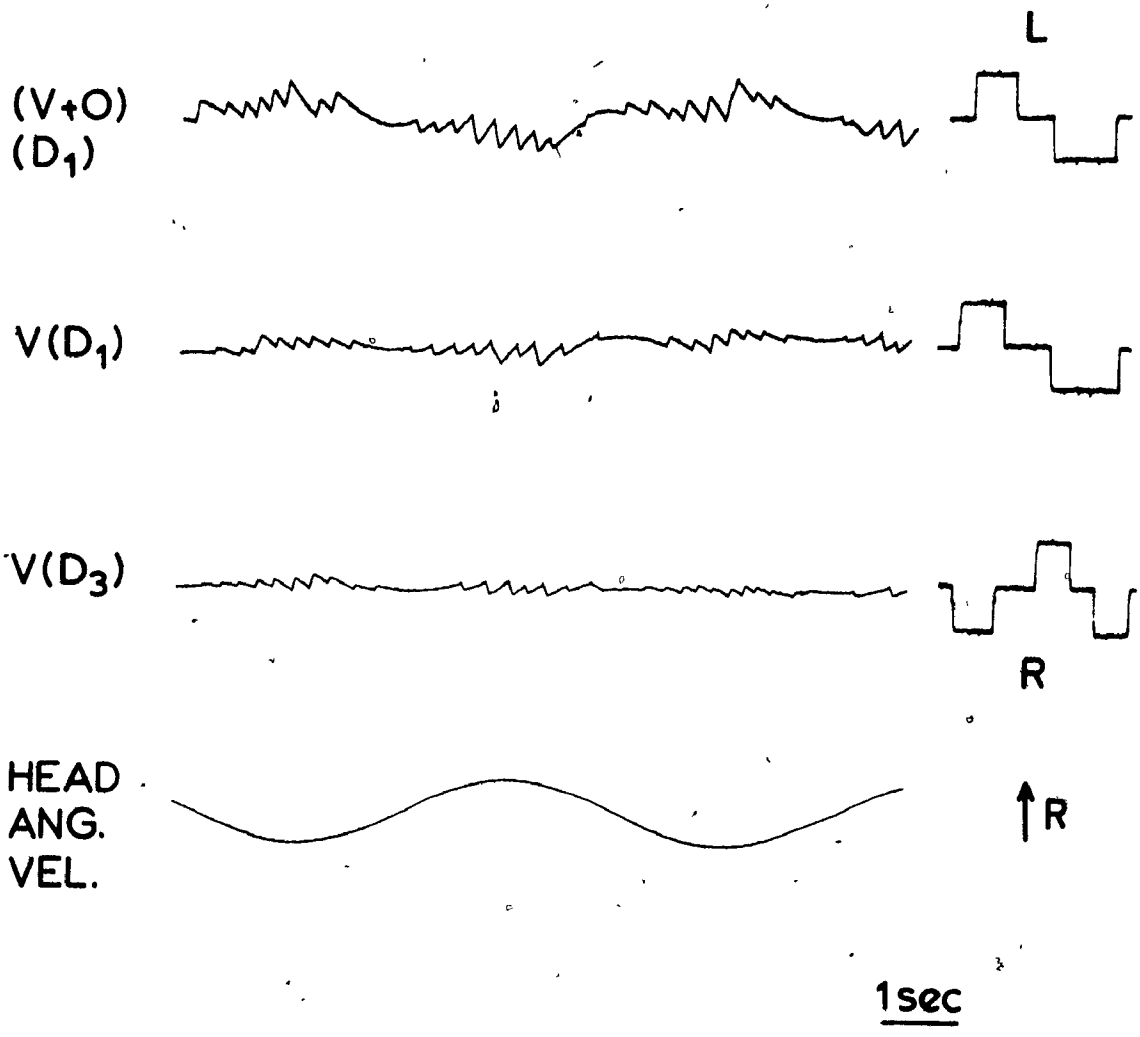
The first 3 experiments, conducted on separate subjects in the following order, lasted 4 (subject T.D.), 17 (A.G.) and 25 (M.J.) days, during which the reversing prisms were worn continuously for 2, 6 and 7 days respectively. Some examples of original records from subject T.D. are shown in Figure 3. As before, the bottom trace of this figure and subsequent similar ones gives the angular velocity of sinusoidal head rotation associated with all the accompanying records of eye movement. Static calibrations of eye angle relative to the head, obtained immediately before each run, are shown on the right side of the figure. Of incidental interest is the consistency with which such calibrations

(Fig. 3 near here)

can be obtained by careful attention to details of EOG electrode application. The top trace shows several cycles of normal compensatory horizontal nystagmus obtained on D_1 with eyes open (V+0) before donning the reversing prisms. From curves of cumulative eye displacement the mean gain of response over the standard 20 cycles of this

Fig. 3.

Extracts from original records of eye position relative to head angular velocity. V+O (D_1) is compensatory nystagmus resulting from complementary vestibular (V) and optokinetic (O) stimuli, and is taken from a control run on day 1 (D_1). V (D_1) is taken from a run in the dark on day 1, when only the vestibular input (V) to the oculomotor system is operative. V (D_3) is from a test in the dark less than 24 hours after the commencement of prism-reversal. The calibrations at the right of this figure all represent 20° displacement either side of center. L = left and R = right.


L
(V+O)
(D1)
V(D1)
V(D3)
R
HEAD
ANG.
VEL.
R
1sec

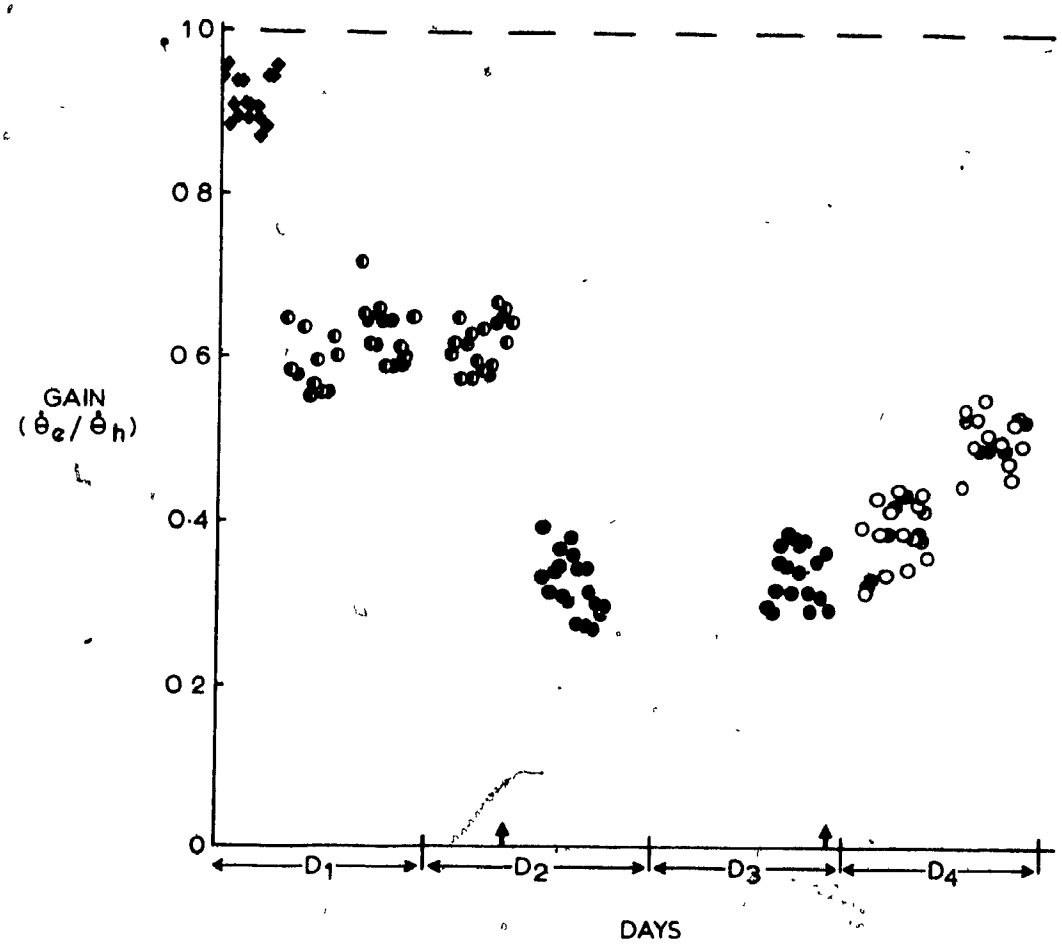
run was 0.92 (S.E.±0.007), which is typical of normal nystagmoid responses to combined vestibular and optokinetic stimulation during the standard oscillatory rotational stimulus described above. The second record from the top (V,D_1) is taken from a test run in the dark on D_1, when only the vestibular input (V) to the oculomotor system is operative. Comparison of smooth phase slopes in this record with those in the top one illustrates the reduction of VOR gain by about one third, which is to be expected on removal of vision in these circumstances (mean gain 0.61, S.E. =±0.006). The third record is an extract from the final test run on D_3 at the end of 2 days exposure to the habituating influence of prism-reversal, again recorded without vision. The additional highly significant ($P << 0.001$) attenuation of VOR gain is visible on simple inspection of the raw record. The mean gain obtained from the whole of this latter run was reduced to 0.33 (S.E. =±0.008), or about 50% of the value obtained during the control run without vision (V,D_1).

(Fig. 4 near here)

Figure 4 shows the cycle by cycle results obtained from subject T.D. throughout the 4 day experiment, each point giving the measured VOR gain, determined from individual cycles of records such as those in Figures 2 and 3, as described in Methods. In this figure and Figures 6, 7 and 13, the ordinate gives the gain, G, of response as defined in equation (1), and the abscissa gives the days, expressed

Fig. 4.

Collected results for one subject over the 4 day experiment. The ordinate gives the vestibulo-ocular gain. (eye angular velocity/ head angular velocity, or $\dot{\theta}_e/\dot{\theta}_h$). The vertical arrows on the abscissa represent the start and termination of vision reversal. Each point gives the measured vestibulo-ocular gain from a single cycle within runs in the dark before (◐), during (●), and after (○) the reversed vision stimulation. A cycle by cycle estimate of gain with normal vision during a control run, before donning the prisms, is illustrated in the top left corner (◆). The upper dashed line gives the maximum turntable angular velocity of 60°/sec attained in each cycle of the standard sinusoidal stimulus. Symbols in this figure are used for the same purposes in subsequent figures, unless otherwise stated.


1·0
0·8
0·6
0·4
0·2
0
GAIN
($\dot{\theta}_e / \dot{\theta}_h$)
D_1
D_2
D_3
D_4
DAYS

as D_1 etc., from commencement of the experimental series as described in Methods. The three control tests (◐), two performed on D_1 and one on D_2, yielded consistent results which were closely similar to those described earlier for normal subjects in these circumstances (Gonshor and Melvill Jones, 1974a). However, after donning the prisms (first vertical arrow on the abscissa) during the morning of D_2, the VOR gain, tested 6 hours later, was found to be consistently about 50% attenuated (●). A similar consistently attenuated VOR was found towards the end of D_3. Then, after removal of the prisms (open circles following the second vertical arrow on the abscissa of Figure 4), two tests on D_4 yielded results indicating progressive recovery of VOR gain throughout the day. However, even after 20 hours of normal activity without vision reversal there was retention of a considerable and highly significant degree of habituation, manifest as a 20% attenuation of VOR gain. Unfortunately, this subject was due to leave on a round-the-world expedition after D_4 and consequently could not be followed to the point of full recovery. Nevertheless this initial experiment clearly indicated that the planned experimental procedure was feasible, as well as demonstrating that marked and consistent habituation of the VOR was to be expected in these circumstances. The closed diamonds in the top left corner of Figure 4 give cycle-by-cycle gain obtained with normal vision during the standard sinusoidal rotational stimulus applied before donning the prisms, and generating a response as illustrated in the top

trace of Figure 3. They show that in this mode the gain of response approximates a value of one.

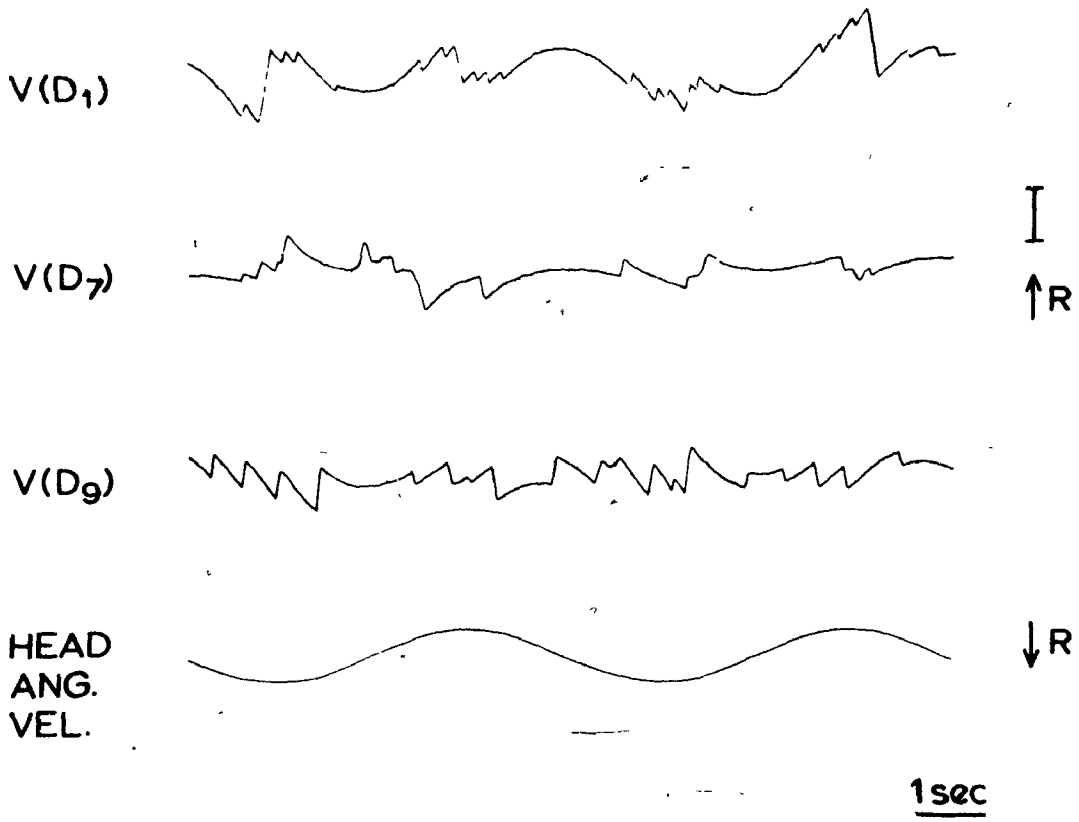
Original records from subject A.G. are shown in Figure 5, in which the format is similar to that of Figure 3. The top and bottom records of eye movement show vestibulo-ocular responses (V) without vision during runs before (D_1) and two days after (D_9) the period of vision reversal. The mean gains obtained from the whole of each of these two runs are 0.65 (S.E.$\pm$0.009) and 0.70 (S.E.$\pm$0.011) respectively. The middle record (V,D_7), taken from the final test run on the final day of prism-reversed vision, shows the now familiar attenuation, but also the beginnings of disorganization of a normally stereotyped nystagmoid response. For example, sometimes there tends to be rounding of normally sharp transitions between saccadic and compensatory phases of eye movement, as well as occasional anomalous patterns of eye movement not observed in normal control records, such as marked but fluctuating directional preponderance (e.g. Fig. 12). The mean gain for the whole of this run (V,D_7) is 0.16 (S.E.$\pm$0.013), which represents a substantial and highly significant ($P \ll 0.001$) suppression of gain relative to the other two records.

(Fig. 5 near here)

Figure 6 shows the collected results obtained from subject A.G. in the 17 day experiment. All symbols in this figure are as in

Fig. 5.

Extracts from original records of eye position relative to head angular velocity in the 17 day experiment with subject A.G. $V(D_1)$, $V(D_7)$ and $V(D_9)$ show respectively the compensatory nystagmus in the dark during a control run (before donning the prisms), a run on the 6th day of vision reversal, and a run 2 days after its termination.


V(D1)
V(D7)
V(D9)
HEAD
ANG.
VEL.
I
R
R
1sec

(Fig. 6 near here)

Figure 4. But here each point is the mean of the individual cycle-by-cycle estimates from each test run, together with vertical bars depicting ± one standard deviation (S.D.). Note particularly that the numbers on the abscissa depict the ends of the corresponding days into the experiment, in conformity with Figure 4. It is striking to see the similarity of this subject's gain attenuation on D_2 and D_3 with the corresponding changes seen in Figure 4 from subject T.D.. Beyond this point in time however the gain continued to decline in subject A.G., although at a progressively decreasing rate, reaching a value of 0.2 on the last test run before removing the prisms. After removal of the prisms the early indication of gain recovery seen in Figure 4 was progressively continued in this subject over a time course bearing a rather close similarity to the first 2 days of fall in gain after initially donning the prisms. A final test run on day 17 confirmed recovery to control conditions. As in Figure 4, the closed diamond at the top left corner of the figure gives the mean gain obtained whilst looking at the surroundings with eyes open, and before donning the prisms.

(Fig. 7 near here)

Figure 7 summarises the results from subject M.J. in the 25 day experiment. Again there was rapid attenuation of VOR gain during the first 2 days after donning the prisms, reaching about

Fig. 6.

Changes in vestibulo-ocular gain ($\dot{\theta}e/\dot{\theta}h$) as a function of the 17 day experiment. The vertical arrows enclose the period of reversed vision. Each point is the mean value for up to 20 cycles of test runs in the dark before (◐), during (●), and after (○) reversed vision stimulation. The filled diamond at the top left represents the mean value for 17 cycles during a run with vision before donning the prisms. The upper dashed line gives the maximum head angular velocity of 60^{o}/sec attained in each cycle of the standard sinusoidal stimulus. Vertical bars depict ±one standard deviation (S.D).

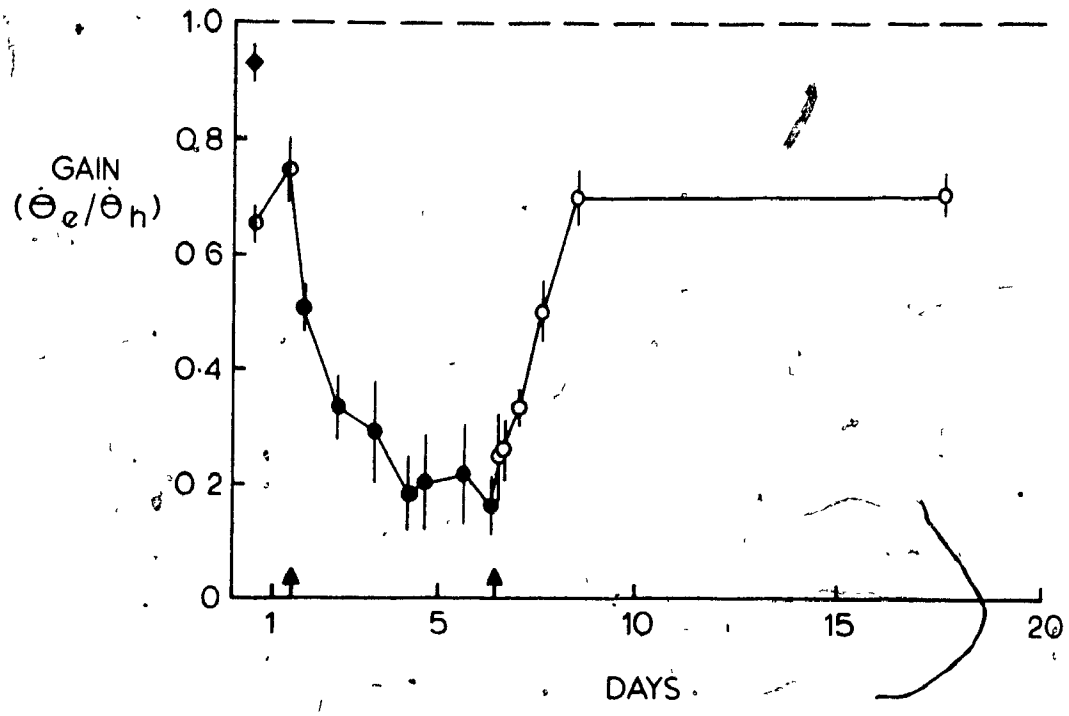
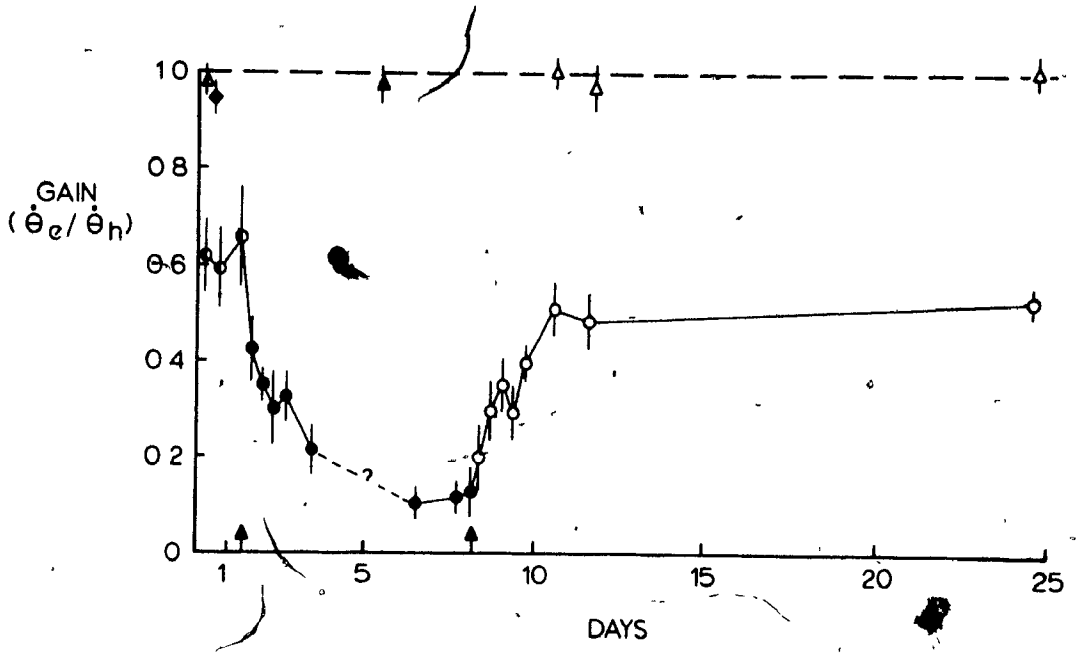

GAIN
($\dot{\Theta}_e/\dot{\Theta}_h$)
1.0
0.8
0.6
0.4
0.2
0
1
5
10
15
20
DAYS

Fig. 7.

Changes in vestibular-ocular gain as a function of the 25 day experiment. Ordinates, points, and dashed lines as in Figure 6. The question mark represents tests run during days 5 and 6 of the experiment, when a combination of low gain and a disorganized nystagmus pattern made analysis impossible. The triangles are mean VOR gains ($\bar{n}$ = 20) obtained from test runs in the dark, with head oscillation in the sagittal plane, before (△), during (▲), and after (△) the period of vision reversal. Vertical bars again depict ±1 S.D.


GAIN
($\dot{\theta}_e / \dot{\theta}_h$)
1.0
0.8
0.6
0.4
0.2
0
1
5
10
15
20
25
DAYS

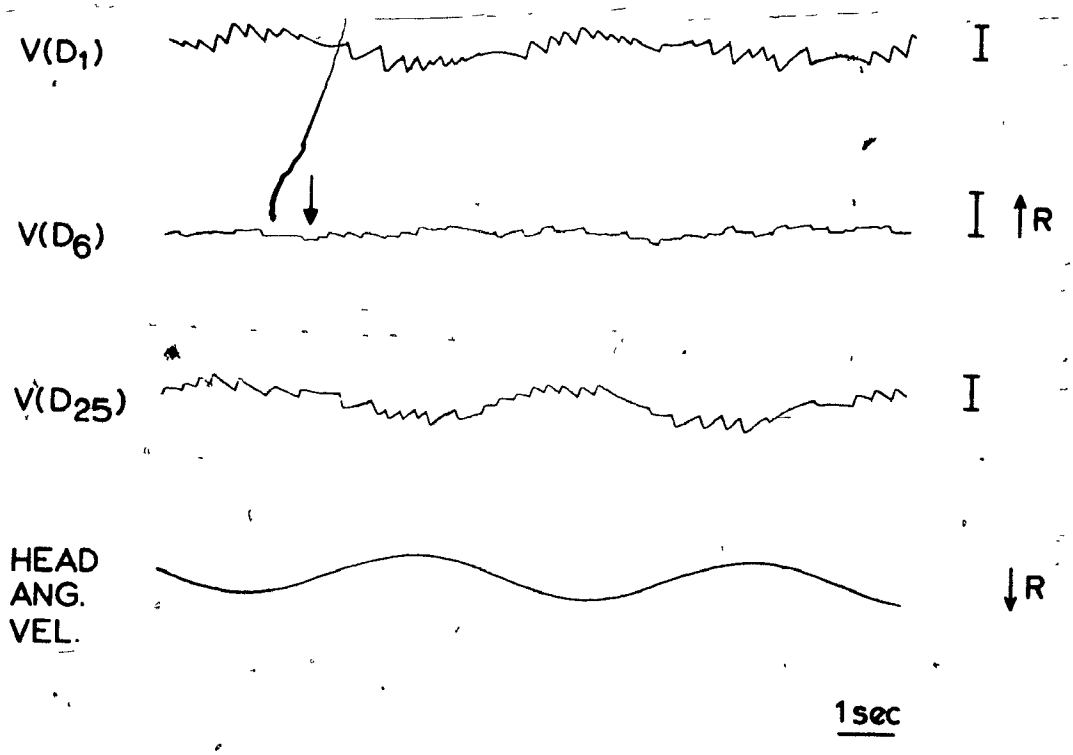
50% attenuation over this period, as in the previous subjects. Furthermore, the recovery of gain after prism removal occurred over a somewhat similar time course to that of the initial habituation. However, in these records high attenuation of gain tended to be associated with consistent disorganization of oculomotor response such that some records were impossible to analyse with satisfactory assurance. The intermittent section of the curve containing a question mark covers the period in which such records appeared. The open and closed triangles give the gain of VOR in the dark measured in the sagittal plane.

(Fig. 8 near here)

The middle eye movement record of Figure 8 illustrates a segment from such a response obtained from subject M.J. As in Figure 5 the upper and lower eye movement records show extracts from two normal responses obtained without vision before (D_1) and a long while after (D_{25}) the period of prism-reversed vision. However, the intermediate record of D_6 is not merely attenuated in amplitude, but also shows portions of response defying meaningful analysis in terms of gain. One tantalising feature of this record (D_6) occurs at the point marked by an arrow. The latter denotes a turnover point, which if compared to the corresponding ones in the records above and below, is seen to be almost 180° out of phase with normal compensation, or approximately reversed in direction. But the transient changing nature of this feature,

Fig. 8.

Extracts from original records of eye position relative to head angular velocity in the 25 day experiment. $V(D_1)$ is a control run in the dark before donning the prisms and $V(D_{25})$ is a run 17 days after termination of reversed vision stimulation. $V(D_6)$ is a record from a test run in the dark on the 5th day of reversed vision, with the arrow pointing to a nystagmic turnover point that appears functionally reversed.


V(D1)
I
V(D6)
I
R
V(D25)
I
HEAD
ANG.
VEL.
R
1sec

together with the very weak signal-to-noise ratio in such records led us at this stage to disregard change of phase as a measurable variable.

Figure 9 shows two cycles from runs performed with the sagittal

(Fig. 9 near here)

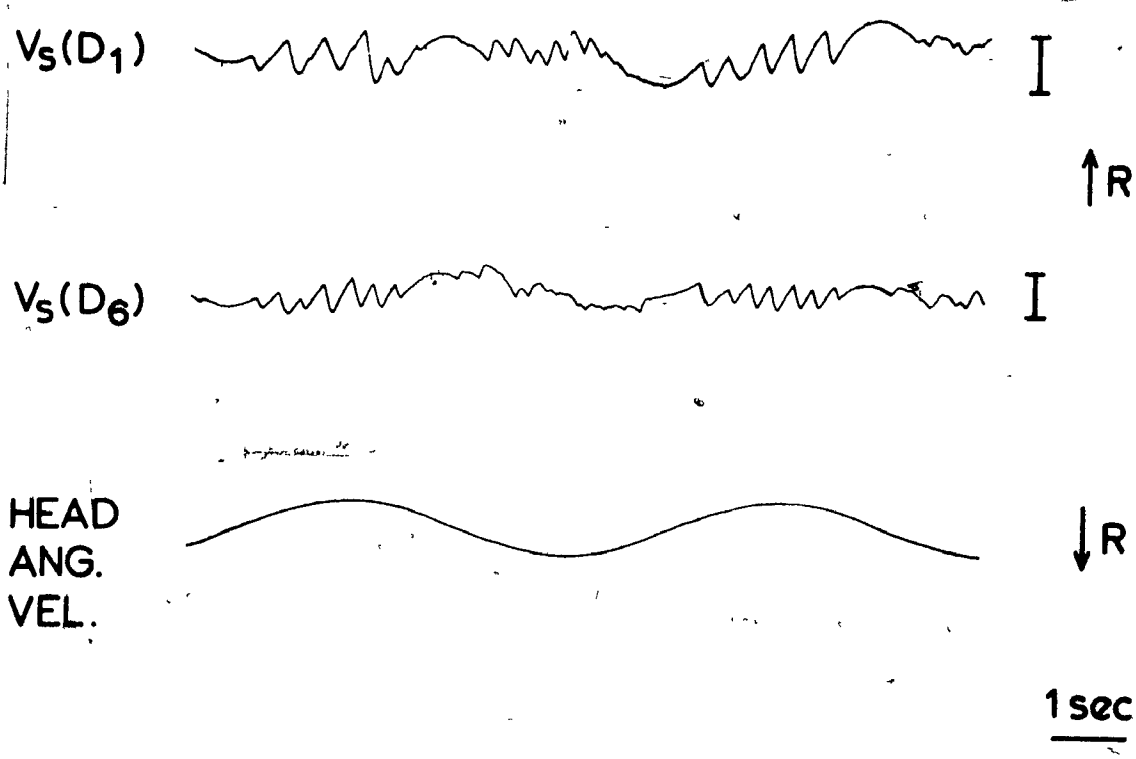
plane of the head parallel to the rotational plane of stimulation. It should be remembered that the "dove" prisms were specifically oriented to reverse vision in a horizontal plane, but not in the sagittal one. These records of vertical ocular nystagmus were obtained during a control run on D_1 and at the height of vision reversal on D_6. Despite the very marked attenuation of horizontal nystagmus on D_6 (middle trace in Figure 8) there is no significant difference between the mean gains of vertical nystagmus depicted in the two runs of Figure 9 ($P>0.5$). This was a consistent feature of all the prism-reversal experiments as exemplified by the diamonds and triangles in Figures 7 and 19, and indicates high geometric specificity in the habituating process. Of incidental interest is the fact that in all subjects tested this way, sagittal VOR gain was consistently close to a value of one, despite the fact that all such measurements were made in the dark.

LONG-TERM EXPERIMENTS

The previous medium-term experiments demonstrated the need for a longer exposure to vision reversal, in order to follow up the

Fig. 9.

Extracts from original records of eye movements relative to head angular velocity in the sagittal plane, in the 25 day experiment. The subject is again rotated at 1/6 Hz and 60^{o}/sec velocity amplitude, but this time with the head rotated through a 90^{o} angle so that it lies on the right shoulder. Thus, a movement of the turntable in the horizontal plane produces <u>head</u> motion in the sagittal plane. $V_s(D_1)$ and $V_s(D_6)$ represent the vestibulo-ocular reflex responses in the dark during a control test run and a run on the 5th day of reversed vision, respectively. R = right going turntable (head) motion, but since this causes the rotated head to move in the sagittal plane, the "R", or right-going movement of the eye relative to the turntable, actually represents an upward movement of the eye relative to the head.


$V_S(D_1)$
I
R
$V_S(D_6)$
I
HEAD
ANG.
VEL.
R
1 sec

impression that more than mere attenuation of gain was at play in the habituation process. For this a 4th subject (A.M.) undertook a 49 day experiment in which the reversing prisms were worn continuously for 27 days. Exactly the same procedures were employed as in the previous medium-term experiments.

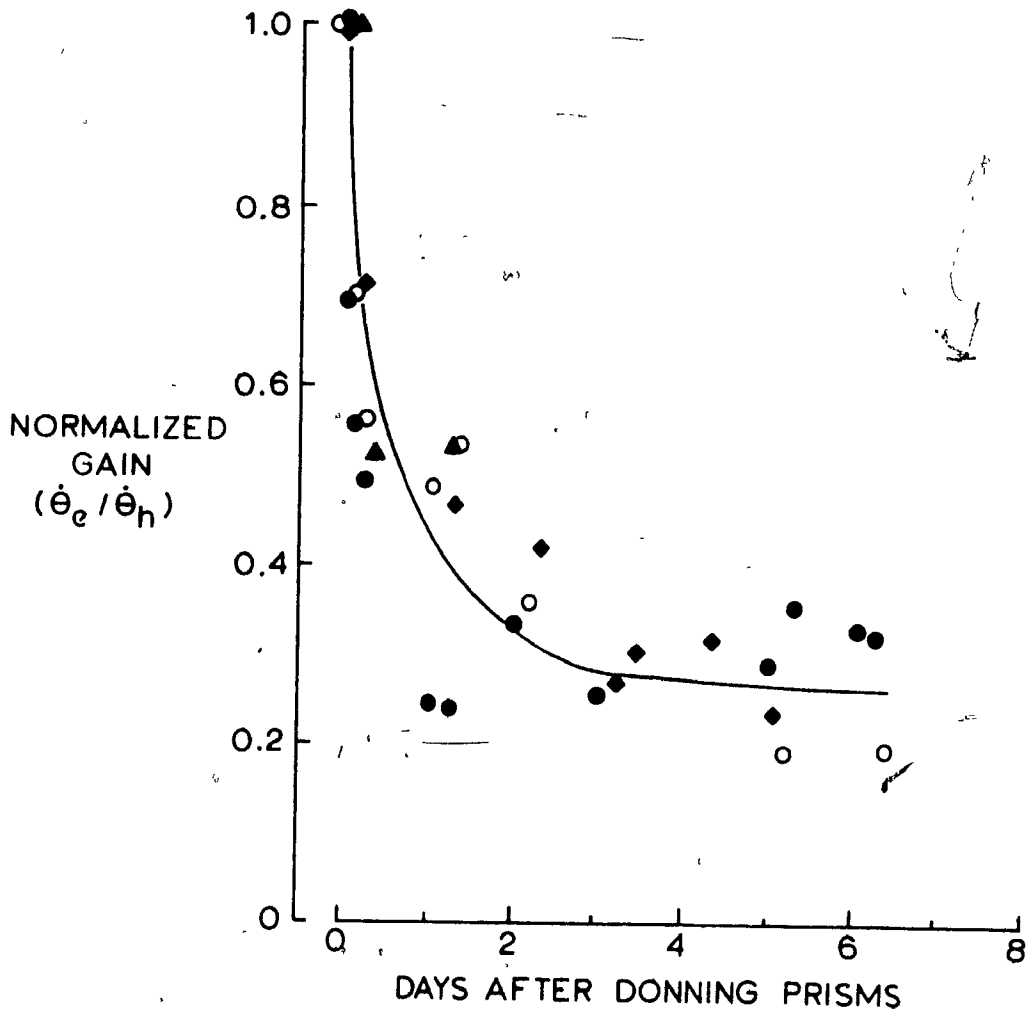
Changes observed during the first week of habituation were generally similar to those seen in the three medium-term experiments. To illustrate this the normalized VOR gain for all four subjects is plotted over the first seven days in Figure 10. Subject A.M. is denoted by the symbol (●) in this figure. The fact that he followed the same general pattern of decline in gain as the three previous subjects is considered particularly important in view of the fact that he was the only individual exposed to more than this duration of prism-reversal.

(Fig. 10 near here)

As already mentioned, a feature which first became systematically apparent in the long-term experiment was the significance of phase of VOR relative to the sinusoidal rotational vestibular stimulus. Figure 11 shows a sequence of records obtained over the first 18 days, chosen to illustrate general features of the progressive changes observed. The format is similar to that of Figures 3 and 5, so that although eye movement records were obtained on separate days, they are all properly referred in time to the standard sinusoidal stimulus, shown as a single trace at the bottom of the figure. Thus, in this

Fig. 10.

Changes of normalized VOR gain during the first few days of vision reversal in the 4 day (▲), 17 day (◆), 25 day (○), and 49 day (●) experiments. The abscissa represents real time after donning the prisms, each number denoting the end of a 24 hour period from 10.00 a.m. on one day to 10.00 a.m. on the following day. The ordinate gives mean VOR gain normalized relative to each individual subject's mean control value, obtained immediately prior to donning the prisms. The curve was drawn by eye.


NORMALIZED
GAIN
($\dot{\theta}_e / \dot{\theta}_h$)
1.0
0.8
0.6
0.4
0.2
0
0
2
4
6
8
DAYS AFTER DONNING PRISMS

figure, the progressive phase lag of eye movement from D_1 to D_{18} is properly related to that of the common stimulus. One should recall that all records were obtained in the absence of vision. The top record is a control response obtained before donning the prisms (V,D_1). V,D_3 is taken from the last test sequence at the end of the second day of wearing the reversing prisms. Considerable attenuation of gain had occurred together with some interesting phase characteristics, which however require cognisance of the features described in connection with Figure 12 for proper interpretation.

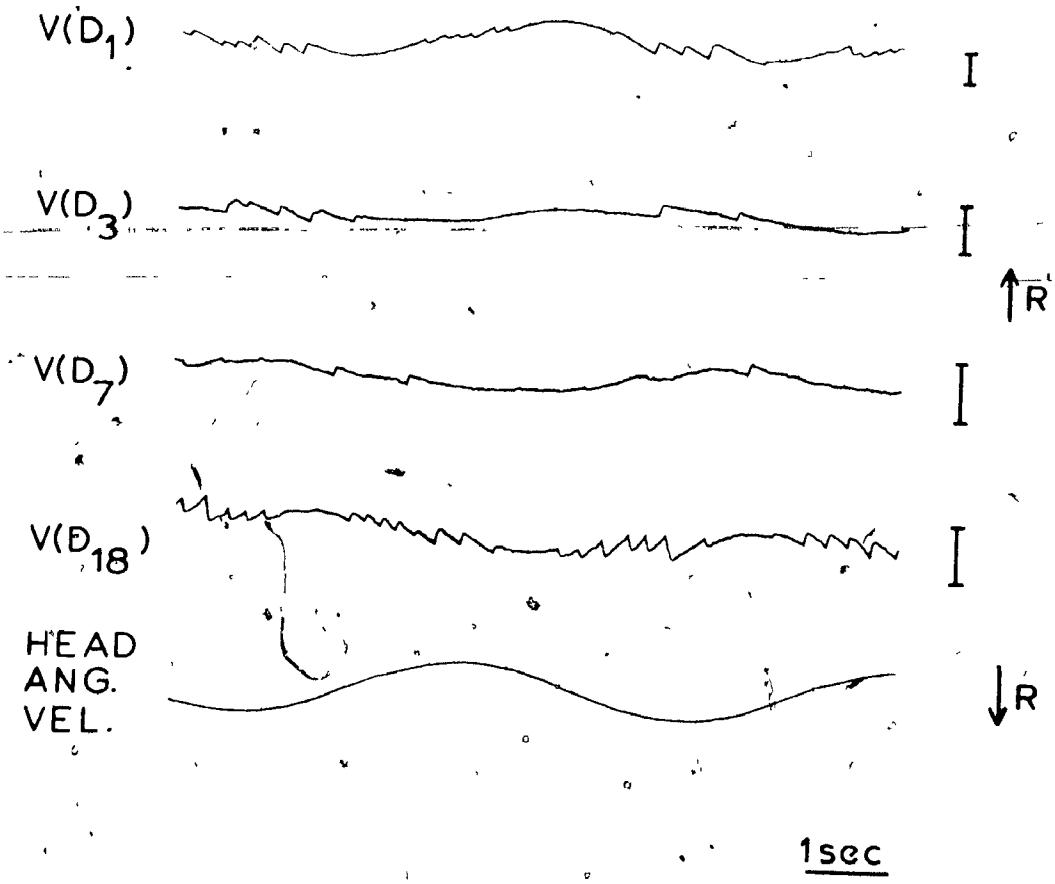
(Fig. 11 near here)

In the subsequent records of this figure there was a progressive, although somewhat erratic tendency for substantial development of phase lag in the response. Thus on D_7, and D_{18}, the mean phases of response were respectively 94^o and 130^o lagged relative to the control response. The important feature here is that a phase shift of 180^o would amount to precise reversal, so that, as evident in the figure, the response on D_{18} represents approximate, but not complete, reversal. An additional important feature is that the gain of this approximately reversed response was considerably restored, although not back to its original value (note the calibrations on the right hand side of the figure).

As will be seen in Figure 13 this became the normal pattern of

Fig. 11.

Extracts of original records from the 49 day experiment, showing the changes in phase of head angular velocity stimulus and eye position response. All records are taken from runs in the dark during a control run (D_1), and runs on the 2nd (D_3), 6th (D_7), and 17th days (D_{18}) after donning the prisms.


V(D1)
V(D3)
V(D7)
V(D18)
HEAD ANG. VEL.
I
R
1sec

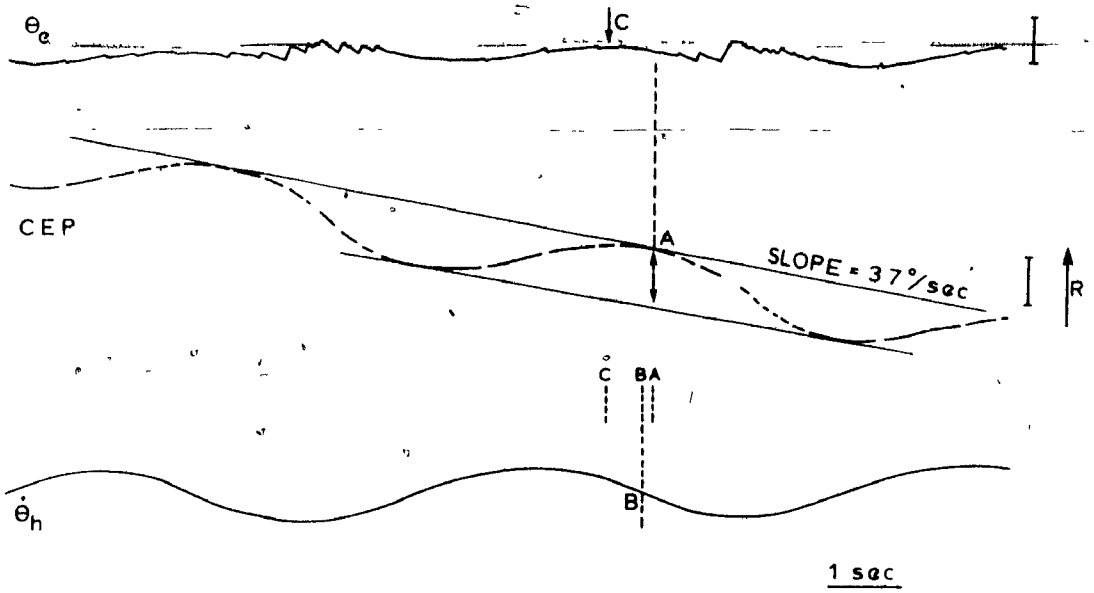
response to be expected during the last two weeks of wearing the prisms. Of particular significance is the fact that without a knowledge of phase it would not be possible to decide whether the record obtained on D_{18} in Figure 11, was normal or the consequence of habituation. That is to say, there was normal interspersion of appropriately placed saccades amongst well defined and organized smooth pursuit movements generating a closely sinusoidal CEP curve. Evidently, not only the smooth compensatory phase of nystagmus had been effectively reversed, but so also had the numerous well organized placements of the saccadic repositioning flicks. Physiological implications of this feature will be discussed later.

Figure 12 is included to point out another characteristic of response patterns often obtained at this advanced stage of the habituation process, seen also in the D_3 trace of Figure 11. The top trace is an original record of 2 cycles from a portion of record obtained on D_8. Here the nystagmus is biased in that almost all saccades are to the right. This can be accounted for by a bias of eye angular velocity (i.e. "directional preponderance") to the left, in this case approximately 4°/sec, as is apparent in the mean "downwards" slope of the CEP curve shown below the original one. This phenomenon was commonly seen during the transitional stage of habituation, even though no subjects exhibited overt directional preponderance during control conditions.

(Fig. 12 near here)

Fig. 12.

Extract from original records (D_8) in the 49 day experiment, showing the effect of directional preponderance on the measurement of phase. The top trace gives the recorded eye positional response to 1/6 Hz sinusoidal oscillation at 60^{o}/sec maximum velocity amplitude (velocity trace at bottom). The arrow at "C" indicates the apparent "turnover" point in this original record. The middle trace is the constructed CEP curve (Fig. 2), showing an angular velocity bias (directional preponderance) of 3.7^{o}/sec. The actual "turnover" point is at the dashed line ("A"), which is determined from the point of tangential contact of the CEP curve with a line parallel to the slope of mean positional drift. The arrow heads at "A" enclose the vertical distance between the points of tangential contact and a straight line joining successive peaks. The dashed line at "B" indicates the point of zero head angular velocity, where a "turnover" would be considered in perfect compensation. B to C represents a phase advancement of 27^{o}, while B to A represents a phase lag of 10^{o}.


θ_e
C
CEP
A
SLOPE = 37°/sec
R
C
BA
$\dot{\theta}_h$
B
1 sec

In addition to the inherent interest of the introduction of such directional preponderance during habituation, it is important to appreciate that when this phenomenon is present the phase of response cannot be obtained directly from points of "turnover" in the original trace of eye displacement (e.g. the point located by the arrow at "C" on the original trace). Rather the phase of the "turnover" must be determined from points of tangential contact ("A") of the CEP curve with lines parallel to the mean drift. The relevant feature to note here is that "A" is phase lagged relative to point of perfect compensation, "B", whereas "C" in the original record gives the misleading appearance of phase advancement.

A confusing feature of the transitional changes between the two extreme patterns of response in Figure 11, was the wide range of variability found from one day to the next, and even from one test run to the next on the same day. These changes are evident in Figure 13 which shows a three dimensional display of the inter-dependence between gain; phase and duration, throughout the whole extent of the long-term experiment. The vertical ordinate gives VOR gain expressed as before in terms of the ratio of mean maximum eye angular velocity to mean maximum head angular velocity ($\dot{O}e/\dot{O}h$). The abscissa gives time in days after commencing the experiment. The third, or z axis, gives the phase lag of ocular movement relative to that which would yield perfect compensation for head movement with normal vision, in accordance with the convention defined at the

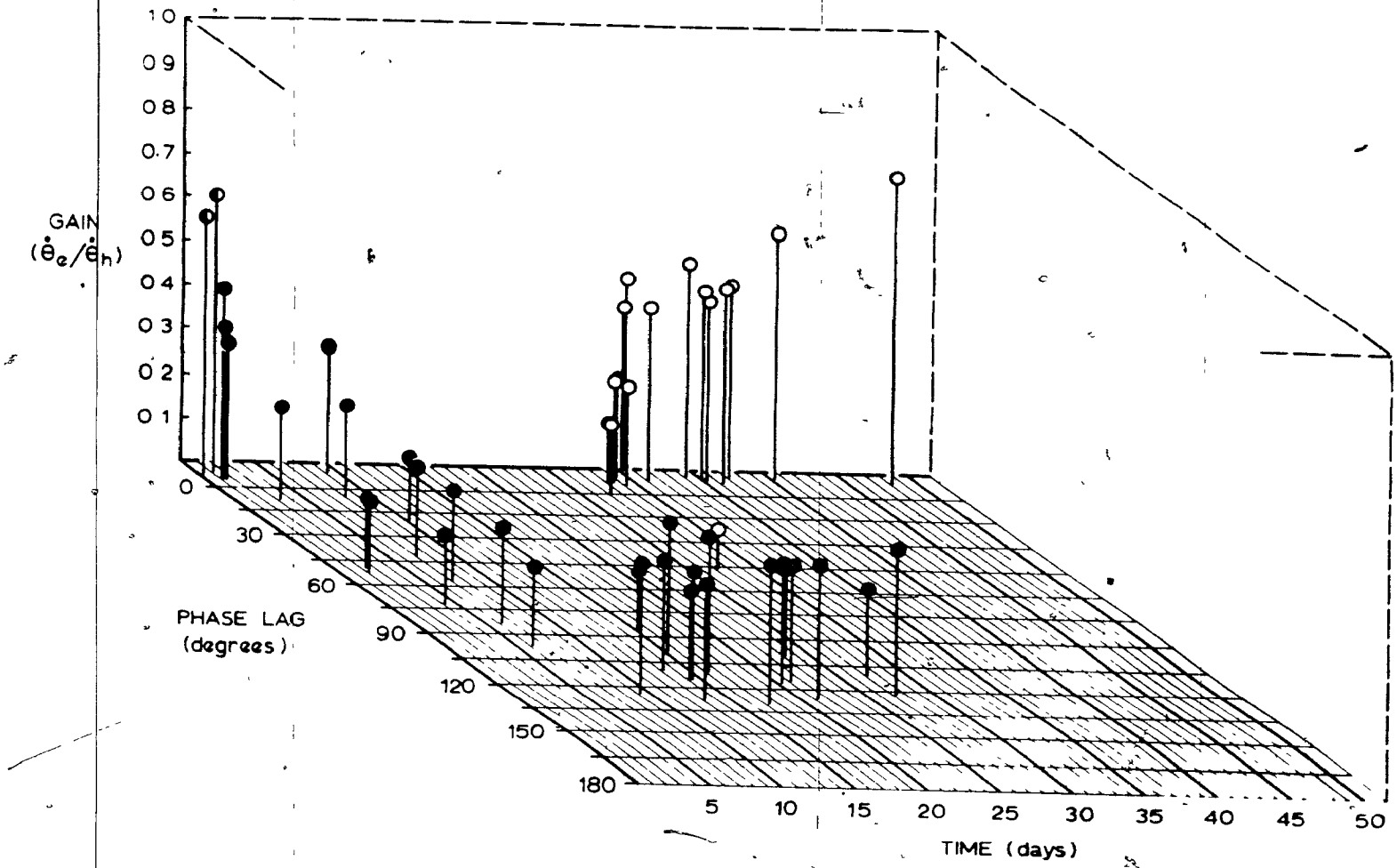
commencement of Results. Half filled circles depict control responses obtained in the absence of vision prior to donning of the prisms. Filled circles depict the period during which the subject wore the reversing prisms throughout the waking hours. Open circles indicate responses obtained after the prisms had been removed and normal vision restored. It may be helpful to emphasise again that the responses plotted in this graph were all obtained in the absence of vision. The lengths of the "stalks" on which these points lie give the scalar magnitude of the gain of response on the same scale as the ordinate.

(Fig. 13 near here)

As already indicated in the raw data presented in Figure 11, after donning the prisms the habituation process manifested itself as a progressive sequence of change in gain and phase. Initially there was rapid reduction of gain without significant change in phase. Thereafter, during the remainder of the first week there was a general tendency for a substantial development of phase lag, at a somewhat further reduced level of gain. It should however be noted that this general pattern of change was by no means smoothly accomplished. Thus, careful attention to detail in Figure 13 shows that during the first two weeks or so the changes incurred fluctuated back and forth from day-to-day and even from one test run to another within a single day. The most striking example of this fluctuation

Fig. 13.

A 3-dimensional view of the simultaneous changes in the vestibulo-ocular gain ($\dot{\Theta}e/\dot{\Theta}h$) and phase as a function of time in the 49 day experiment. Each point is the mean value for up to 20 cycles of a run, and is placed according to both its mean gain and phase values. The points are also placed according to the actual elapsed time between the start of the experiment and the test run they represent. Each day number on the abscissa indicates the end of a 24 period, starting at 10.00 a.m. on one day and terminating 10.00 a.m. on the following day (see also Table 1). The points are the results of test runs in the dark before (◐), during (●), and after (○) reversal of the visual field.

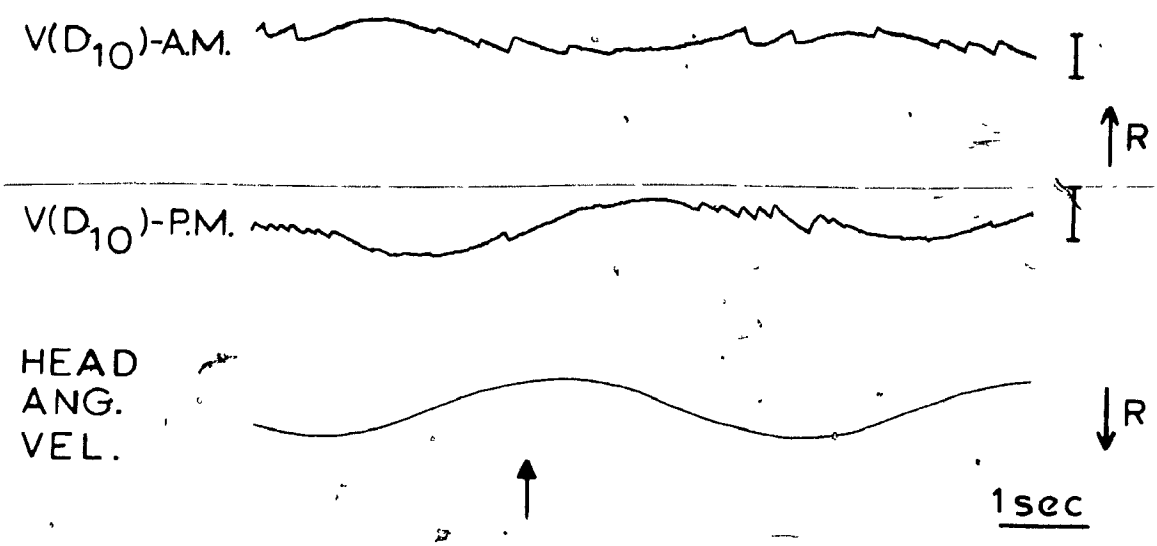

GAIN
$(\dot{\theta}_e/\dot{\theta}_h)$
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
30
60
90
120
150
180
PHASE LAG
(degrees)
5
10
15
20
25
30
35
40
45
50
TIME (days)

was observed on D_{10} from which samples of morning and evening records are separately illustrated in Figure 14. Here, the top record was obtained at 10.00 a.m. and shows a well defined "reversed" pattern of response. The bottom trace was obtained at 5.00 p.m., and here the phase of response had reverted completely back to the initial control value, although the gain remained substantially (about 50%) below the normal control gain. Of course, in this instance one was particularly careful to review directional calibrations of head and eye records in view of the possibility that these may have been accidentally reversed between morning and evening sessions. Fortunately, this possibility is absolutely excluded by the fact that the morning response was consistently in the region of 120^{o} phase lag, whilst the evening response was almost precisely in phase with the control responses obtained on D_1. Since the difference between the respective mean values is highly significantly less than 180^{o} ($P \ll 0.001$), there can be no simple ambiguity of directional calibration, and hence the observation must be a real one. Such extreme variability from one set of tests to the next in the same day was only seen on this one occasion. The uniqueness of this observation raises the question of whether the subject could have removed his prisms over a period of waking hours unknown to us. Although this cannot of course be absolutely excluded, the fact that his whole day was under minute-to-minute observation by his full-time companion makes this possibility unlikely.

(Fig. 14 near here)

Fig. 14.

Extracts from original records of runs in the morning (D_{10}-A.M.) and afternoon (D_{10}-P.M.) of day 10 in the 49 day experiment. Eye response to head angular velocity in the morning run is about 130° phase lagged, so that at the vertical arrow, whilst the head is rotating to the left, "compensatory" slow phase eye movements due to VOR are directed also to the left, with saccades placed appropriately for this reversed slow phase movement. The phase relationship in the afternoon run reverts back to the normal compensation seen prior to reversing the visual field (Fig. 2), i.e. whilst the head is (at the arrow) rotating left, compensatory slow phase eye movement is directed to the right.


V(D10)-A.M.
I
R
V(D10)-P.M.
I
HEAD
ANG.
VEL.
R
1sec

Returning to Figure 13, it can be seen that after the first two weeks of exposure to vision reversal the situation more or less stabilised to one in which the phase lag of VOR was around 110° to 130°, and the gain about one half the normal control values. Of considerable additional interest is the fact that during the last two weeks of vision reversal the subject was able to move about with something approaching normal facility. Moreover, he had regained his normal hearty appetite, which, as with the medium-term subjects, had been somewhat depressed in association with the nausea, and general lethargy and malaise, experienced in the early phase of vision reversal (Gonshor, 1974b).

The next feature to note in Figure 13 is the pattern of recovery after removal of the prisms. Thus, although it took effectively one further month to regain normal conditions, the time course of events was dramatically different from that of the original habituation to prism-reversal. The first standard test run, conducted one half hour after removal of the prisms, is seen as the first open circle. Already there were large changes in both phase and gain. Two hours later, the phase of response had reverted to a value which slightly "overshot" the normal control value, and thereafter no marked change of phase was subsequently seen. However, the gain of response remained highly attenuated for two to three days, and subsequent recovery to the normal control value was extended over a prolonged two to three week period.

These striking phenomena are well illustrated in the original

records of vestibularly driven eye movements shown in Figure 15. The top three traces are taken from standard test runs in the dark performed (i) just before, (ii) half an hour after and (iii) two hours after removal of the prisms on D_{28}. In $D_{28-(i)}$ there was both substantial phase lag (115^{o}), and attenuation of VOR gain (60%). In $D_{28-(ii)}$ the phase is only 80^{o} lagged and there is considerable additional attenuation of gain and seen in the first open circle of Figure 13. In $D_{28-(iii)}$ the phase has reverted nearly to normal, although the gain was still well below the control value. 24 hours later (D_{29}) the gain was still low, with the interesting additional feature that saccades were absent in some stretches of record, as in the figure. Nearly four weeks after prism-removal (D_{49}) a normal response was again obtained, as already noted in connection with Figure 13.

(Fig. 15 near here)

In Figure 13 the time scale is so compressed that it is often not possible to identify the exact sequence of events. In view of the high physiological significance of the changes observed and the difficulty of indicating statistical reliability of means in Figure 13, mean values of gain and phase together with their standard errors are given for each test run in Table 1.

(Table 1 near here)

Fig. 15.

Samples from original records, showing the changes in vestibulo-ocular gain and phase after removal of the prisms. $V(D_{28})$ represents test runs in the dark, (i) before the prisms are removed, (ii) half an hour after removal of the prisms, and (iii) 2 hours after. $V(D_{29})$ is from a run less than 24 hours after removal of the prisms, and $V(D_{49})$ represents a test run on the last day of the experiment.

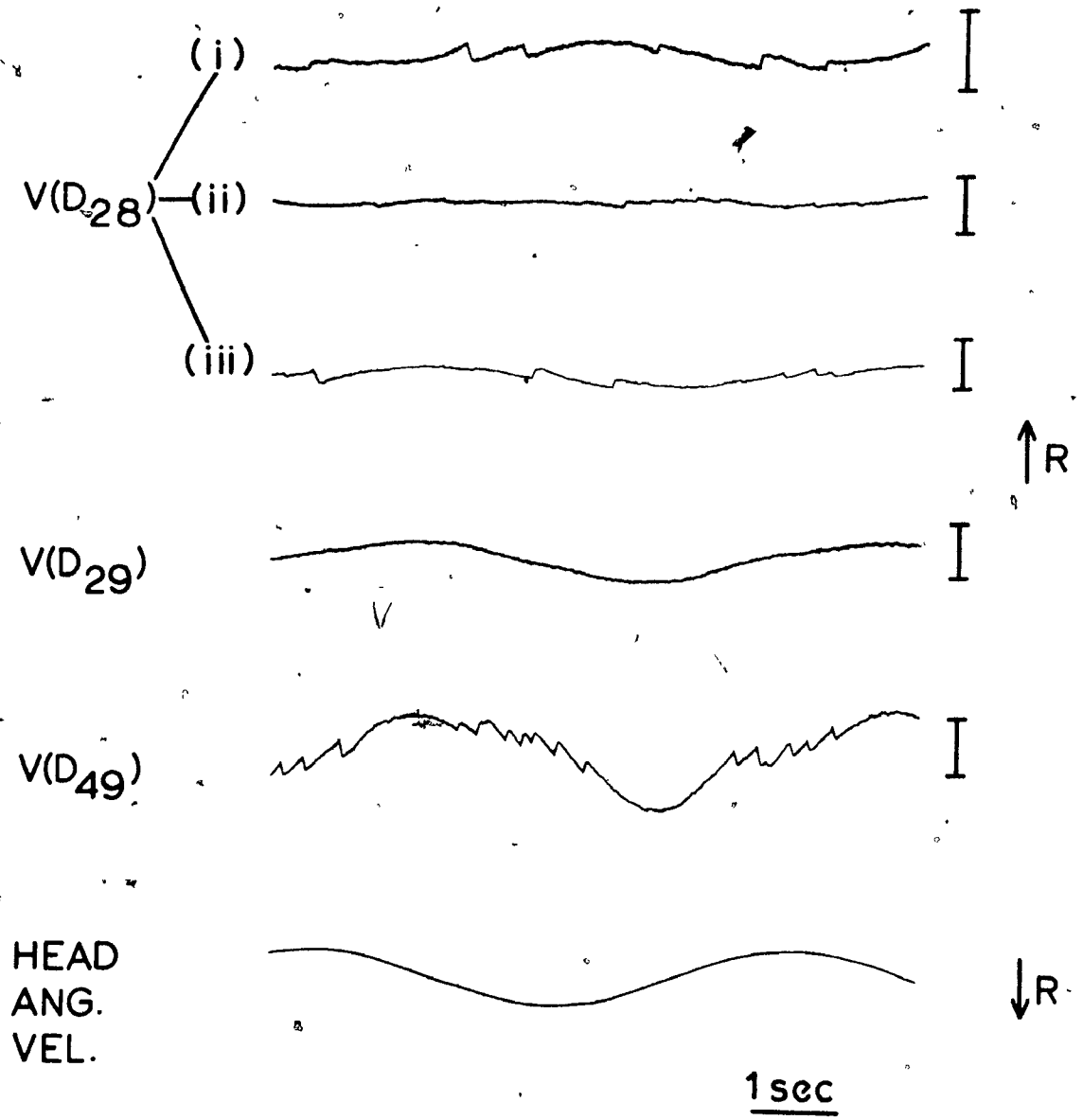

(i)
V(D28)
(ii)
(iii)
R
V(D29)
V(D49)
HEAD
ANG.
VEL.
R
1 sec

TABLE 1

Assessments of gain and phase for the 49 day experiment. The only day numbers shown are those in which at least one test was performed. Tests on days where more than one was performed are denoted as A, B, C, and D. "Time", denotes the time in each day (hours) when a complete test session commenced. The vestibulo-ocular reflex gain (eye angular velocity/head angular velocity) is shown as a mean value for each run, ±S.E. of the mean (n). Phase values represent the degrees of phase advancement (+) or phase lag (-) with respect to perfect compensatory eye movement. The values are given as mean phase change, in degrees, for a run, S.E. of mean (n). Unless otherwise stated, the n value for each phase measurement is 10.

TABLE 1

DAY	TIME	MEAN GAIN	MEAN PHASE
1	10	0.581±0.017(18)	+7.2±0.36(18)
2A	10	0.632±0.008(18)	+7.6±0.48(19)
	12	PRISMS ON	
B	13	0.423±0.010(18)	+5.0±1.11
C	15	0.336±0.007(21)	+4.0±1.44
D	18	0.298±0.005(14)	+4.0±0.98
3A	10	0.147±0.009(18)	-52.0±8.29(16)
3B	17	0.144±0.006(18)	-50.0±1.81
4	10	0.201±0.014(15)	- 8.0±6.59
5	10	0.149±0.010(18)	-67.0±5.13(18)
7A	10	0.173±0.011(18)	-94.0±3.99
B	17	0.198±0.013(14)	-83.0±6.82
8A	11	0.197±0.012(16)	-57.0±8.82
B	16	0.207±0.012(18)	-40.0±6.95
9	11	0.203±0.013(15)	- 5.0±5.86
10A	10	0.288±0.008(17)	-125.0±2.23
B	17	0.280±0.009(19)	+9.0±4.96
11	10	0.132±0.010(16)	-20.0±10.52
14A	10	0.259±0.008(19)	-128.0±1.45
B	15	0.265±0.009(13)	-109.0±4.34
15A	10	0.203±0.013(12)	-115.0±4.83
B	15	0.242±0.011(18)	-115.0±4.02
16A	10	0.293±0.015(20)	-99.0±11.77
B	17	0.142±0.008(19)	-86.0±5.54
17	10	0.299±0.015(15)	-110.0±3.77

DAY	TIME	MEAN GAIN	MEAN PHASE
18	11	0.312±0.024(17)	-130.0±2.79
21	14	0.270±0.031(14)	-116.0±3.88
22A	11	0.263±0.009(12)	-115.0±4.74
B	19	0.299±0.012(14)	-125.0±2.25
24	11	0.191±0.008(19)	-99.0±1.89
28A	10	0.185±0.007(14)	-110.0±2.75
B	15	0.325±0.011(27)	-122.0±1.16
	17:30	PRISMS OFF	
C	18	0.089±0.005(20)	-76.0±7.88
D	19:30	0.154±0.007(23)	0.0±2.14
29A	14	0.133±0.005(20)	+5.0±2.92
B	18	0.233±0.007(16)	+6.0±1.22
30A	10	0.223±0.004(18)	+9.0±1.20
B	17	0.224±0.005(19)	+5.0±1.45
31A	10	0.363±0.009(20)	+15.0±1.42
B	17	0.467±0.009(20)	+14.0±1.25
32	11	0.380±0.016(7)	+13.0±1.00
35	11	0.482±0.010(10)	+10.0±1.24
36A	10	0.412±0.009(17)	+10.0±1.11
B	16	0.396±0.001(13)	+8.5±2.60
37	11	0.425±0.009(14)	+7.0±0.87
38	11	0.426±0.010(19)	+11.0±1.06
41	13	0.552±0.007(19)	+10.0±0.46
49	13	0.694±0.016(12)	+9.0±1.56

Statistical reliability of measurement of gain is seen to be similar to the other three subjects, as depicted in Figures 4, 6 and 7 (note that the vertical bars in Figures 6 and 7 give standard deviations). However the reliability of mean estimates of phase varied widely. For example in tests conducted on control days (D_1, D_{2A}) the variability within a test run was on the same order of magnitude as the accuracy of measurement (S.D. = 1.56^{o} and 1.93^{o} respectively), whilst during the period of initial habituation (e.g., D_3 - D_{11}) there was more than a tenfold increase in the variability. Thereafter, except for occasional runs with high variability (e.g., D_{16A}), consistency within runs tended to improve. After the return to normal vision, except for the test made half an hour later (D_{28C}), consistency tended to improve further, quickly (D_{29B} onwards) returning to levels similar to those seen on the original control days.

Figures 16 and 17 add perhaps some insight into both the short and long-term variability of phase. Both these figures plot results projected on the gain-phase plane of the three dimensional display in Figure 13. In Figure 16 the half filled circles give the values of gain and phase obtained from single cycles of a control run prior to donning the prisms. The closed circles give corresponding values obtained during the afternoon run on D_8. Evidently, there was wide variability of phase, but not gain, from cycle-to-cycle during this run. The closed circles with cross (⊗) give similar

data obtained from the noon test run of D_{18}. Of particular interest is the apparent continuity links between the three sets of data, suggesting that some physiological criteria are forcing a particular pattern of relationship between gain and phase, even when there is variability of these parameters within a run

(Fig. 16 near here)

This conclusion is strongly supported by the data in Figure 17, which plots the mean values of gain and phase obtained on individual days throughout the whole seven week experiment. The similarity of interdependence between the gain and phase in this plot and the preceding one (Fig. 16) suggests that such fluctuations are by no means arbitrary in nature. Physiological implications of these observations will be discussed below, and developed in a subsequent article, which explores a simple but plausible neurophysiological model that could readily account for these apparently complex interrelations.

(Fig. 17 near here)

As with the earlier medium-term experiments, all test runs were followed immediately by measurement of vestibulo-ocular response in the absence of vision with the sagittal plane of the head in the plane of turntable rotation. Figure 18 shows sample records of "vertical" nystagmus obtained during this form of stimulation, the upper trace being obtained during a control run on D_2 before donning the prisms,

Fig. 16.

Changes in vestibulo-ocular gain ($\dot{\Theta}e/\dot{\Theta}h$) as a function of the phase relationship between stimulus (1/6 Hz oscillation at 60^{o}/sec velocity amplitude) and response (eye movement relative to the head). Each point represents the phase and gain value for one cycle in a run before vision reversal (◐), and in runs 7 days (●), and 17 days (✱) after donning the prisms. It is seen that control values for phase are slightly phase-advanced at this frequency, and that the reversed visual stimulus causes substantial phase-lag.

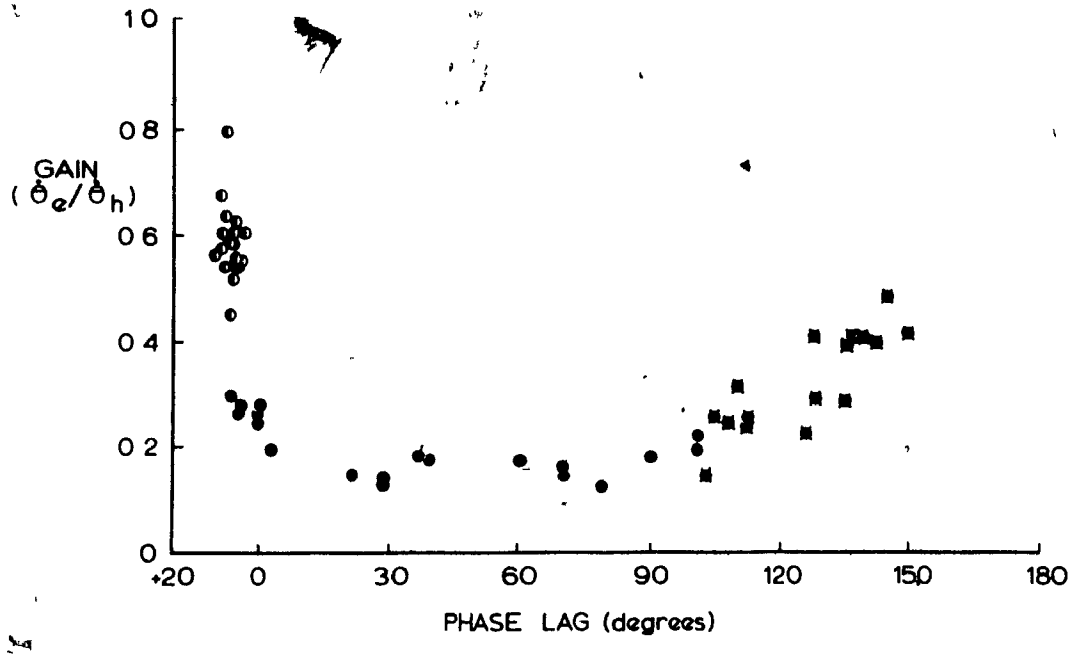
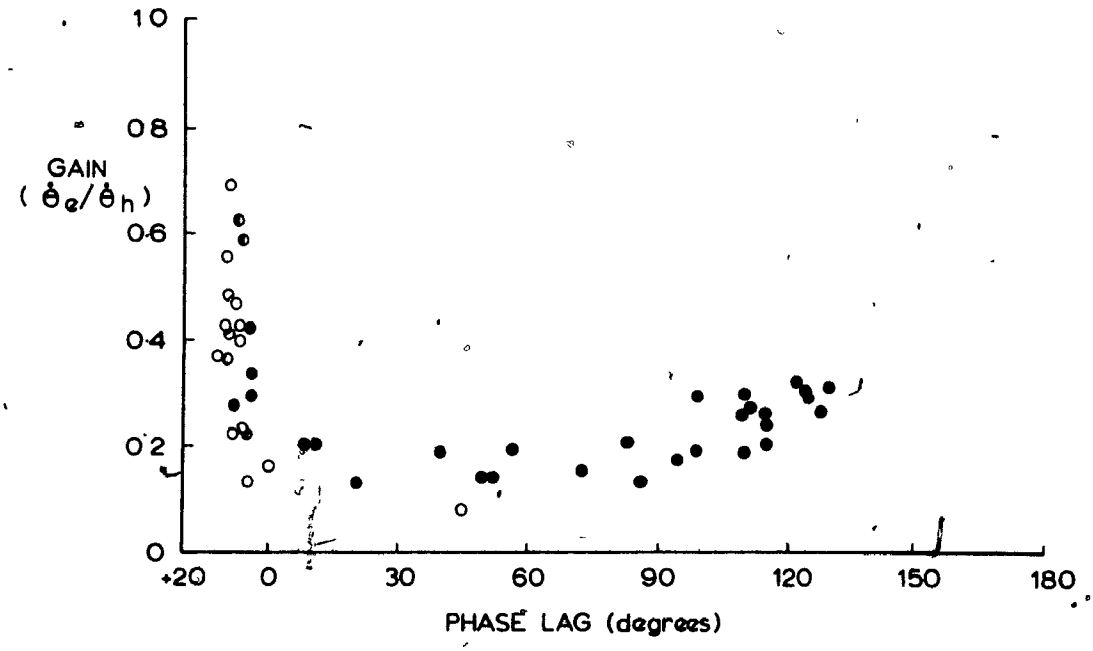

GAIN
(θ_e/θ_h)
1.0
0.8
0.6
0.4
0.2
0
+20
0
30
60
90
120
150
180
PHASE LAG (degrees)

Fig. 17.

The gain-phase relationship of stimulus and response in the 49 day experiment. Each point represents the mean values of gain and phase for an entire run (up to 20 cycles) before (◐), during (●), and after (○) reversal of vision.


1·0
0·8
GAIN
(θ̇c/θ̇h)
0·6
0·4
0·2
0
+20
0
30
60
90
120
150
180
PHASE LAG (degrees)

and the lower trace on D_{28}. Evidently, despite radical changes of both gain and phase in the horizontal plane of the head between these two days, there was no significant change in either of these characteristics in the sagittal responses obtained before and at the height of the habituation process ($P < 0.5$).

(Fig. 18 near here)

Figure 19 shows there was no significant change in the sagittal response from beginning to end of the seven week experiment. From this and the previously mentioned observations in other subjects, it seems one may conclude with assurance that the habituating process is subject to high specificity with respect to the plane of vision reversal.

In addition, these latter observations permit the use of the sagittal response as an internal control, indicating that gain attenuation even in the horizontal plane is unlikely to have been due simply to failure to maintain an adequate level of arousal. Of incidental interest is the fact that sagittal VOR gain was consistently close to one, whereas the normal control response in the horizontal plane was consistently close to 0.6. Implications of this difference will be discussed below.

(Fig. 19 near here)

Fig. 18.

Extracts from original records of eye position relative to head angular velocity in the sagittal plane, in the 49 experiment. $V_s(D_2)$ is a control run just prior to donning the prisms, whilst $V_s(D_{28})$ is from a run on the 27th, or final day of prism-reversal. Format is as in Fig. 9.

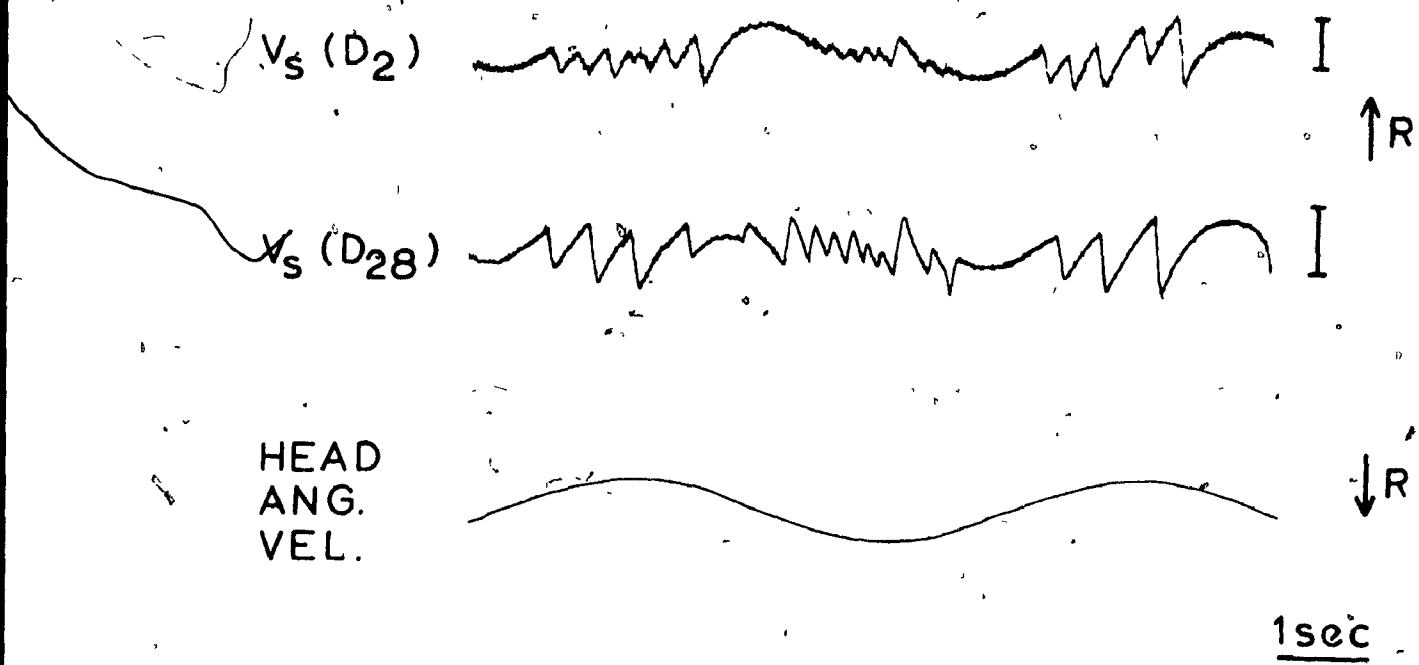
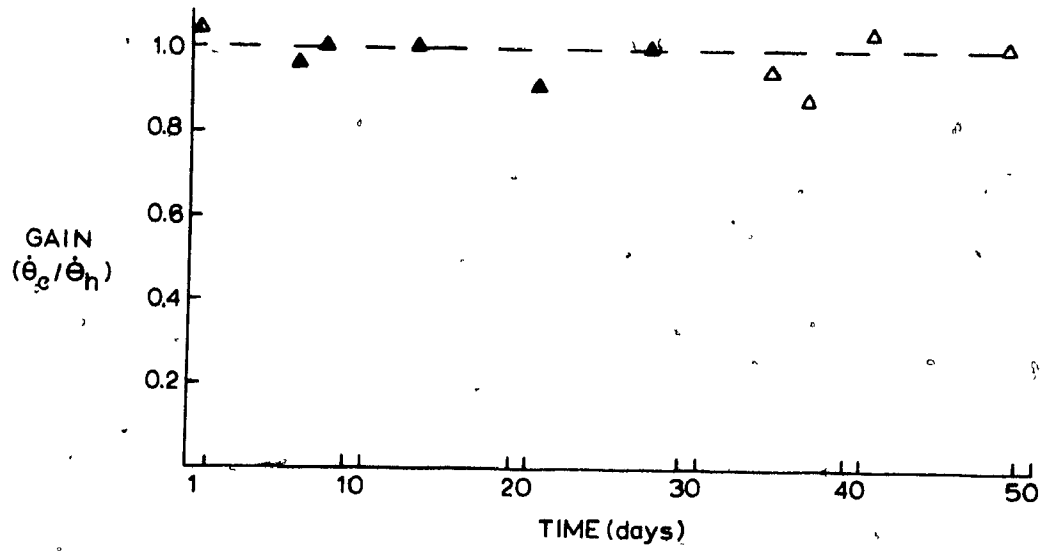

V_S (D_2)
I
R
V_S (D_{28})
I
HEAD
ANG.
VEL.
R
1sec

Fig. 19.

The changes in vestibulo-ocular gain ($\dot{\theta}e/\dot{\theta}h$) during oscillation in the sagittal plane, in the 49 day experiment. Each point represents the mean value for an entire run (20 cycles) in the sagittal plane before (△), during (▲), and after (△) vision reversal. Typical cycles within such runs are seen in Fig. 18.


GAIN
$(\dot{\theta}_c/\dot{\theta}_h)$
1.0
0.8
0.6
0.4
0.2
1
10
20
30
40
50
TIME (days)

DISCUSSION

What is Habituation?

As a general concept, habituation has been described as a gradual waning of responses to repetitive stimuli applied without reinforcement (Thorpe, 1950, 1963). Humphrey (1933) saw it as an adaptive process which permits an animal to ignore stimuli which do not have significance for preservation. He interpreted this as a form of learning with a universal character throughout the animal kingdom. Thompson and Spencer (1966) were more detailed in their description of the habituation process, and specified the following criteria: (1) Repeated stimulation causes response decline, the latter being (2) more rapid with frequent rather than with spaced stimulus presentation; (3) habituation is commonly specific for a given stimulus or input; (4) the magnitude of the habituated response can be restored by withholding the stimulus; and (5) the habituation rate increases with each new series of trials separated by intervals of spontaneous recovery.

Previous Findings

In a similar fashion, investigators of vestibular habituation have for many years considered habituation to be an attenuation, or response decline, due to monotonous repetition of an indifferent, useless, or inadequate stimulus (Forsmann, Henriksson and Dolowitz, 1963), which could often be returned to its full intensity by

countering the concomitant loss of arousal with specific mental tasks (Collins 1964a). For prolonged and repetitive vestibular stimulation the response attenuation could therefore be accounted for in part by a transient arousal factor as well as an adaptation to the vestibular stimulus per se (Guedry, 1965a, 1974).

However, most of these vestibular experiments have employed sustained cupula deflection as the adequate sensory stimulus. But this is not a normal occurrence in natural life, and the question arises whether similar attenuation of physiological response would take place using stimuli which are within the frequency and angular velocity range of natural semicircular canal stimulation. Some insight into the answer to this question was provided by the first experiment of this series (Gonshor and Melvill Jones, 1974a), in which aroused subjects were rotated sinusoidally in the dark at 1/6 Hz and 60^{o}/sec velocity amplitude for up to 1hr/day (200 cycles), for 3 days. No significant changes in the measured vestibulo-ocular reflex (VOR) were detected, which contrasts strongly with the reductions observed during similar, or even shorter, durations of unilateral rotational stimulation of man (Collins, 1964a), rotational and caloric stimulation in cat and dog (Collins and Updegraff, 1966), and caloric stimulation in monkeys (Komatsuzaki et al, 1969). This led us to the conclusion that repetitive vestibular stimulation in itself does not necessarily lead to response decline. What then are the criteria responsible for establishing a changed relationship between stimulus and response.

The second experiment in this series (Gonshor and Melvill Jones, 1974b) set out to examine the possibility that such change would be

generated when its occurrence represents a functional advantage. For this a mirror-reversed visual tracking task was superimposed on the non-habituating sinusoidal vestibular stimulation used in the previous experiment. The results were striking. During periodic tests of VOR gain performed in the dark each day of the three day experiment, and with the subject highly aroused, there was marked attenuation in the VOR to the previously non-habituating stimulus. The results of this experiment raised an important issue. Should, and could one still consider habituation to be mere attenuation to monotonous stimuli; or does habituation really represent an attempt by the organism systematically to restructure its neurological characteristics in such a manner as to optimize new stimulus-response relations? In the above experiment, for example, the ultimate goal of such reorganisation would extend beyond mere attenuation to complete reversal of the vestibulo-ocular reflex. The former calls for a suppression of activity, in contrast to the latter which would necessitate excitation of relevant components of the reflex response. Evidence against the theory of simple depression of activity is provided by experiments at the neuronal level by Precht, Shimazu and Markham (1966). Following unilateral labyrinthectomy in the cat, they recorded from vestibular neurones in the vestibular nuclei. After initial depression of activity in the acute stage (3-4 days after the operation), they obtained recovery of spontaneous discharge of Type I neurones in the chronic, or "central compensation" stage (30-45 days after the operation). In Type II neurones on the side of

the chronic labyrinthectomy the threshold for frequency response to angular acceleration returned to almost normal range. This indicates that mere attenuation of response is most probably a component of a much more complex interaction taking place at the neuronal level.

Present Findings

In the second experiment simple attenuation was found to occur, but only when system was faced with vision reversal. However, the relatively short duration of that 3 day experiment did not permit an answer to the question of whether reversal of the VOR would ultimately occur. Thus there was a need for a longer term approach, which led to the present experiment.

1. Changes in Gain and Phase

The outcome described in results above lead one to the conclusion that neither simple attenuation to zero gain, nor a simple reversal of the VOR takes place. Rather, there are a complex series of changes in both gain and phase, falling into 5 recognizable stages. The first stage is a rapid and significant decrease of the VOR gain to 30 or 40% of its pre-stimulus level. Within the first two stimulus days the phase changes at this stage are not marked. The second stage (days 3 to 14) comprises almost exclusively large and continuously varying changes of phase. In the third stage (days 14 to 28) plateau levels of both gain and phase are reached, which for the 1/6 Hz frequency used in this

experiment amounted to 40% of pre-stimulus gain values and 125° phase lag respectively. The fourth stage takes place immediately after removal of the prisms and last only a few hours. During this time the phase returns rapidly to normal, whilst the gain drops slightly. This extremely rapid recovery of normal phase is striking and may be an important clue in determining the underlying physiological mechanisms responsible. The fifth and final stage consists of a slow return over 3 to 4 weeks to normal VOR gain with no further change of phase. It is interesting that the medium-term experiments in the present study demonstrated almost exclusively the changes of stages one and five. It was only with the 49 day experiment that the complex but highly systematic changes in phase and gain were manifest in an analyzable form. Attempts are now underway to elucidate these interactions by means of systems modelling, and preliminary results seem to indicate that a rather simple model of sine-wave summation in a feedforward network may account for many of the present results.

2. Geometric Specificity

The results demonstrated a high degree of geometric specificity, in that response modification was strictly confined to the plane of vision reversal. Similar specificity has been observed in conventional attenuation experiments (Guedry, Collins and Graybiel, 1964), where lack of transfer of vestibulo-ocular changes to different planes of rotation was shown in subjects allowed free movement in a slow rotation room being rotated continuously in one direction. In

this connection it is interesting to note that each parallel pair of canals is functionally specifically related to approximately parallel pairs of extra-ocular muscles in each eye (Lorente de Nó, 1933; Szentágothai, 1950). In experiments with dogs and cats, Szentágothai (1950) stimulated individual canals with artificially induced endolymph currents, and found short latency responses in only one muscle of each eye. Confirmation comes from cat experiments (Cohen, Suzuki and Bender, 1964) in which high frequency repetitive pulse stimulation of primary afferent vestibular fibers from one canal produced short latency excitation in one corresponding oculomotor nucleus. This same specificity of one canal to one muscle relationship has recently been observed in rabbits (Ito, Nisimaru and Yamamoto, 1973a, b), with the added important feature that the same canal has a short latency inhibition on the antagonist muscle.

3. Directional Preponderance

The directional preponderance outlined in Figure 12 was a response characteristic seen during the period of most rapid change in the reversed vision environment. It is thought that this may represent the transient imbalance in differential input to the oculomotor system, derived from the bilateral vestibular one. In this regard some recent relevant findings have been reported by Mathog (1972) with tests of the vestibular system during sinusoidal angular acceleration. Normal subjects showed negligible directional preponderance and variability, whereas subjects suffering from Menière's disease or surgical labyrinthectomy produced marked

directional preponderance. Furthermore, in those patients who recovered from their injuries, there was a tendency to return to symmetrical nystagmus.

It is clear that the attenuated responses seen in selected situations of repetitive stimulation are not alone responsible for the response changes seen in the present experiments, but rather it seems that a complex series of changes occur, the ultimate goal of which is no different from that required in normal action; minimization of image slip on the retina so as to assist fixation of the visual image during head rotation.

4. Effect of Subject Age

The results of these experiments negate any differences due to age, since similar results were obtained from subjects ranging in age from 20 to 50.

5. Subjective Effects

The subjective effects coincident with vision reversal have long been of great interest to psychologists (Harris, 1965; Howard and Templeton, 1966). The complete reversal in perception of the visual world, reported by many of these experimenters, was not confirmed in any of the present experiments, although visual-motor coordination in the reversed visual environment improved through to the last day of vision reversal. Fatique, dizziness, depression and nausea, often experienced during conditions of vision reversal, were encountered as well by the subjects in the present experiments, so that modifications were made in the protocol of the final 3 experiments to minimize their

effect. It is interesting in this regard that in the recent flights of the "Skylab" orbiting space station, astronauts have reported very similar symptons, complaining of nausea and fatique, and exhibiting an unusual degree of overall lethargy (Homick, Reschke and Miller, 1974).

In accounting for the lethargy, fatique and nausea, several possibilities come forth: (1) The effects may be due in part to the fact that motor patterns, which have become internalized into mature automatic response are now forced to change, making it necessary for the subject to consciously produce each movement of the new patterns. This could account especially for the fatique, lethargy, and depression that is observed. (2) The subjective symptons may be caused by the antagonism in the vestibular and reversed vision stimulation. The importance here would be the conflict of input information rather than any vestibular effect per se, since no such symptoms are in evidence under normal circumstances, where no antagonism takes place. (3) The possibility exists that the subjective symptoms are a direct effect of the habituation process itself. That is, the symptoms may be an external manifestation of imbalance in the central nervous system, consequent to changes in neuronal elements as they move towards a physiological goal of optimisation in the condition of vision reversal.

Possible Mechanisms Responsible for Vestibulo-Ocular Changes

What mechanisms are responsible for the changes in vestibulo-ocular reflex produced in the present experiments, and where might

they operate in the nervous system?

1. The Reticular Formation

An area of the central nervous system that may play an influential role in the final oculomotor response to a given vestibular stimulus is the reticular formation of the brain stem. Lorente de No (1933), after interupting the basic three-neurone arc (Szentagothai, 1950) by lesioning the medial longitudinal fasciculus (MLF), observed that components of all the vestibular reflexes of the ocular muscles could still be elicited. If however the MLF was left intact, but the reticular formation and pons lesioned, the reflexes were abolished. Furthermore, both anatomical (Brodal and Pompeiano, 1957; Brodal et al, 1962; Hauglie-Hanssen, 1969), and neurophysiological (Eccles et al, 1967) evidence exists for circuits connecting the reticular formation with vestibular and cerebellar nuclei, and the cerebellar cortex, therefore placing the reticular formation in close contact with those centers that have important relationship to the vestibulo-ocular reflex pathway.

However, to what extent could known reticular formation characteristics contribute to the observed changes in gain and phase in the present experiments?

Gain: It is well established that the reticular formation is the prime center for the control of arousal (Moruzzi and Magoun, 1949). Furthermore, numerous experiments have shown that vestibulo-ocular gain will decrease with lack of arousal (Wendt, 1951; Guedry and

Lauver, 1961; Collins and Guedry, 1962), therefore implicating the reticular formation as an important center for control of vestibulo-ocular gain. Although this may be the case, in the present experiments arousal was maintained at all times, therefore negating that reticular formation effect.

Phase: It has been postulated that an important function of the reticular network's influence on the oculomotor nuclei may be as an integrator between neural information flowing from vestibular to oculomotor nuclei (Cohen, 1971; Skavenski and Robinson, 1973). However, even if one were to postulate complete reversal of this integrator, it could only produce a maximum of 90^{o} phase shift in the final response; much less than the 130^{o} phase lag observed. Although this does not rule out the reticular formation, it does cast doubt on its being the prime mover in the present case.

Saccades: Evidence that the reticular formation is performing its normal function comes from the present observations that saccades are not changed dynamically, indicating no interference with the normal triggering and synchronization of saccade discharge described by Robinson (1964). In addition, the saccades are always appropriate in direction for the smooth pursuit, even when the latter is reversed. This favours the view that the signal modification is taking place "upstream" of the reticular formation. The smooth pursuit and saccades would then be driven by the reticular formation as before vision reversal, but with a modified incoming signal.

2. Vestibular Efferent System

The vestibular system is a second mechanism by which changed patterns of stimulus-response could be brought about. Efferent nerve fibers have been shown to project directly to the peripheral vestibular end organ (Leidler, 1916; Engstrom, 1958; Gacek, 1960), and their effect seems to be an inhibitory one (Llinás and Precht, 1969). Efferent fibers show increased discharge frequency during angular accelerations in the ipsilateral and contralateral directions (Precht, Llinás and Clarke, 1971). Since the increase in frequency due to contralateral rotation must come from impulses arising in the contralateral labyrinth which eventually reach the efferent neurone through multisynaptic chain, it allows for the possibility that a feedback system may be responsible in part for the adaptation to on-going vestibular stimulation.

Recently, extralabyrinthine inputs to the efferent fibers, such as passive movement of limbs and cutaneous stimulation, have been described (Schmidt, 1963; Llinás and Precht, 1969). Schmidt, Wist and Dichgans (1970) observed a close relationship between saccadic eye movements and modulation in discharge of efferent fibers in the peripheral vestibular nerve, with the efferent discharge modulation occurring about 100 msec before the start of the optokinetically induced saccades. This modulation persists after the eye muscles are paralyzed, indicating an independence from proprioceptive eye muscle afferents.

It seems clear that various sensory inputs can influence the

vestibular end organ via efferent fibers. The functional meaning of this innervation is still not understood, although it seems doubtful that it could, on its own, account for the type of vestibulo-ocular changes manifest in the present series of experiments.

3. The Cerebellum

Although the reticular formation and efferent vestibular system undoubtedly can play a role in modification of the vestibulo-ocular reflex, it is the cerebellum that has received the most experimental attention. As far back as 1935 Halstead gave experimental evidence suggesting strongly that cerebellar lesions could affect the habituation of vestibular nystagmus in pigeons. Di Giorgio and Pestellini (1948), Di Giorgio and Giulio (1949), and Menzio (1950), were able to show that guinea pigs with lesions of the tuber vermis did not show habituation. Ablation of the nodulus in the cat led to prolonged vestibular reactions to rotatory and caloric stimulation, positional nystagmus, and disequilibrium (Fernandez and Fredrickson, 1963). On the other hand, stimulation of the nodulus in that study led to partial inhibition of nystagmus. Very recently Ito, Shiida, Yagi and Yamamoto (1974a, b) have investigated the influence of the cerebellum on the VOR during head rotation with various forms of visual stimulation. Their results indicate that visual signals which were able to change vestibularly induced eye movements with an intact cerebellum were unable to do so after removal of the flocculus. Removal of other portions of the

cerebellum, as well as large areas of the cerebral cortex did not have a similar effect.

In addition to ablation studies a very close relationship of the cerebellum and the vestibular system has been demonstrated by comparative anatomical studies (Allen, 1924; Dow, 1936; Jansen and Brodal, 1958; Walberg and Jansen, 1964; Brodal, 1960; Brodal et al, 1962; Angaut and Brodal, 1967). Both primary and secondary vestibular afferents enter the vestibulo-cerebellum; travelling mostly to the flocculus, nodulus, ventral uvula and paraflocculus (Brodal and Høivik, 1964), which in turn send Purkinje axons back to the vestibular nuclei either directly (Angaut and Brodal, 1967), or by way of the fastigial and other cerebellar nuclei (Brodal, 1960). Moreover, these cerebello-vestibular terminations coincide with the sites of projection of vestibular primary afferents (Angaut and Brodal, 1967; Gacek, 1969). Corroborating neurophysiological evidence has recently been reviewed in detail by Eccles et al (1967). Specifically, direct eighth nerve primary afferent fibers activate Purkinje cells in the vestibulo-cerebellum via mossy and climbing fiber systems in the frog (Llinás, Bloedel and Hillman, 1969; Precht and Llinás, 1969), and by means of mossy fibers to the flocculus and nodulus in the cat (Eccles et al 1967; Precht and Llinás, 1969). Monosynaptic inhibition by Vermal Purkinje axons of Deiters neurones; receiving excitatory otolith input (Peterson, 1967), has been demonstrated by Ito, Yoshida and Obata (1964). Similarly, termination of floccular fibers onto portions of the vestibular neurones concerned

with semicircular canal function (Shimazu and Precht, 1965) has recently been found to be inhibitory in nature (Ito, Kawai, Udo and Sato, 1968; Shimazu and Smith, 1971; Baker, Precht and Llinás, 1972a), as well as being the major cerebellar action on the vestibulo-ocular reflex (Ito et al, 1970). That this floccular inhibition is exerted on both excitatory and inhibitory transmission was finally demonstrated by Baker et al (1972b). The suggestion that the vestibulo-ocular reflex may be under a direct cerebellar control is further substantiated by findings that ipsilateral horizontal angular rotation will cause changes of discharge frequency in floccular Purkinje cells (Llinás, Precht and Clarke, 1971) very similar to those seen in vestibular second order neurones in the vestibular nuclei of the brain stem (Shimazu and Precht, 1965).

Ito (1970) has postulated that by receiving vestibular afferents and sending Purkinje axon input to the vestibular nucleus neurones in the cat (directly to oculomotor nuclei in fish - Kidokoro, 1968), the vestibulo-cerebellum acts as a "feedforward" control system. More specifically, the flocculus is able to modulate the vestibular neurones so as to produce the most exact eye compensation for changes in head position. It is interesting that when the flocculus is destroyed or impaired, eye compensation is impaired during rotation (Dow and Manni, 1964), and post-rotatory nystagmus is changed (Lorente de Nó, 1931). Of more direct relevance is the fact that removal of the cerebellum substantially modifies the transfer function relating rotational eye

response to rotational stimulation of the canals (Carpenter, 1972).

How does the flocculus "learn" what optimum compensation is necessary on a moment by moment basis. The most logical means would be input from the visual system, and such visual information has very recently been demonstrated to reach the flocculus through a network leading from the accessory optic tract, to the central tegmental tract, through to the inferior olive, finally reaching the flocculus Purkinje cells as a climbing fiber input (Maekawa and Simpson, 1972; 1973). This latter input is reflected in a depression of certain vestibulo-ocular reflexes, which in the rabbit occurs only in those pathways which arise from the horizontal canals and innervate the ipsilateral horizontal eye muscles (Ito, Nisimaru and Yamamoto, 1973c). No such visually-effected depression was found for the posterior and anterior canals, or when the ipsilateral flocculus was lesioned. With such a system at work, image slip on the retina due to insufficient eye compensation would initiate signals to the cerebellum, that alterations in performance are required to minimize the blurring of the visual field.

Experiments by Klinke (1970) have raised the intriguing question of whether active optokinetic drive and subsequent reduction in image slip, such as described above, is necessary to produce the vestibular modification. Klinke worked with completely motionless and relaxed (Flaxedil) gold fish, recording from vestibular primary afferents while providing an optokinetic stimulus in the form of a moving pattern of

stripes. Although eye movements were not possible, due to the muscle paralysis, modulation of primary vestibular afferent activity was obtained. He postulated, therefore, that the intention to move the eye is in itself a sufficient input to produce a change in firing patterns in vestibular units, in such a manner as to assist retinal image stabilisation during the actual performance of active body motions. This would be an elegant example of the psychological principle of "efference copy" (von Holst, 1954), which states that the voluntary command to act, in addition to sending motor input to the muscles, also sets up in the nervous system an image, or "efference copy" of the message, and the "reafference" or sensory activity that arises as a result of the motor action is compared to this copy. Therefore if the eye muscles are paralysed, the voluntary attempt to move the eyes, say due to an optokinetic stimulus, produces an efferent copy but no moving retinal image. The environment should therefore appear to move in the direction of the voluntary effort to move the eyes.

Although eliminating muscle movement, this experiment does not eliminate retinal image slip, which indeed would produce the effects of the postulated efferent copy. Hence, one cannot assume efference copy is at play until vision is excluded in those experiments. Until then it must be assumed that Klinke's effects were due to image slip on the retina.

Thus, not withstanding Klinke's findings, it appears plausible that the vestibulo-ocular reflex system can be driven by purely retinal

optokinetic stimuli to facilitate what amounts to optokinetic tracking. Neurophysiological observations similar to those of Ito et al (1973c) have been observed in experiments on alert monkeys (Henn, Young and Finley, 1974). They recorded from units in the medial vestibular nucleus during visual stimulation, consisting of horizontal motion of projected stripes on a cylindrical screen. Results showed that even though there was no head movement, and thus no vestibular stimulation, cells in the vestibular nucleus were nevertheless affected, such that a unit which was normally excited by head acceleration to the left was now also excited by motion of the stripes to the right. In the case of man this produces a sensation of turning to the left. They contend that modification of the vestibular units could explain the human psychophysical phenomenon of "circular vection" (Dichgans and Brandt, 1972), in which a sensation of self-rotation can be induced without vestibular stimulation by a moving visual surround.

The pathway from the retina to floccular Purkinje cells is not the only feedback from the ocular region. Rapid stretch of the oculomotor muscles in the cat have generated clear field potentials in the cerebellum (Fuchs and Kornhuber, 1969), mostly in lobules V, VI, and VII of the cerebellar vermis (Baker et al, 1972c). This pathway seems to play a role in control of saccades (Ron and Robinson, 1973) and be involved in continuous updating information prior to its execution (Wolfe, 1971) with feedback provided by extra-ocular muscle spindles. It is noteworthy that the vermis has connections

to portions of the vestibular nuclei by way of the intracerebellar nuclei (Jansen and Brodal, 1942), although it avoids many of the areas of terminations of the direct cerebellar fibers (Brodal, 1960). Recent neurophysiological evidence indicates that this input is inhibitory on the target neurones in the vestibular nuclei (Precht, personal communication). The relationship of all the ocular inputs to the cerebellum has still to be determined.

Because visual information comes to the cerebellum by way of climbing fibers, while vestibular afferents utilize the mossy fibers, Ito (1973) has suggested that this differential input to the flocculus allows the climbing fibers to produce changes in transmission through the synapses transferring mossy fiber signals to Purkinje cell dendrites. This fits well with the suggestion that the cerebellum acts here as a "perceptron" (Marr, 1969), with the mossy fibers providing information on the state of the vestibular signal, while the climbing fiber visual input corrects the discrepant performance of the cerebellum through changes in transmission through the synapses which transfer mossy fiber signals to the dendrites of Purkinje cells.

The results of the present experiments bear out the intimate relationship of the visual and vestibular systems. Not only can the vestibulo-ocular reflex be excited or suppressed by appropriate retinal stimuli, but the influence can be so versatile as to bring about effectively complete reversal of the vestibulo-ocular reflex of man as a retained response consequent upon long-term optical reversal of vision. The implication of vestibular cerebellum participation in

long-term visual modification of the vestibulo-ocular reflex has very recently been similarly demonstrated in rabbits (Ito, Shiida, Yagi and Yamamoto, 1974a), with the feature that no such modifications took place in those rabbits whose flocculus had been removed beforehand. Although unable to achieve the reversals of response seen in the present study, Robinson (oral presentation, Stockholm Symposium, 1974) has shown that attenuation of normal vestibulo-ocular response induced in cat by vision reversal, is abolished by removal of the vestibular cerebellum.

The cerebellum therefore appears at this time to be a prime candidate for the mechanism responsible for producing the vestibulo-ocular changes in these experiments. If this assumption is borne out by future neurophysiological experimentation it would prove to be an important example of how the cerebellum, and for that matter the central nervous system in general, can radically alter the input-output characteristics of a stimulus response relationship when there is a functional need to optimize for a clearly defined physiological goal.

CHAPTER 6

IMPAIRMENT OF VISUAL FIXATION ASSOCIATED WITH CHANGES IN THE VESTIBULO-OCULAR REFLEX INCURRED BY LONG-TERM VISION REVERSAL IN HUMANS

SUMMARY

1. Functional impairment of visual fixation during both fixed and continuously varying frequencies of head oscillation, optokinetic response to target oscillation, and saccadic performance, were investigated during long-term vision reversal in humans.

2. Tests of voluntary, sinusoidal head oscillation, showed that the gain (eye angle/head angle) of response decreased as a function of the days of reversed vision stimulation. For 1.75 Hz and 3 Hz oscillation, gain fell 80% and 60% respectively, with no concomitant phase changes.

3. Voluntary head oscillation through frequencies from 0.15 to 6.25 Hz showed increasing gain with frequency, from 0.5 Hz upward. Control tests produced no concomitant phase shifts, but similar tests during the 4 week period of reversed vision produced a continuum of phase shifts as a function of frequency.

4. The vision reversal produced no change from the normal characteristics of optokinetic and saccadic performance.

5. It is concluded that changes in the vestibulo-ocular reflex due to long-term vision reversal do cause functional impairment in visual fixation.

INTRODUCTION

The present report describes a continuation of the study on adaptability in the vestibulo-ocular reflex arc, begun in a series of previous articles (Gonshor and Melvill Jones, 1974a, b, c). In the most recent study subjects were exposed to a prismatically-reversed visual environment for prolonged time periods, lasting up to 27 days. During each day, tests sessions were held, each session encompassing a variety of experiments. In that study (Gonshor and Melvill Jones, 1974c) a detailed account was given of one of these tests: Vestibulo-ocular response, in the dark, to low frequency oscillatory rotation (1/6 Hz, and 60^{o}/sec velocity amplitude). The results showed that the reversed visual environment had caused profound changes in the vestibulo-ocular response, amounting to a functional reversal of the reflex.

It was of further interest to examine what effects such profound vestibulo-ocular reflex changes would have if the subject was permitted brief periods of vision, whilst not wearing the reversing prisms. Put another way, the object of the present experiments was to examine what functional deficits the subject incurred due to the changed vestibulo-ocular reflex. These experiments include the following measurements:

(A) Vestibulo-ocular response during,

1. Voluntary high frequency head oscillation at 1.75 and 3 Hz.
2. Voluntary head oscillation at continuously varying frequency.

(B) Optokinetic response in the absence of head movement.

(C) Saccadic performance in the absence of head movement.

METHODS

A detailed protocol for the entire experimental period has already been described in a previous article (Gonshor and Melvill Jones, 1974c). Briefly, 4 subjects were used in experiments lasting 4, 17, 25, and 49 days. Within these time periods they were required to wear reversing prisms for 2, 6, 7, and 27 days respectively. The prisms were of the "erecting" or "dove" type, and therefore permitted reversal of vision in only one plane of rotation; in this case the horizontal plane. The first day (D_1), and a portion of the second day (D_2), were always reserved for control runs. From D_2 onward, subjects wore the prisms during all waking hours of what will hereafter be called "vision reversal" days. Test sessions were held almost every day in the before, during, and post-vision reversal periods.

Measurement of head and eye movement

Head Movement. To measure high frequency and low amplitude head oscillations, a method was used that has previously been designed and constructed by Outerbridge and Melvill Jones (1971), employing principles detailed earlier by Robinson (1963). In this method two Helmholtz coils, fixed to the turntable which rotates the subject, receive an input from an oscillator, and produce a high frequency, and linear alternating

magnetic field. A light pick-up coil, fixed to the moving head, and midway along the axis of the Helmholtz coils, produces an oscillating voltage proportional to the sine of the angle between the magnetic field and the plane of the pick-up coil. Subsequent rectification then yields a proportionate DC voltage registering horizontal head rotation. Several benefits obtained by the use of this method are that linear movements of the head produce only very minor output variations due to linearity of the magnetic field, and there is negligible mechanical interference due to high frequency head motion, since the only moving component is a light pick-up coil with its fine output wire.

In the present experiment the pick-up coil was 1.5 cm in diameter and had 30 turns of insulated copper wire wound on a plexiglass holder. The support apparatus consisted of a light steel wire frame which fitted over the head. This frame attached to a plastic cylindrical post which in turn held the pick-up coil. This post separated the coil from small field distortions produced by the steel wire and allowed for adjustment of the angular position of the coil relative to the head.

Slip of the pick-up coil relative to the head has previously been assessed by Outerbridge (1969). In his experiment the head was voluntarily oscillated and the coil output compared with the output from an angular potentiometer connected to a suitable dental bite system. He showed that negligible slip occurred except at the highest frequency, namely 6 Hz. At this frequency the amplitude ratio and

phase of the pick-up coil output relative to a potentiometer measurement of head position was +0.12 and -5° phase lag respectively.

Eye Movement. Movements of the eyes in all the tests of these experiments were recorded by DC electro-oculography (EOG), as described elsewhere previously (Gonshor and Melvill Jones, 1974a).

Measurement of Subjective Blur

During head oscillation the subject was requested to assess the degree of apparent distortion of the radial lines on the target disc. (Fig. 1). This method has been found to provide a reliable index of small degrees of retinal image slip (Melvill Jones and Drazin, 1962). In this test, a 4 point scale was utilized by the subject to estimate blurring.

0 = No perceptible distortion

1 = Just perceptible distortion

2 = Apparent compression and extension of near horizontal lines

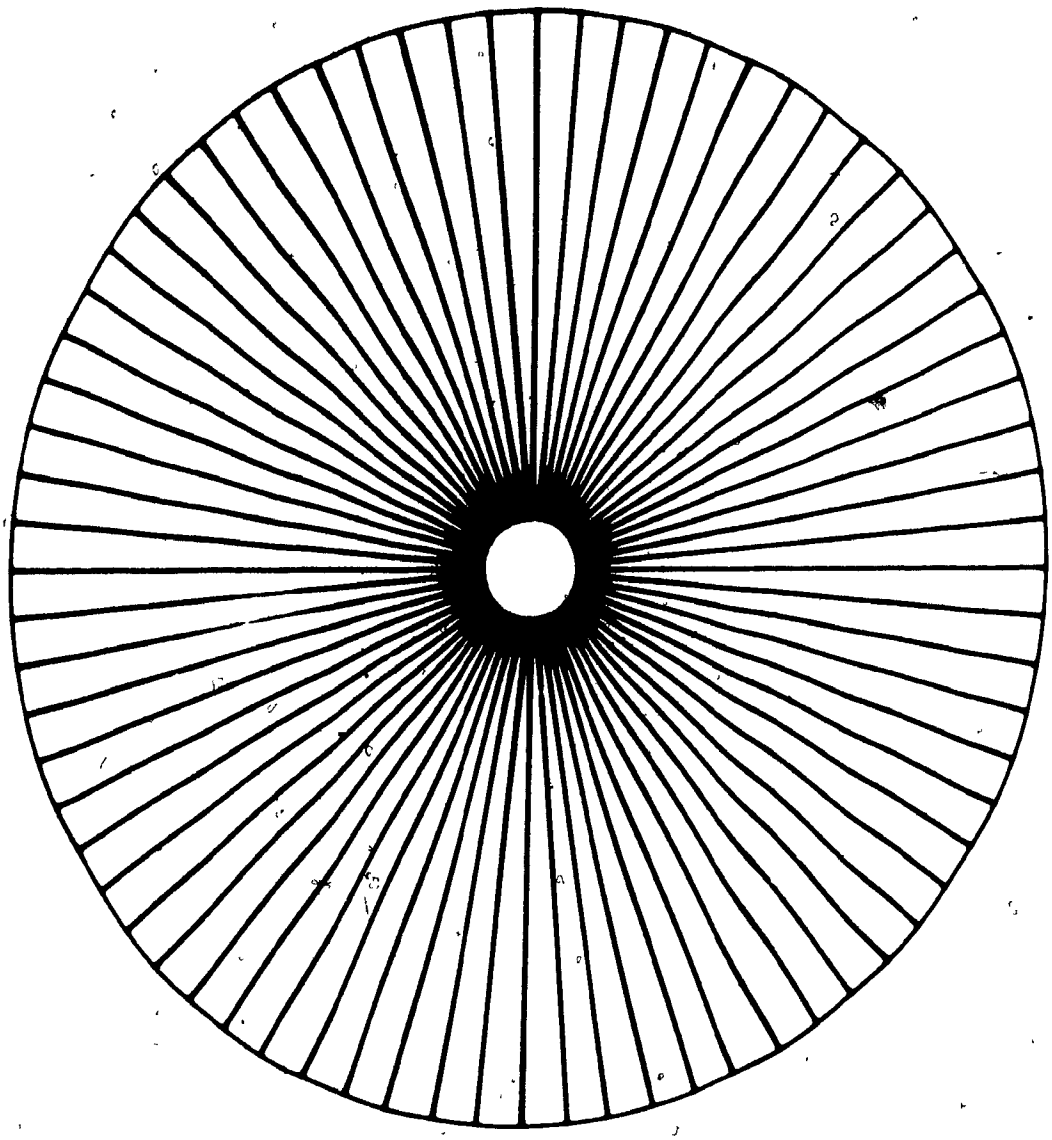
3 = Strongly established horizontal line standing out clearly against a blurred background.

Intermediate estimation values (e.g. 2.5, 3.5, etc.) were utilized when the subject felt that the extent of blur lay somewhere between the whole number values.

(Fig. 1 near here)

Fig. 1.

Radial Line Disc.



(A) Responses During Active Head Movement

1. . Steady State Responses At 1.75 and 3 Hz

Since the oscillatory head movement was voluntarily driven, a method was devised to keep both the head excursion amplitude and frequency constant. The output of head position from the pick-up coil was fed to an oscilloscope, where the horizontal plane oscillation of the head was monitored as an up-down movement of the scope beam. Two marker lines were placed on the scope face, representing a peak-to-peak head movement of 10^{o}. The subject was then instructed to practise moving the head in such a manner as to smoothly oscillate the beam from one marker line to the next. After several cycles of this practice procedure the subject continued the head oscillation, whilst fixating for the remainder of the run on the center point of a radial line disc attached above the scope face (Fig. 1). Both the practice and fixating procedures were performed during each run. The output from the oscilloscope led to both pen and tape recorders for permanent records.

To keep the frequency of head movement constant, the subject was instructed to follow a sinusoidally oscillating auditory tone. A high frequency tone of approximately 1000 Hz was modulated by a low frequency waveform generator, whose frequency was determined by the needs of the experiment. This modulated output was amplified and fed into a speaker which produced the desired frequency of tone modulation. After experimenting with various wave shapes, it was

found that the subject could move the head with the greatest ease and smoothness when following a sine wave tone. The records in Figures 2 and 3 show simultaneously recorded eye and head movement at modulated frequencies of 1.75 and 3 Hz respectively. From these records one sees that for the most part the subject was able to exercise a fair measure of control over both the excursion amplitude and frequency of the head oscillations. Eye movement calibrations consisted of eye movement to markers 10^{o} either side of a center point. Head movement calibration was accomplished by fixing the pick-up coil in the center of the magnetic field of the Helmoltz coils, and then manually rotating the turntable 10^{o} left and right. Both calibrations were performed before and after each test run. At the completion of the run at each frequency the subject gave an estimate of subjective blur, in the manner already described above.

2. Continuously Changing Frequency

After oscillating the head at 1.75 and 3 Hz, the subject was asked to voluntarily oscillate the head, with eyes open, through a sweep of frequencies from low to high and back to low. Instructions were to attempt to keep the amplitude of excursion constant at all times, and to fixate on the center of the radial disc. The frequency range employed extended approximately from 0.2 to 6 Hz. The position records of both head and eye were analyzed for gain (in this case θ_e/θ_h), by measuring the peak-to-peak displacements of the eye and head,

and then plotting the resulting ratio with respect to time or frequency. Phase measurements of stimulus and response were also estimated from peak values.

(B) Optokinetic Response In The Absence Of Head Movement

For quantitative information of visual following capability during the experiment the subject followed a radial line disc, which moved sinusoidally in the horizontal plane. The subject's head was fixed by means of a dental bite at a distance of 33 cm from the target. The peak-to-peak amplitude of target oscillation was constant at 7^{o}, subtended at the eye. Each subject was presented with a randomized series of frequencies, ranging from 0.4 to 3.6 Hz. For each frequency, the subject was instructed to fixate on the central portion of the radial disc until completion of the run. During this fixation period, the subject made an assessment of the degree of apparent distortion of the radial lines on the disc, according to the method of subjective blur estimation described above. In addition, the amplitudes of excursion of the target (constant) and the eye were obtained, and the resulting gain ($^{\Theta}e/^{\Theta}t$) was plotted as a function of the frequency of target sinusoidal oscillation.

(C) Saccadic Performance

The normal characteristics of human saccadic eye movement have

already been described in detail by Robinson (1964) and Fuchs (1967). In this experiment the subject, head fixed in position and without wearing the prisms, voluntarily moved the eyes to markers 10^{o} either side of a center marker. After initial calibration the subject produced a total of ten, to-and-fro eye movements, as quickly as possible, using the left and right markers. A final calibration was performed immediately after the experiment. High speed U-V paper galvonometer (flat frequency response; 0-3000 ±5%) recordings permitted an observation of the dynamics of the swift saccadic jumps.

RESULTS

(A) Response During Active Head Movement

1. Steady State Responses At 1.75 and 3 Hz

This series of tests was conducted during experiments of 17, 25 and 49 days, with vision reversal lasting 6, 7 and 27 days respectively. During each of the following tests the subject made voluntary head motions of approximately 10^{o} peak-to-peak amplitude with eyes open (without the goggles), while attempting to fixate on the center of a radial disc target 200 cm from the bridge of the nose. This relatively long distance was used to minimize the angular arc of lateral eye displacement subtended at the eye. Sinusoidal oscillations at both 1.75 Hz and 3 Hz were performed during each

test in random order.

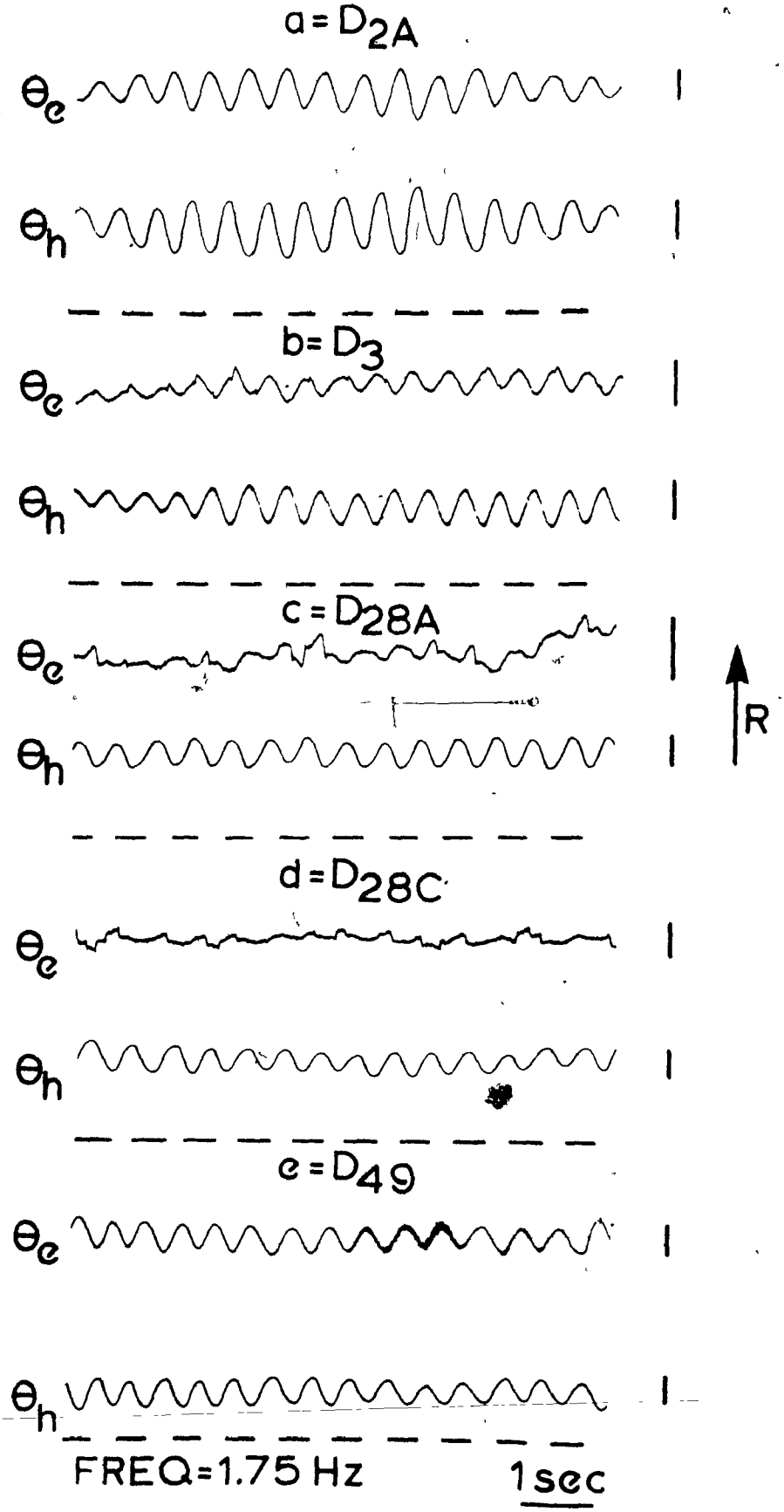
(Fig. 2 near here)

Figure 2 shows portions of original records at 1.75 Hz from selected days of the 49 day experiment. Figure 2a is a portion of a test run on day 2 (pre-vision reversal). The lower trace gives the subject's head position relative to space ($^{\Theta}h$), the upper trace being the resulting eye position relative to the head ($^{\Theta}e$). Note that due to the voluntary nature of the head motion, there was considerable variation in the amplitude of excursion during this particular test. Several features become apparent in Figure 2a. First, the gain of response (compensatory eye angle/head angle, or $^{\Theta}e/^{\Theta}h$) is very close to a value of 1 throughout, with the head and eye positions 180^{o} out of phase, as one expects for complete, and normal compensatory eye movement at this frequency. Secondly, the motion throughout the cycles is one of smooth pursuit, since the arc of head motion is not large enough to invoke saccadic flicks. This again is indicative of normal behaviour.

With only several hours of visual reversal (Fig. 2b), there is evidence of a rapid decline in the gain of response. This resulting decrease in efficiency of eye compensation for head movement makes pure smooth pursuit inadequate, so that saccades are introduced to return the fovea intermittently to the visual fixation point. The

Fig. 2.

Specimen records of voluntary head oscillation from tests in the 49 day experiment. All oscillations are in the horizontal plane, with eyes open (no prisms), at 1.75 Hz. θ_e represents the angular position of the eye relative to the head throughout the cycle. Similarly, θ_h denotes angular position of the head relative to space. (a) is a test before vision reversal (D_{2A}). (b) and (c) represent tests on the 2nd (D_3), and final day (D_{28A}) of vision reversal. (d) and (e) are tests less than 1 hour (D_{28C}) and 3 weeks (D_{49}) after termination of vision reversal. All calibrations = 10°, and R = right going movement. The same notation will be used in all the subsequent figures, unless otherwise stated.


a = D2A
θe
θh
b = D3
θe
θh
c = D28A
θe
θh
R
d = D28C
θe
θh
e = D49
θe
θh
FREQ=1.75 Hz
1 sec

records from D_{28} (Fig. 2c) represent the type of response observed from the second week of vision reversal until the latter's termination. That is, an almost complete breakdown of normal smooth pursuit compensation due not only to greatly attenuated smooth pursuit gain, but also to the frequent interjection of saccades. Figure 2c is also a good example of the subject's ability to produce consistent head oscillations at the desired amplitude - in this case for more than 15 cycles - therefore allowing sufficient cycles for meaningful averaging and statistical analysis.

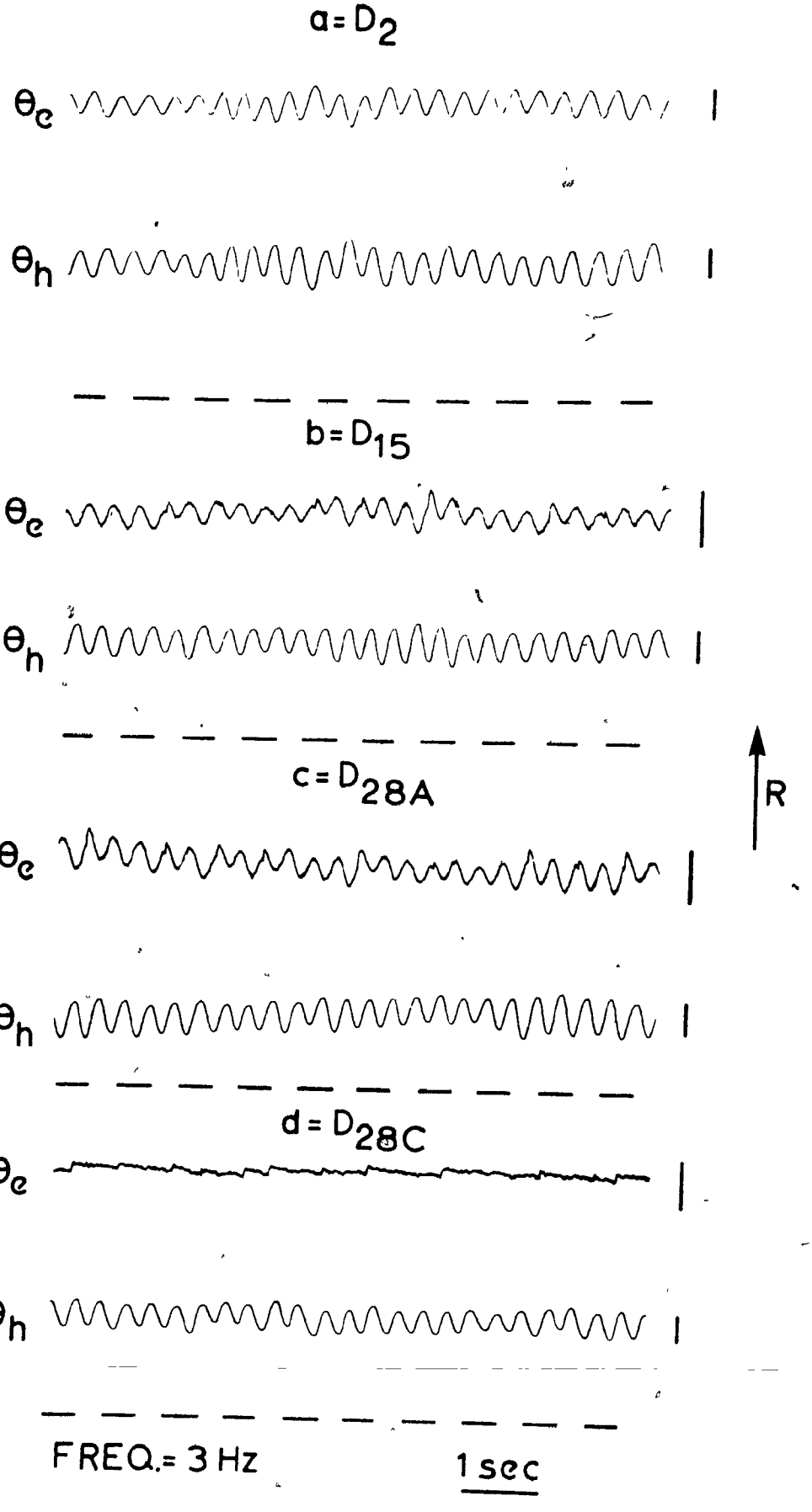
The rapidity of return to normalcy after removal of the prisms is seen in Figure 2d, which represents a test less than one hour after terminating (post) vision reversal. The efficiency of smooth pursuit eye compensation has begun to return as evidenced by the increased amplitude of response as well as the decrease in the frequency and amplitude of saccades. Note the variable calibration of eye movement. Figure 2e is a record made 3 weeks post-vision reversal, and shows the virtual return to normal smooth pursuit conditions.

(Fig. 3 near here)

Selected records from tests at 3 Hz are found in Figure 3. In Figure 3a one sees a portion of a pre-vision reversal test, showing normal compensatory smooth pursuit eye movement, similar to that

Fig. 3.

Extracts from original records of voluntary head oscillation at 3 Hz, in the 49 day experiment. (a) is from control test prior to donning the prisms (D_2). (b) and (c) represent tests on the 14th day (D_{15}) and the final day (D_{28A}) of vision reversal. (d) is a test less than 1 hour after removal of the prisms (D_{28C}). Symbols as in Fig. 2.


a = D2
θe
θh
b = D15
θe
θh
c = D28A
θe
θh
d = D28C
θe
θh
R
FREQ.= 3 Hz
1 sec

already observed for 1.75 Hz (Fig. 2a). Vision reversal again has the effect of disrupting this smooth pattern of response, but to a much lesser degree than at 1.75 Hz. Therefore the response at 3 Hz on D_{15}, although it exhibits decreased amplitude and interspersed saccades, is best compared to the 1.75 Hz test on D_3 (Fig. 2b), to which it comes closest.

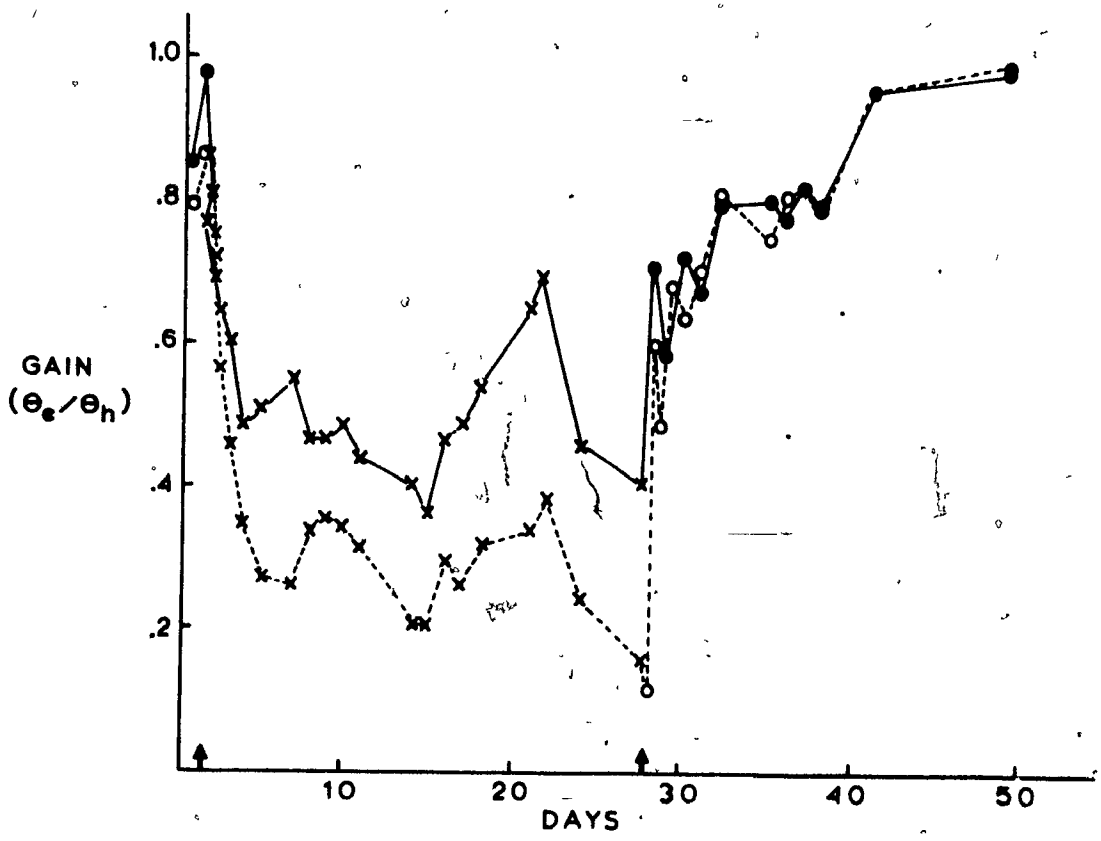
A response of interest occurred during a 3 Hz test, less than 1 hour post-vision reversal (Fig. 3d). The normal compensatory smooth pursuit eye movement is almost obliterated by a response bearing striking resemblance to vestibular nystagmus resulting from unidirectional rotation. To test if it could be due to a lack of fixating, the subject was instructed to do so, and still this response remained. It is most probably the low amplitude eye response to the head oscillation, with a substantial directional preponderance.

(Fig. 4 near here)

The similarity in the pattern of changes in response to voluntary head oscillation at 1.75 and 3 Hz, becomes apparent in the analyzed results of the entire 49 day experiment, in Figure 4. The ordinate shows gain of the smooth pursuit component of response ($^{\Theta}e/^{\Theta}h$) as a function of days in the experiment. To measure smooth pursuit, a method previously utilized and described was used (Gonshor and Melvill Jones, 1974a). In this method the saccadic portions of the response are omitted, leaving only the sequential compensatory

Fig. 4.

Changes in smooth pursuit gain ($^{\dot{\Theta}}e/^{\dot{\Theta}}h$) as a function of the 49 day experiment. The vertical arrows enclose the period of reversed vision. Each point is the mean value for up to 20 cycles of voluntary, sinusoidal head oscillation at frequencies of 1.75 Hz (– – – –), and 3 Hz (———). "x" represents runs during the period of vision reversal.


GAIN
(θ_e/θ_h)
1.0
.8
.6
.4
.2
10
20
30
40
50
DAYS

smooth movements in the cycle, the latter now describing the total change in eye position which would have occurred if the eye were capable of unrestricted rotation in the orbit. The ratio of this peak-to-peak eye displacement, or "cumulative eye position" (after Meiry, 1965), to that of the head, produced the measurement of gain ($^{\Theta}e/^{\Theta}h$). Each point in Figure 4 represents the mean vestibulo-ocular gain obtained from 10 cycles of head oscillation at 1.75 Hz (dashed lines) and 3 Hz (continuous lines). The vertical arrows on the abscissa enclose the period of vision reversal from D_2 to D_{28}.

The gain of response for both frequencies in the pre-vision reversal control runs is fairly close to one. However, it rapidly falls during the first four days following the start of vision reversal. From this point the gain for both frequencies varies considerably from day to day, although there does appear to be a general trend towards a small further decline up to the 28th day. Throughout the vision reversal period the gain of the vestibulo-ocular response at 3 Hz remains 10 to 30% higher than that for 1.75 Hz. This may be due to an increased gain with frequency, but also to the higher accelerations experienced during the head oscillation at 3 Hz, where frequency and amplitude are kept at a constant level, as for 1.75 Hz. In the post-vision reversal period gain values for 1.75 and 3 Hz on the same day become almost indistinguishable. Upon termination of vision reversal the resultant increase in gain follows the similar

rapid pattern of change evidenced in the earlier decrease. Within 4 days the gain for both frequencies has returned almost to its pre-vision reversal level, the remaining increase to the previously unattained gain of one taking a further 2 weeks.

It is of great interest to compare the results of gain for these intermediate frequencies with those obtained for the 1/6-Hz rotations in the dark reported earlier (Gonshor and Melvill Jones, 1974c).

At 1/6 Hz, the gain change followed an almost identical pattern, decreasing rapidly after initiation of vision reversal, and then plateauing the decrease, to reach a low gain of 0.15 on D_{28}. This is the same gain level reached for the 1.75 Hz oscillation on D_{28}, although in this case the head movement was voluntary, and performed whilst fixating on a visual target. The post-vision reversal gain increases for 1/6 Hz again followed an almost identical pattern to that of the intermediate frequencies. The importance of this result is discussed below.

Figure 5 shows the change in normalized gain, as a function of the days after donning the prisms, for the 49 day (●), 25 day (○), and 17 day (x) experiments. Only the first 7 days are depicted, and only the results obtained before removal of the prisms. The abscissa represents real time, with each day number denoting the end of its 24 hour period (starting at ten in the morning). Each point is the mean of 10 cycles in a test run at 1.75 Hz head oscillation. Notwithstanding the considerable scatter, it is clear that in all the

experiments a very significant decrease in gain does occur in spite of the subject's attempt at fixation. Thus it appears that a substantial functional deficit is produced by the decrease in vestibulo-ocular gain.

(Fig. 5 near here)

Subjective Blur Estimation. Apart from the strictly objective eye movement data, tests at 1.75 Hz and 3 Hz included a subjective estimation of blur, in order to obtain information on the functional impairment of vision. As noted in Methods, the procedure followed here closely paralleled the methods used by Melvill Jones and Drazin (1962).

(Fig. 6 near here)

The blur estimation method was used for the first time during the 17 day experiment (6 days reversed vision), the results of which are shown in Figure 6. For interpretation of this figure it should be recalled that these tests are performed with eyes open and the reversing prisms removed. The left-hand ordinate gives a measure of the gain of response of eye to head angle during horizontal plane oscillation at a frequency of 1.75 Hz. The right hand ordinate gives the apparent distortion of the radial disc according to the system described in Methods; the highest number represents the greatest amount of blurring. The abscissa denotes the days of the total experiment, with arrows

Fig. 5.

Changes of normalized gain during the first few days of reversed vision environment in the 17 day (x), 25 day (○), and 49 day (●) experiments. The abscissa represents real time after donning the prisms, each number denoting the end of a 24 hour period from 10:00 a.m. on one day to 10:00 a.m. on the following day. The ordinate gives mean gain normalized relative to each individual subject's mean control value for a run of head oscillation at 1.75 Hz, obtained immediately prior to donning the prisms. Note that during these runs the eyes are open, and the prisms are not worn.

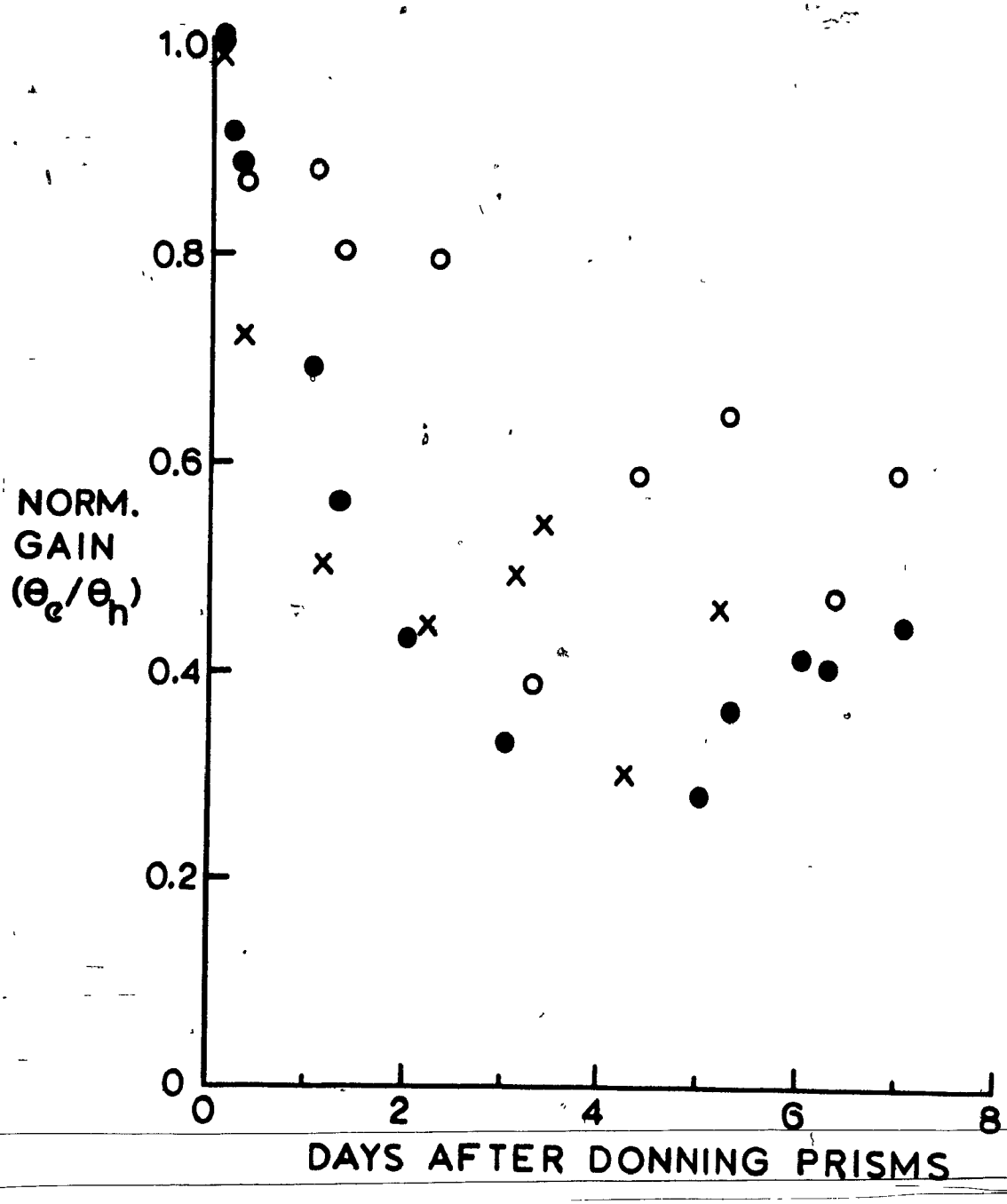
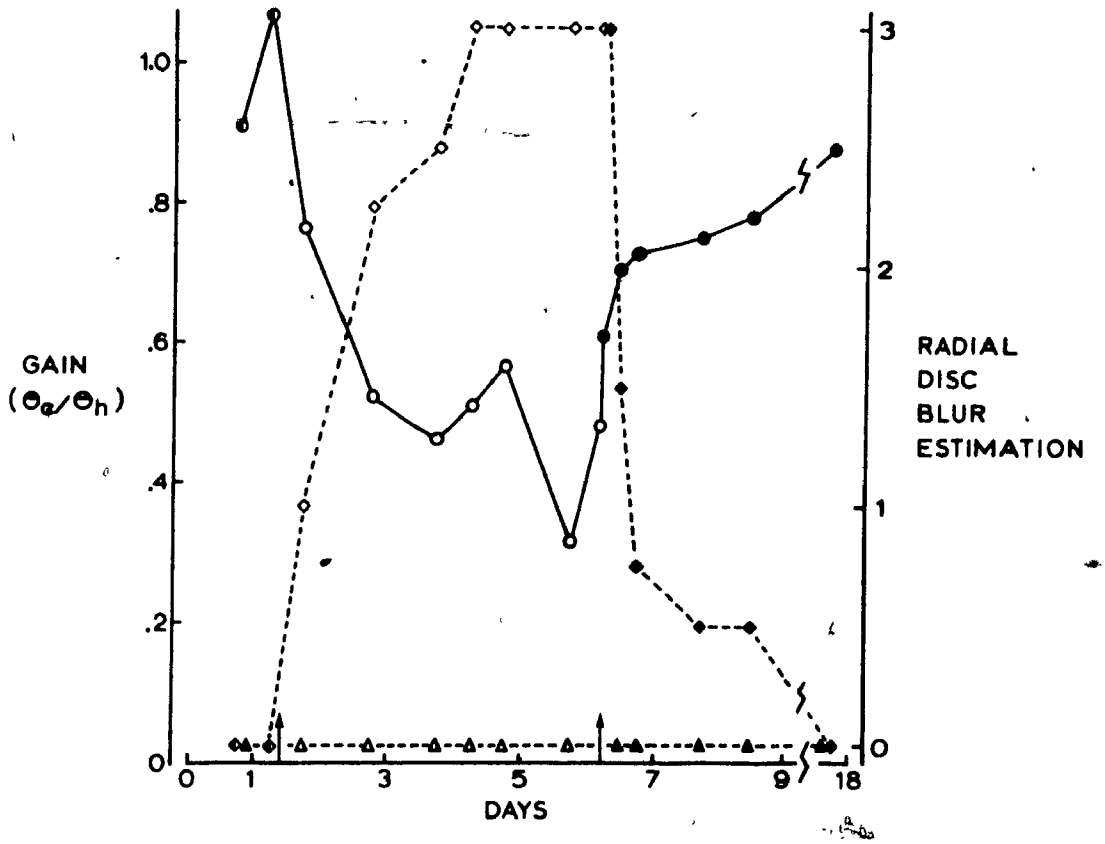

1.0
0.8
0.6
0.4
0.2
0
NORM.
GAIN
(θ_e/θ_h)
0
2
4
6
8
DAYS AFTER DONNING PRISMS

Fig. 6.

Changes in gain and blur estimation during the 17 day experiment. The left-hand ordinate gives gain of response during voluntary head oscillation (eyes open, no prisms) at a frequency of 1.75 Hz. The right-hand ordinate gives the subjective estimate of a radial disc blur; the highest number of the 3 point scale denotes the greatest amount of blurring. The abscissa denotes the days of the experiment, with the vertical arrows enclosing the 6 days of reversed vision. Note the break in the abscissa between D_9 and D_{18}. Each point representing gain of response is a mean of 10 consecutive cycles in a run before (◐), during (○), and after (●) vision reversal. In similar fashion each diamond is the subject's single estimate of blur, made at the end of a run. The subject's blur estimation for vertical (sagittal) plane head oscillation at 1.75 Hz are similarly presented by means of triangles. There was no change in this latter estimate from beginning to end of the experiment.


GAIN
(θe/θh)
1.0
.8
.6
.4
.2
0
0
1
3
5
7
9
18
DAYS
3
2
1
0
RADIAL
DISC
BLUR
ESTIMATION

enclosing the 6 day period of vision reversal. Note the break in the abscissa line between days 9 and 18. Each point, representing gain of response (circles), is a mean of 10 consecutive cycles at 1.75 Hz, whilst each diamond gives the subject's blur estimation, made at the end of a run. The decay in gain of compensatory eye response for this subject followed closely the 1.75 Hz response of the subject in the 49 day experiment (Figure 4), falling almost 70% in the first 5 days of reversed vision, and with a similar slope of decay (see Figure 5). The development of retinal image slip due to this decay in smooth pursuit gain is manifest by the subjective impression of increased distortion of the radial disc, so that by the fourth day of prism reversal maximal blur was being registered, and remained so for the remaining two days of reversed vision. To determine what effects there were in planes other than the horizontal, blur estimations were obtained after several cycles of head oscillation at 1.75 Hz in the sagittal plane (triangles). The total absence of change is apparent in the straight line at "0" level for radial disc distortion, indicating the high degree of specificity with respect to plane of rotation. In this regard, it is important to recall that the "dove" prisms were aligned so as to cause reversal only in the horizontal plane; i.e. no vision reversal in the sagittal plane. Similar results to those in the 17 day experiment were also obtained for the 25 day experiment.

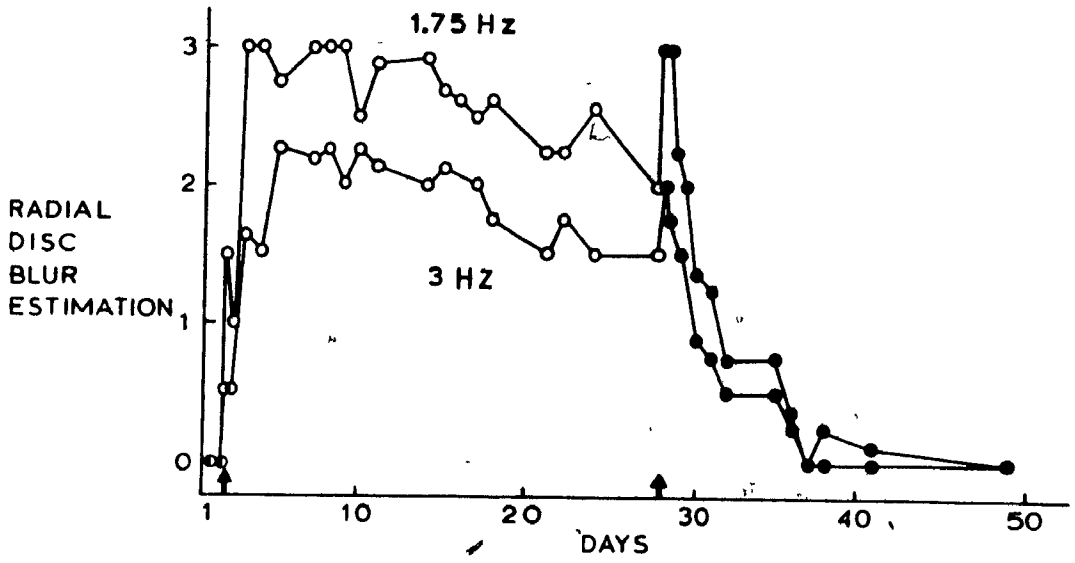
(Fig. 7 near here)

Results from blur estimations at 1.75 and 3 Hz during the

Fig. 7.

Subjective estimates of radial disc blurring obtained during the 49 day experiment. The ordinate gives blur estimation on a 3 point scale, the highest number denoting maximum blur. The vertical arrows enclose the period of reversed vision (D_2 to D_{28}). The tests were voluntary, sinusoidal head rotation at 1.75 Hz and 3 Hz.

Each point represent a value for blur obtained at the termination of a run of 1.75 Hz or 3 Hz voluntary head oscillation before (◐), during (○), and after (●) vision reversal.


1.75 Hz
3 HZ
RADIAL
DISC
BLUR
ESTIMATION
3
2
1
0
1
10
20
30
40
50
DAYS

49 day experiment (Fig. 7), show clearly the rapid increase in blur after the start of vision reversal to a level of maximum blurring. This is similar to results in Figure 6. After the first 10 days there is a somewhat decreased estimation of blur at both frequencies, as though a seeming improvement in smooth pursuit eye movement were taking place. However, when compared with the gain data from Figure 4 for these tests, one sees that throughout the experiment fluctuations in blur estimation follow closely the corresponding gain changes. This is further evidenced in the post-vision reversal period where the blur decreases rapidly toward zero in the first 4 days, following almost identically the corresponding increase in gain of smooth pursuit following. It is of interest that the subject reported zero blur on D_{37} for both frequencies, when the gain (Fig. 4) was at 0.8, or still below perfect compensation. Similar results can be seen in Figure 6. It is not certain whether the subject perceives an absolutely still field when estimating zero blur, or accepts a small range of permissible relative motion whilst still giving a zero value. From work by Melvill Jones and Drazin (1962) it would appear that extensive image slip must take place before visual acuity is greatly affected. Finally, the higher gain observed at 3 Hz (Fig. 4) results in a closely corresponding lower level of blur estimation in Figure 6 for each of those tests, again underlining the sensitivity of the blur method.

2. Response to Continuously Varying Frequency Of Head Oscillation

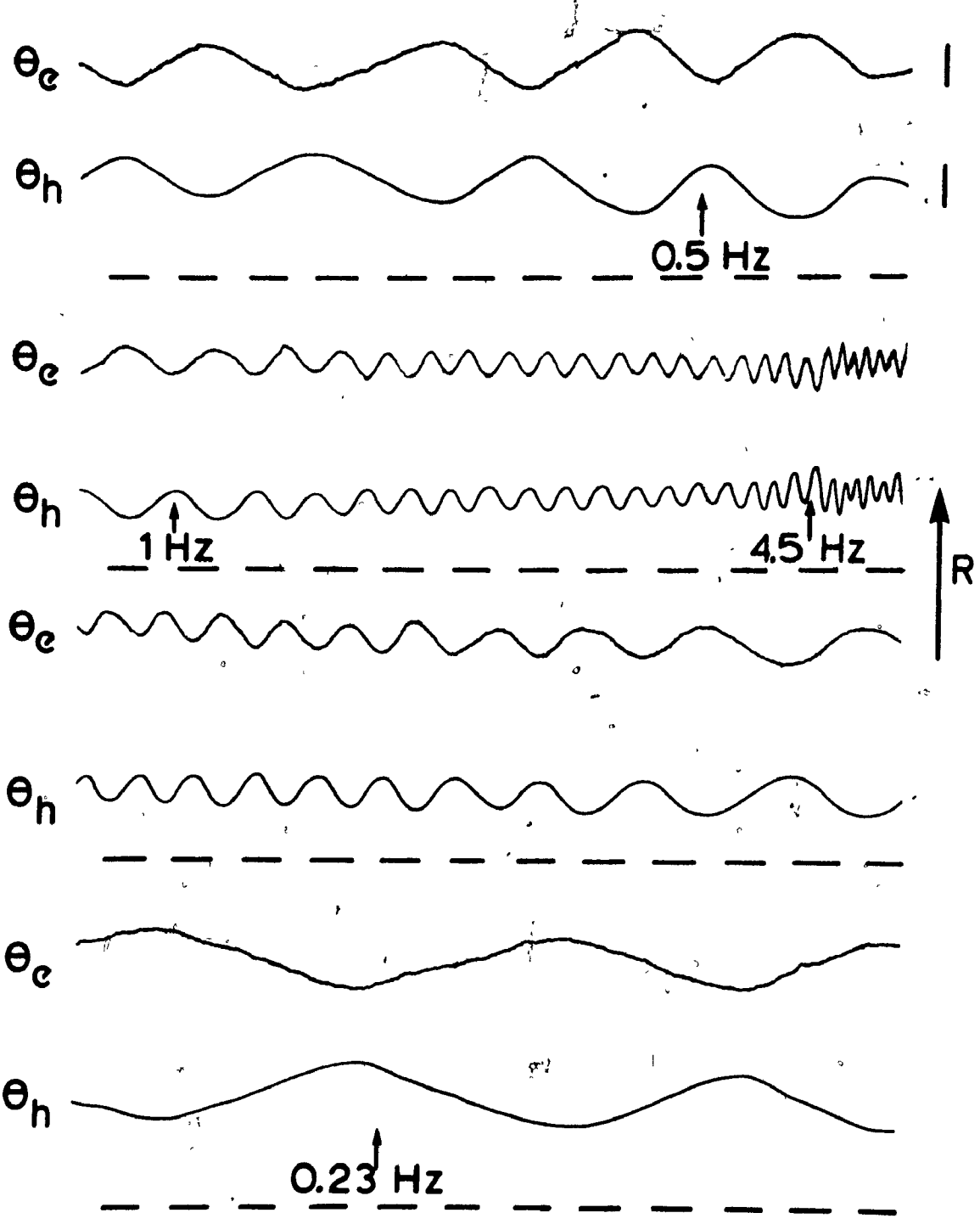
Some of the most intriguing results derived from tests in which the subject, with eyes open (no prisms), whilst looking at a stationary target, produced a voluntary series of to-and-fro oscillations, the frequency of which varied from less than 0.2 Hz to above 6 Hz, and back. An example of responses obtained in these circumstances is seen in Figure 8, which shows four extracts from

(Fig. 8 near here)

portions of a control run during a pre-vision reversal test. It is apparent that the subject was quite capable of producing sinusoidal-like oscillations of the required amplitude throughout the frequency spectrum. Furthermore, the resulting compensatory eye movement was almost exclusively smooth pursuit in nature, as is to be expected at this amplitude of head excursion (Jones and Milsum, 1965).
The gain of this response (eye displacement/head displacement, or θ_e/θ_h), as a function of the frequency of oscillation, is depicted in Figure 9a. The results were obtained from a control run before reversal began (D_1-○), as well as from runs 8 days (D_{36}-◆), 9 days (D_{37}-◐), and 13 days (D_{41}-△) after termination of the reversed vision stimulation. Each point represents the gain calculated from one cycle of a run on each of the four days represented. As the frequency is increased from 0.15 upward the gain also increases, but with no accompanying phase changes. Possible explanations for this behaviour will be discussed below.

Fig. 8.

Extracts from original records of head and eye movement, taken from a control run (D_1) in the 49 day experiment. The entire run (not shown here), consists of voluntary, sinusoidal head oscillation through a frequency range of 0.2 to 6.5 Hz. The subject's eyes are open (no prisms), and he is attempting to fixate on a stationary target.



DAY 1 - Variable Frequency 1 sec

(Fig. 9 near here)

With introduction of vision reversal the resultant decrease in vestibulo-ocular gain disrupts the smooth pursuit eye compensation, causing it to change to a nystagmoid form of response, whose characteristics vary with each test session, as well as with changes in frequency within a test. In Figures 10a to 10d one sees examples of the variations in response to head oscillations at about 0.5 Hz, on various days of the experiment. Figure 10a is taken from a pre-vision reversal run (D_1), and shows the normal compensatory eye response to head rotation, already described in Figure 8. The gain for this cycle is 0.8.

(Fig. 10 near here)

Because vision is permitted, the eye position record (θ_e) represents, in this case, a response due to synergistic action of both the vestibular and optokinetic inputs, with a gain close to 1 (see Figure 9a). It will be seen below that with the head still, whilst following a moving target, the optokinetic input at 0.5 Hz is by itself capable of producing an ocular response with a gain of 1 (Fig. 13).

The effects of vision reversal on the compensatory smooth pursuit at 0.5 Hz is shown in Figures 10b, c, and d. In Figure 10b (D_{22}) the smooth pursuit nature of compensation has become a

Fig. 9.

Changes in gain ($^{\theta}e/^{\theta}h$) as a function of frequency of head oscillation. The abscissa denotes the frequency (Hz) of voluntary, sinusoidal head oscillation. The horizontal dashed line denotes the peak-to-peak amplitude of the head excursion in each cycle.

(a) Measurement of gain during runs in the pre and post-vision reversal periods of the 49 day experiment. Each point gives the gain for one cycle in a run on D_1 (○), D_{36} (◆), D_{37} (◐), and D_{41} (△).

(b) Gain measurements for runs during the period of vision reversal. Each point is the gain for one cycle in a run on D_{11} (▽), D_{14} (●), D_{15} (▲), D_{17} (◑), and D_{28} (⊙). Gain measurements at 1.75 and 3 Hz (X), obtained during the D_{15} run, are included as a comparison to values shown in Fig. 6. The regression lines are calculated from 2 Hz upward for (a) $y = 0.0748x + 0.7310$ ($r = 0.8687$) and (b) $y = 0.0819x + 0.1378$ ($r = 0.8786$).

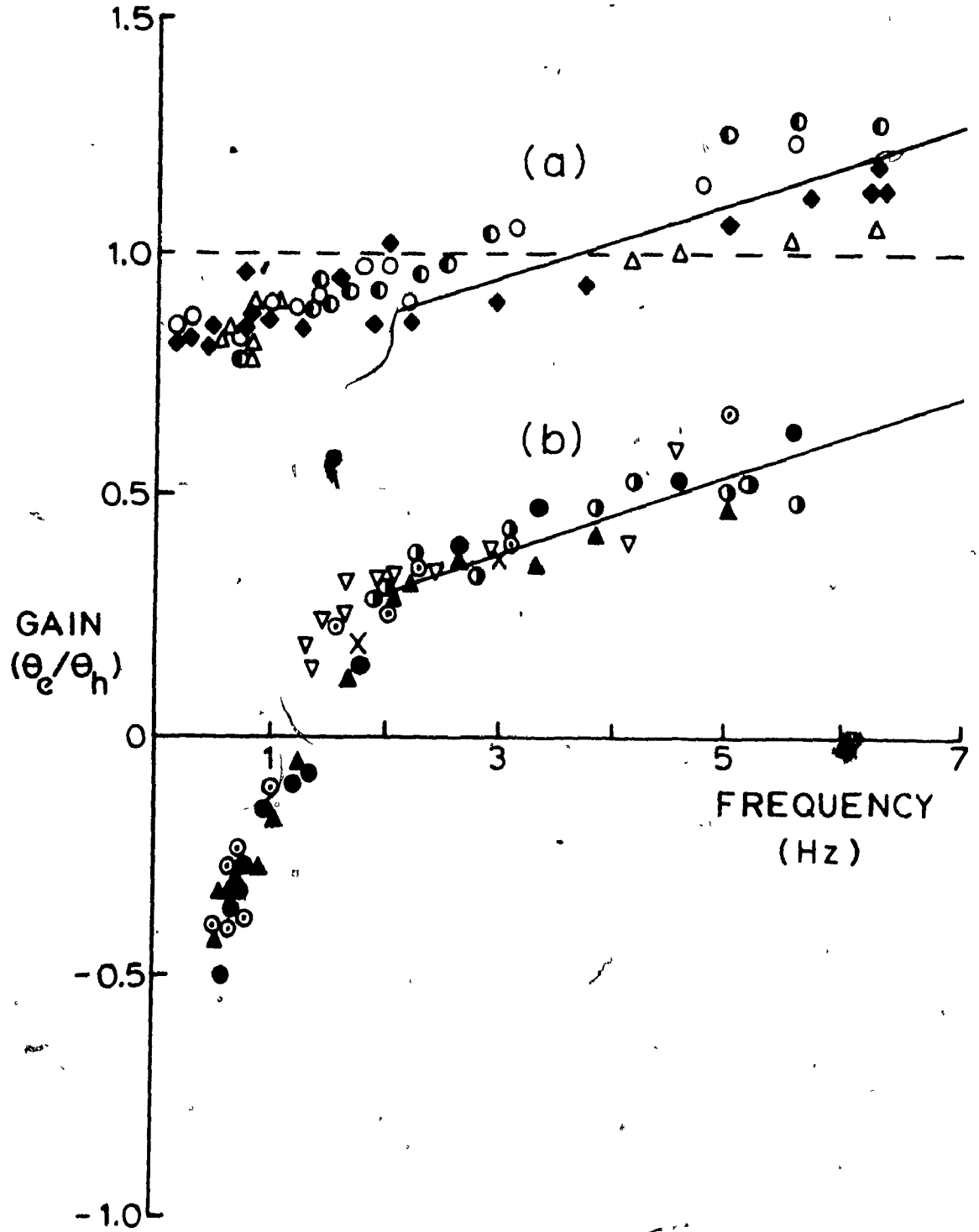
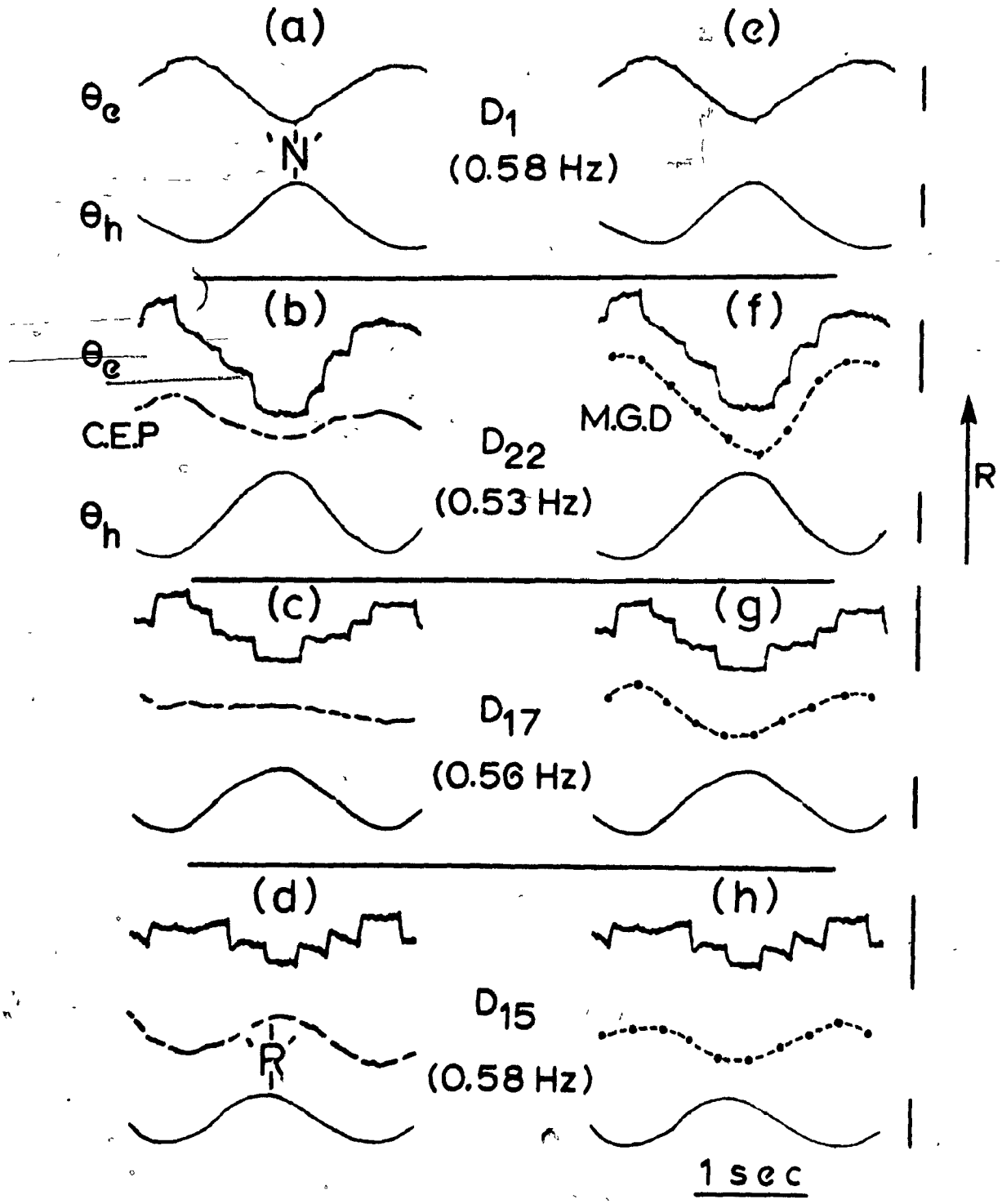

1.5
1.0
0.5
0
-0.5
-1.0
(a)
(b)
GAIN
(θ_c/θ_h)
1
3
5
7
FREQUENCY
(Hz)

Fig. 10.

Specimen records from runs of variable frequency head oscillation on (a) D_1, (b) D_{22}, (c) D_{17} and (d) D_{15}, of the 49 day experiment. All four groups are at a frequency close to 0.5 Hz. In addition, parts b, c, and d also include a calculated "cumulative eye position" (CEP) record. Lines "N" and "R" join the points of maximum head movement to the left with the corresponding maximum excursion of the eye, revealing normal compensation in the D_1 cycle and reversal of normal compensation in the D_{15} cycle respectively. Figs. 10e to h give a measure of the mean gaze direction (MGD) of eye movement for the cycles of head movement already depicted in Figs. 10a to d. In parts f, g, and h the MGD is produced by dividing the cycle of eye movement into 10 segments, and choosing a point which represents the average height of the cycle for that segment. Symbols as in Fig. 2.


(a)
(e)
θ_e
'N'
D_1
(0.58 Hz)
θ_h
(b)
(f)
θ_e
C.E.P
M.G.D
D_{22}
(0.53 Hz)
θ_h
R
(c)
(g)
D_{17}
(0.56 Hz)
(d)
(h)
D_{15}
R
(0.58 Hz)
1 sec

distinctly nystagmoid form of response. With the saccades removed, the cumulative eye position (CEP) exhibits a highly attenuated gain (0.34), but still properly phase related to the stimulus. During later tests the gain of response frequently reached a "0" level, as exemplified in the CEP tracing from the 0.56 Hz portion of a run on D_{17} (Fig. 10c).

With effectively no smooth pursuit available, the subject's eye response through the entire cycle is saccadic in nature, resembling very closely the response seen when scanning a stationary scene from side to side, while holding the head fixed in space. A third variation of response is exemplified in a 0.58 Hz portion of a run on D_{15} (Fig. 10d). Again the response is dominated by saccades, and interspersed with smooth pursuit movements of low gain. The low gain is evident in the accompanying CEP trace (gain = 0.42). However, a closer look at the phase of this CEP curve reveals that it is completely reversed with respect to normal compensation for the head movement. This is easily verified by comparing the directions of movement of the eye (Θe) and head (Θh) at lines "N" and "R" in Figures 10a and 10d respectively. Possible explanations of these results are discussed below.

The changes in vestibular-optokinetic interaction depicted in Figure 10 serve to focus attention on the action of still another input to the eyes - the saccade. No matter how variable the vestibulo-ocular gain and the direction of CEP, the requirement that fixation be maintained brings about a normal saccadic response, such that the fovea is always

brought back to the point in space which is commensurate with proper fixation. This occurs regardless of the direction in which the smooth pursuit component is moving, as shown in Figures 10e to 10h. In this case the cycles from Figures 10a to 10d have been divided into 10 segments, and a point representing average height of the curve for that segment chosen. The result gives the MGD, or mean gaze direction (Mishkin and Melvill Jones, 1966). This response, which is under visual control, exhibits normal compensatory behavior throughout the frequency range.

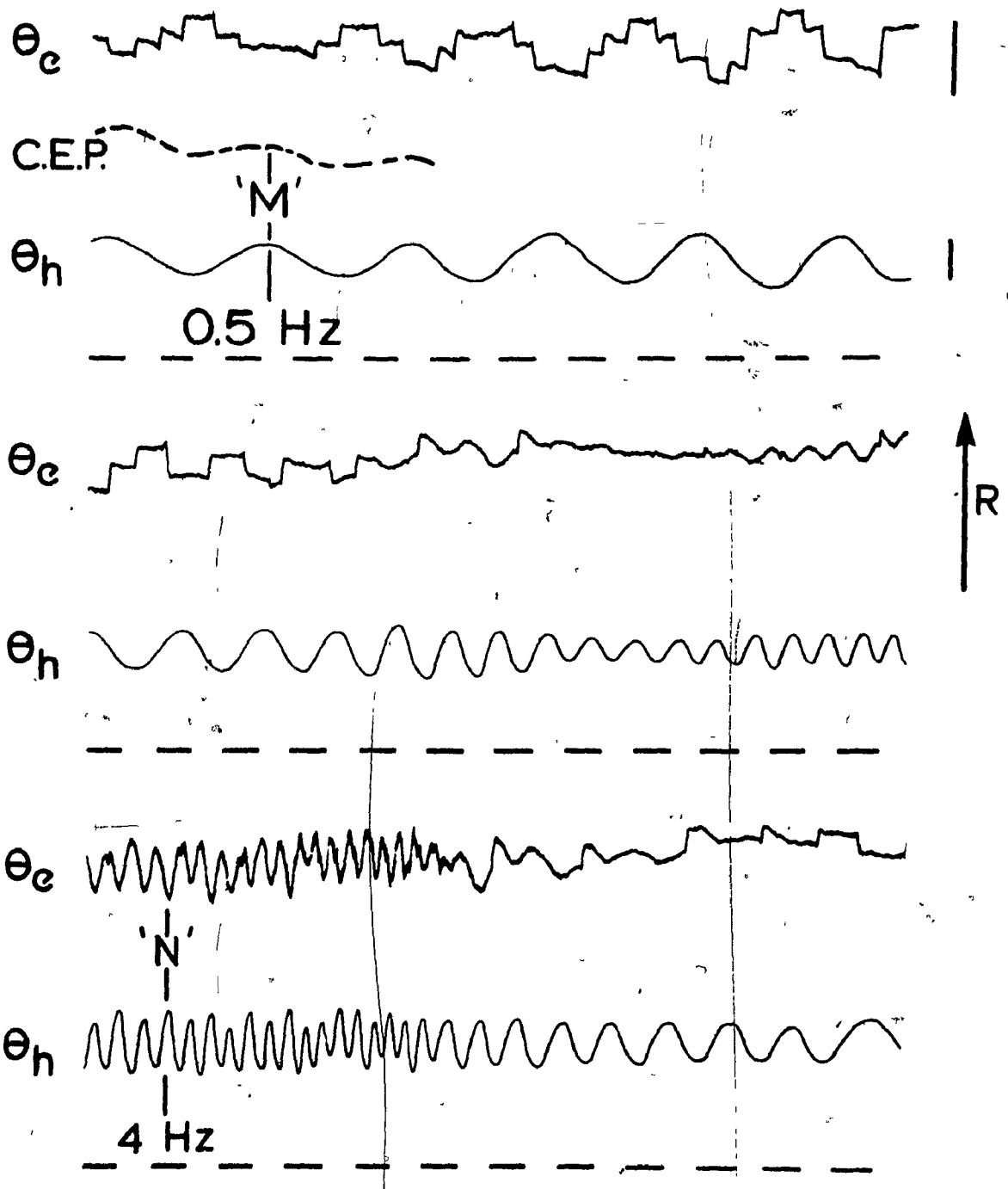
(Fig. 11 near here)

Figure 11 represents a portion of the run on D_{15}, including both the high and low frequency head movements produced voluntarily by the subject. The smooth pursuit component of response at 0.5 Hz on this day was already shown to be reversed (see Fig. 10d). However, as the frequency of head movement is increased, the completely reversed vestibulo-ocular response to the head movement at line "M" along the CEP and Θ_h curves, returns to normal compensation ("N").

The return to this normal phase relationship is accompanied by changes in the vestibulo-ocular gain, as outlined in Figure 9b. Here one sees a measure of vestibulo-ocular gain as a function of the frequency of voluntary head oscillation. Because an insufficient amount of data was available for a meaningful gain-phase measurement at the various frequencies, and since most values were either much greater or much less than 90^o phase shifted with respect to the

Fig. 11.

Extracts from original records, showing a portion of the run of variable frequency head oscillation on D_{15}, in the 49 day experiment. Head and eye movement are shown, as well as the cumulative eye position (CEP) for several cycles. Lines "M" and "N" are drawn at the point of maximum head deviation to the right, and show the change from complete reversal of eye compensation at 0.5 Hz to a normal compensatory eye movement at 4 Hz. Symbols as in Fig. 2.



DAY 15 - Variable Frequency 1 sec

stimulation, all points with phase values less than 90^{o} were placed as positive gain. Any point with phase values greater than 90^{o} were placed in the negative gain portion of the ordinate. The horizontal dashed line represents the peak-to-peak amplitude of head rotation in each cycle. Each point represents the gain measurement for a selected cycle in a test run on days 11 (▽), 14 (●), 15 (▲), 17 (◑), and 28 (⊙). Specific values for cycles at 1.75 and 3 Hz (X) from the run on day 15 are also included as a comparison to the values previously described for these intermediate frequencies (Fig. 4). It becomes apparent in Figure 9b that in the 0.5 to 1.75 Hz frequency range not only is the beforementioned phase relationship changing from one of complete reversal to one of normal compensatory response, but the gain is decreasing to almost zero. At higher frequencies the changes are purely those of increasing gain with frequency, very much like the relationship seen in Figure 9a. This close relationship is very apparent from the regressions performed on both Figures 9a and 9b, starting from 2 Hz upward. Results show that there is no significant difference between the two regressions ($P < 0.5$).

The responses obtained here for the oscillations at 1.75 and 3 Hz, follow closely the results from the separate tests of oscillations at these two frequencies (Fig. 4), and therefore act as a good indicator of the validity of the present measurments. One should note again that this reversed response was seen only on several occasions, and cannot be said to indicate a uniform trend of response.

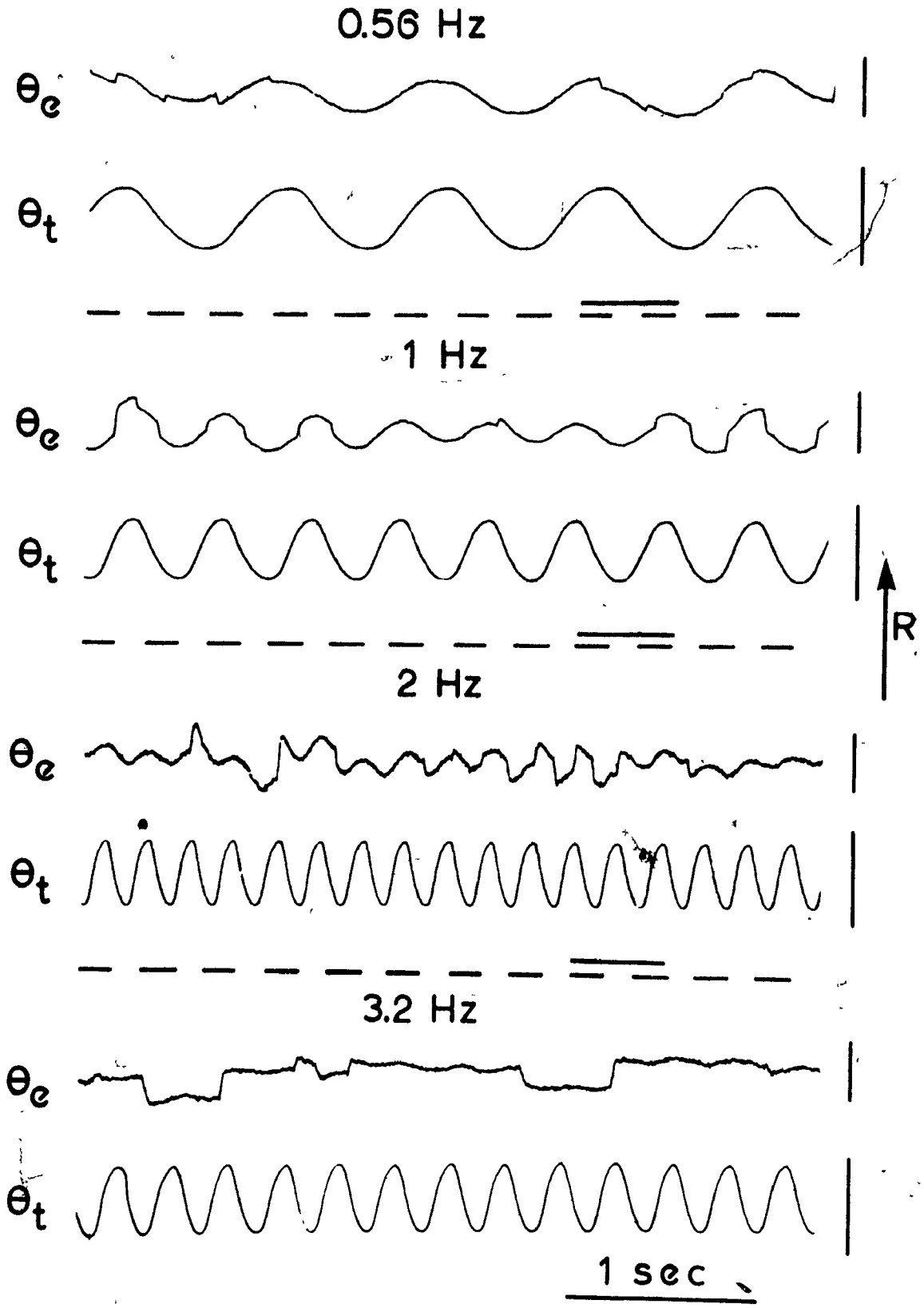
However, even on days where no apparent reversals took place, the same pattern of gain change occurred. That is, a decrease of gain from 0.5 to 1.75 Hz, and then a rise in gain with increasing frequencies.

(B) Optokinetic Response In The Absence Of Head Movement

From the information already provided in this and a previous article (Gonshor and Melvill Jones, 1974c), it is evident that prismatic reversal of the visual field - in this case the horizontal plane - has a profound effect on the vestibulo-ocular reflex. Because the vestibulo-ocular and visual following reflexes form a complex integrated system, tests were performed to determine what, if any, changes took place in the optokinetic or visual following mode of operation. Tests were performed three times during the 49 day experiment: Before donning the prisms, on the final day of vision reversal, and on the final day of the experiment. The methods of DC electro-oculography and radial disc distortion were used to obtain both objective and subjective data from the subject. A previous study by Melvill Jones and Drazin (1962) had made use of the moving radial disc to determine the response characteristics of pilots to many frequencies of target movement. Their methods have been utilized here and the results used as control comparisons for the present tests. A sample of object and eye movement records from this experiment are shown in Figure 12. One sees clearly that

Fig. 12.

Extracts from original records showing optokinetically generated eye movement in response to a target movement at 0.56, 1.0, 2.0 and 3.2 Hz. Θe, or eye angle, gives the position of the eye relative to the head, while Θt denotes the target's position in space. The horizontal bar at the lower right of each extract represents 1 sec. Static calibrations = 10^{o}, and R = right-going movement.


0.56 Hz
θe
θt
1 Hz
θe
θt
R
2 Hz
θe
θt
3.2 Hz
θe
θt
1 sec

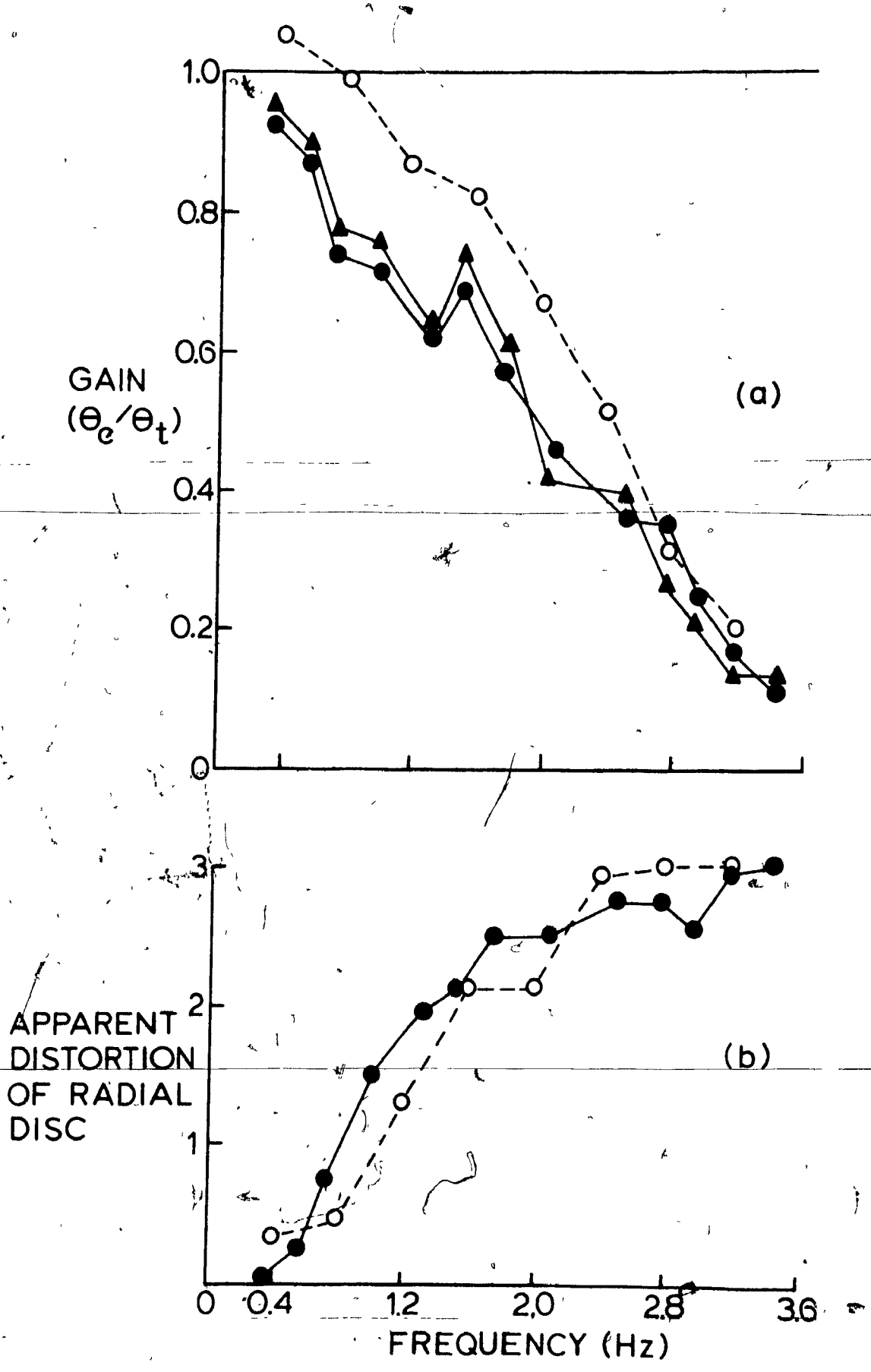
with increasing frequency of object movement from 0.56 to 3.2 Hz, there is a progressive loss in ability of the velocity of the smooth pursuit to match the target velocity, associated in turn with an increase in the number and amplitude of the saccadic repositioning flicks.

These records were averaged over 10 cycles for each frequency, in order to obtain a measure of the gain of response (eye angle/target angle, or $^{\Theta}e/^{\Theta}t$) as a function of the frequency of target movement (Fig. 13a). The solid lines in Figure 13a denote the response of a subject during a control run on D_1(▲), and a run on D_{28}(●), the final day of vision reversal. The dashed line is taken from similarly recorded and analyzed data in the study of Melvill Jones and Drazin (1962). All the lines show clearly that increasing frequency produces a steady decrease in gain. More importantly, comparison of the D_1 and D_{28} shows no significant difference in the slopes of response decay with frequency increase. There is also good agreement with the Melvill Jones and Drazin results, although slightly lower values of gain were obtained from this experiment at the lower frequencies. The lack of marked differences is interesting since a portion of the results derived from this experiment come from a test performed on D_{28}, when the greatest changes, if any, would be expected to have taken place.

(Fig. 13 near here)

Fig. 13.

Change in optokinetic gain ($^{\theta}e/^{\theta}t$), and apparent distortion of the radial disc, as a function of frequency. The abscissa measures frequency of target (radial disc) sinusoidal oscillation in the range from 0.4 to 3.6 Hz. (a) The solid lines denote the response of a subject during a D_1 control run (▲), and a run on D_{28} (●), each being the mean gain for 10 cycles in a run. The open circles (○) are from similarly analyzed results of Melvill Jones and Drazin (1962). (b) The apparent distortion is on a 3 point scale, with the highest number denoting maximum distortion. Each point represents the subjective value of distortion for the runs with the corresponding mean gain values, on D_{28} (●), and the Melvill Jones and Drazin study (○).


1.0
0.8
0.6
0.4
0.2
0
GAIN
(θ_e/θ_t)
(a)
3
2
1
0
APPARENT
DISTORTION
OF RADIAL
DISC
(b)
0.4
1.2
2.0
2.8
3.6
FREQUENCY (Hz)

The subjective response to the target motion on D_{28}, and in the Melvill Jones and Drazin (1962) study, is shown in Figure 13b, where the ordinate gives the apparent distortion of the radial disc on the 3 point scale, and the abscissa shows the same frequency range as Figure 13a. It is evident that there are no differences in the slopes as frequency is increased, leading one to conclude from both this subjective and the previous objective test, that no large scale changes of visual following capability occurred during the period of vision reversal.

(C) Saccadic Performance

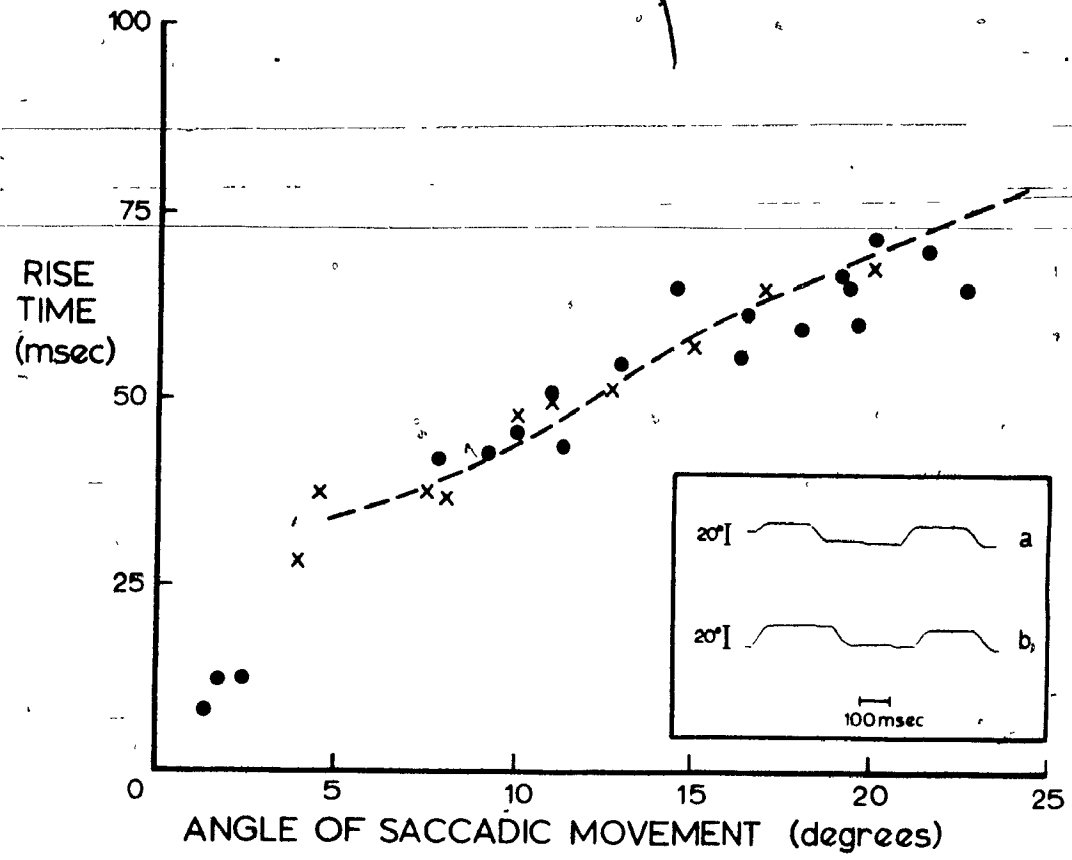
During the entire period of these experiments, tests were conducted to determine if any changes were taking place in the dynamic characteristics of saccadic eye movements induced by attempting to change between stationary fixation points separated by 10^{o}, with head still. Examples of such saccadic jumps are seen in the insert of Figure 14, where (a) is from a test prior to donning the prisms (D_1), and (b) from a test on D_{17}.

(Fig. 14 near here)

The remainder of Figure 14 is a plot of the measured rise time against angle of saccadic jump, for saccades distributed in size range between 2 and 23^{o}. These are taken from tests on D_1 (●)

Fig. 14.

A plot of saccadic rise time (msec) as a function of the angle of saccadic movement. The insert shows specimen records of saccades obtained during, (a) a control test on D_1, and (b) a test on D_{17}. The angle of saccadic movement is distributed in size from 2 to 23°. Each point represents the rise time value for an individual saccade on D_1 (●) and D_{17} (x). The dashed line gives Robinson's (1964) data for normals.


100
75
50
25
0
RISE
TIME
(msec)
5
10
15
20
25
ANGLE OF SACCADIC MOVEMENT (degrees)
20°
a
20°
b
100msec

and D_{17} (x). The broken line gives the mean data from Robinson's (1964) experiments on normals. It can be seen that the individual points from both days of this experiment lie very close to this line. Analysis also shows no statistical difference between the results of the two days shown in this figure and the other days in the experiment, not shown here. It therefore appears that just as with the optokinetic tracking, the control of saccadic eye movement is not affected by the adaptability to the reversed visual environment.

DISCUSSION

Previous Findings

In a previous article (Gonshor and Melvill Jones, 1974c), a report was made of the long-term adaptive capability of the vestibulo-ocular reflex, when placed in an environment where new optimization criteria are required. This new environment was created with the imposition of a left-right reversal of the visual world, by means of prisms. Such a situation produces an antagonism of the two, normally synergistic, inputs to the eye muscles. That is, the inertially driven vestibular system, and the optokinetic or visual tracking system, are now forced to operate in such a manner as to move the eyes in opposing directions for a given movement of the head. In the low frequency and amplitude range of head motion, the visual control was shown to dominate during passive sinusoidal rotation (Gonshor and

Melvill Jones, 1974b), producing in due course a resultant attenuation of the vestibulo-ocular reflex gain. The decrease would be expected, since the raison d'etre of the entire system is presumably to minimize retinal slip, and allow clear image stabilization whilst the head is in motion. Since the vestibulo-ocular reflex would be driving the eyes in the wrong direction for image stabilization in the reversed visual world, its attenuation would be warranted.

Much more marked changes were observed during the experiments with prolonged visual reversal (Gonshor and Melvill Jones, 1974c). Here, the subject was allowed complete freedom of movement, such as walking, climbing, etc. In such circumstances it would not be sufficient to merely decrease the vestibulo-ocular gain, since freeing the skull platform brings in frequencies and angular velocities which far exceed the dynamic limits of the visual system alone. More specifically, the optokinetic system responds to retinal slip, and will tend to compensate for fixation errors, independently of their origin. However, visual tracking accuracy in man begins to fall off rapidly as the target's relative angular velocity increases above 30^{o}/sec (Miller, 1958), and its frequency above 0.7 Hz (Melvill Jones and Drazin, 1962). Therefore, to achieve image stabilization above those values, one must have a properly functioning vestibular system, with its much higher frequency and velocity response (Jones and Milsum, 1965). For example, a running man will generate a fundamental frequency of about 4 Hz/sec, and if one assumes 5^{o}

amplitude of head movement, the maximum head angular velocity becomes about 125°/sec; well beyond the capabilities of the visual tracking system. A subjective impression of these capabilities can easily be obtained by holding one's hand at arm's length and shaking it from side to side. The image becomes blurred at very low frequencies. This is then compared to the clarity one obtains by holding the hand still and moving the head through those same frequencies. In the latter case the reflex eye movement is under strong vestibular control, and in this regard Robinson (1968) has shown that vestibular plus optokinetic reflexes are faster than the optokinetic reflexes alone. Therefore, because a properly functioning vestibular system is necessary for proper image stabilization at high frequencies of head movement, in the case of a reversed visual environment the situation would call for a reversed vestibulo-ocular reflex of high, rather than attenuated, gain.

In a preceding article (Gonshor and Melvill Jones, 1974c) a detailed account was given of the main test for vestibulo-ocular gain. Briefly, the test was horizontal, sinusoidal rotation in the dark, at 1/6 Hz and 60°/sec velocity amplitude. This stimulus frequency had already been shown not to cause vestibulo-ocular gain attenuation due to the oscillation per se (Gonshor and Melvill Jones, 1974a). When interspersed with rotations during which antagonistic visual and vestibular inputs were introduced, test oscillations in the dark at this same frequency did show significant attenuation of ~~the vestibulo-ocular reflex gain~~ (Gonshor and Melvill

Jones, 1974b). In the long-term reversal experiments, the gain of the vestibulo-ocular reflex decreased dramatically, with accompanying large phase changes. Some of the details of these change have already been noted in the results of this article.

Present Findings

A question still remained as to the extent to which these large vestibulo-ocular changes, recorded in the dark, would affect image stabilization, if normal vision was periodically permitted. That is, what, if any, functional impairment was taking place due to this massive change in the vestibulo-ocular reflex. It is this query which led to the inclusion, in the final series of long-term experiments, of the tests described in this article. The tests were specifically designed so as to permit maximum utilization of all stabilization systems. Therefore, in the head oscillation tests the subject produced voluntary high frequency head movements while fixating on a stationary target. Such a task would, under normal circumstances, require the proper utilization of the vestibular system, visual tracking, and neck proprioception, in order to produce adequate image stabilization.

1. Head Oscillation at 1.75 and 3 Hz

The tests at 1.75 and 3 Hz were chosen because these frequencies are well above the limits at which visual tracking by itself can produce adequate image stabilization. For example, the drop in optokinetic gain at 1.75 Hz is in the order of 40% (Fig. 13),

whereas the drop in gain observed during 1.75 Hz voluntary head oscillation (Fig. 4), reaches a value as low as 0.18; that is, an 80% decrease from the pre-vision reversal gain of 0.82. This latter decrease is too great to be accounted for simply by the loss of optokinetic gain. Rather, it is most likely due to the substantial decrement in vestibulo-ocular reflex gain. This clear functional impairment is substantiated by the almost total blurring of the radial line disc, at a frequency where, under normal circumstances, no blurring is experienced during head oscillation (Fig. 7).

The increased gain seen at 3 Hz (Fig. 4), appears at first to be anomolous. The torsion-pendulum model of the vestibular end organ (Steinhausen 1933; van Egmond, Groen and Jongkees, 1949) would predict that in the frequency range of 0.1 to 5 Hz, essentially constant amplitude ratio and zero phase are maintained in the mechanical components of the transducer. This being the case, one would expect that at 3 Hz the attenuated gain should be at the same level as at 1.75 Hz. However, recent experimental evidence has modified the conclusions drawn from the torsion-pendulum model. Benson (1970) rotated human subjects in the dark and measured vestibulo-ocular gain (peak eye velocity/peak turntable velocity) as a function of increasing frequency (0.01 to 5 Hz). In all the experimental subjects a rising gain was consistently observed, with the gain plot inflecting at 0.5 Hz and increasing with frequency at a rate of +5 db/decade. Benson notes that it is significant that the gain of the vestibulo-ocular reflex increases in the frequency range where stabilization

of the eye due to pure visual following undergoes a rapid decay. Similar results have been obtained in experiments on squirrel monkeys (Fernández and Goldberg, 1971), in which recordings were made in the primary afferent neurones of the semicircular canals, while stimulating sinuosidally in a frequency range from 0.0125 to 8 Hz. Just as in Benson's results, the gain enhancement also inflects at 0.5 Hz, reaching in this case a 10 db increase by 8 Hz.

This new evidence therefore might well account for the 0.1 to 0.2 increase in gain as the frequency of head oscillation increases from 1.75 to 3 Hz (Fig. 4). It is also in agreement with the enhancement in gain that is observed in this experiment during the control runs of variable frequency head oscillation (Fig. 9a), and may be responsible for the gain changes observed in the variable frequency tests during the vision reversal period.

2. Head Oscillation at 0.5 Hz

The various patterns of compensatory eye movement at 0.5 Hz (Fig. 10), including a reversed response with respect to normal compensation for voluntary head movement, represent possible clues to the mechanisms at work in producing the extensive changes seen in results. During the vision reversal portion of the 49 day experiment, 0.16 Hz oscillation in the dark (Gonshor and Melvill Jones, 1974c), resulted in decreases of vestibulo-ocular gain to as low a value as 0.13, or 20% of the 0.6 pre-vision reversal gain. However, at 0.16 Hz one eventually reaches a plateau level of phase

shift which, although very pronounced, does not extend beyond 130° phase lag relative to normal compensation; that is, a 50° phase-advancement with respect to complete reversal. In addition, the gain at this plateaued phase rises to a value of 0.3 (50% pre-vision reversal). This plateau for 0.16 Hz is exceeded in the 0.5 Hz tests.

In Figure 10 the CEP curve represents a combined response, due almost entirely to inputs from the vestibular and visual following (optokinetic) systems. Several possibilities exist as explanation for the observed response changes. That the changes are due to attenuation of the optokinetic portion of the response is unlikely, since separate daily tests of optokinetically generated eye movement showed that its normal characteristics are maintained throughout the entire experiment (Fig. 13). This would leave the vestibulo-ocular input as the most probable primary candidate for the changes taking place. In this light, one can conceptualize the CEP curve as representing the final output of a basically normal optokinetic input together with a completely reversed vestibulo-ocular input to the oculomotor system. Now, in the case of D_{22} (3 weeks vision reversal), oscillation in the dark at 1/6 Hz has already been shown to produce a vestibulo-ocular reflex gain of 0.3, with phase lag of 125° (Gonshor and Melvill Jones, 1974c). To produce the attenuated CEP curve on D_{22} for the 0.53 Hz head oscillation, whilst attempting fixation (Fig. 10b), would require a 180° reversal of the vestibulo-ocular reflex to the oculomotor system, although with a gain still

lower than the optokinetic input at that frequency. Similarly the flat CEP curve of Figure 10c could be due to the resultant of two inputs of equal magnitude but opposite sign.

The completely reversed CEP in Figure 10d is quite interesting when one considers that it is occurring in spite of active attempts at fixation. Although again the response may be due to transiently higher vestibular gain in the vestibular to optokinetic gain ratio, a possible influence may come from a third influence of eye movement; neck proprioception. Under normal circumstances, man does not apparently make much use of neck receptors as a source of input for compensatory eye movement, relying almost entirely on the vestibulo-ocular reflex and its vastly higher gain. Compensatory eye movements resulting from neck receptors stimulation do occur (Meiry, 1966), although only with a gain of 0.1 at the 0.5 Hz frequency. This result is confirmed in the monkey (Dichgans, Bizzi, Morasso and Tagliasco, 1974), where experiments have shown that in the normal animal ocular stabilization is due almost entirely to the vestibulo-ocular reflex, with neck afferents playing a negligible role. However, of interest to the present discussion is the finding in the same study (Dichgans et al, 1974), that upon bilateral labyrinthectomy there is an eventual 90% recovery of compensatory eye movement, which the authors attribute in great part to a potentiation of the neck-to-eye loop, as well as to a "reprogramming of compensatory eye movement" from a central nervous system center lying upstream from the central

oculomotor mechanism.

The labyrinthectomy of Dichgan's monkey is in the present study replaced by a dramatically altered vestibulo-ocular reflex, due to the vision reversal. The decreased VOR during vision reversal could cause the neck-to-eye loop gain to be enhanced, although one would also have to invoke a reversal of the neck input to the eyes in order to allow it to aid in the production of the reversed CEP curve in Figure 10d. Perhaps Dichgan's "preprogramming" center plays a role in the activation of such changes.

As a final comment to the results of 0.5 Hz head oscillation, one sees that not only is the gain of the reversed vestibulo-ocular reflex higher at 0.5 Hz than at 0.16 Hz, but the phase at 0.5 Hz must be 180^{o} reversed from normal to produce the responses seen in Figure 10. This is of great interest, since with the knowledge that the phase at 0,16 Hz plateaus at 130^{o}, and extends now to 180^{o} shift at 0.5 Hz, it implies that the changes taking place in the vestibulo-ocular system have a probable frequency dependence.

Possible Mechanisms

In a preceding article (Gonshor and Melvill Jones, 1974c), it was postulated that the large changes in gain and phase observed may be due to the effect of multisynaptic vestibulo-ocular pathways, and their superposition on the basic disynaptic vestibulo-ocular reflex. One such multisynaptic pathway, involving the cerebellum has recently come under intensive investigation. The experimental evidence shows

that the pathway travels from the vestibular end organ by way of primary and secondary afferents to the vestibulo-cerebellum (Brodal and Høivik, 1964; Angaut and Brodal, 1967), activating Purkinje cells via mossy and climbing fibers in the frog (Precht and Llinás, 1969) and by mossy fibers in the cat (Eccles, Ito, and Szentágothai, 1967; Precht and Llinás, 1969). Axons from Purkinje cells are then sent either directly to the vestibular nuclei (Angaut and Brodal, 1967), or by way of the fastigial and other cerebellar nuclei (Brodal, 1960), their terminations coinciding with the sites of projection of vestibular primary afferents (Gacek, 1969). The final common path of the two inputs then produces the output to the oculomotor nuclei and eye muscles. The importance of this proposed pathway lies in the fact that the cerebellar output from the Purkinje cells is inhibitory on the second order neurones in the vestibular nuclei, which are simultaneously receiving excitation from primary afferents of the canals (Ito, Kawai, Udo and Sato, 1968; Shimazu and Smith, 1971). An efferent arm to this cerebellar-mediated pathway has very recently been added with the discovery in the rabbit of a direct visual input to the flocculus by way of the accessory optic tract, to the central tegmental tract, then onto the inferior olive, and finally through climbing fibers to floccular Purkinje cells (Maekawa and Simpson, 1972, 1973). This visual input has since been shown to be capable of modulating central vestibular neurone activity, which always operates to reduce image slip upon the retina (Ito, Nisimaru and Yamamoto, 1973c; Ito, Shiida,

Yagi and Yamamoto, 1974b). Our current observations have demonstrated that this retinal influence can be so versatile as to bring about effectively complete reversal of the vestibulo-ocular reflex of man as a retained response due to long-term vision reversal. The strong implication of vestibular-cerebellum participation in visual modification of the vestibulo-ocular reflex has very recently been demonstrated in rabbits (Ito et al, 1974a, b), and although unable to achieve a reversal of vestibulo-ocular response, Robinson (Oral presentation, Stockholm Symposium, 1974) has shown that the attenuation of normal vestibulo-ocular response induced in the cat by vision reversal, is abolished by removal of the vestibular cerebellum. Therefore, there seems to exist strong evidence that the vestibulo-cerebellar pathway may play an important role in the plastic modulation of vestibulo-ocular responses induced by normal and abnormal patterns of retinal image movement. A modelling study of this overall system is now underway and results will be available in a subsequent article.

The model predicts that with increasing frequency both the gain and phase lag should increase, the latter to 180°; that is, a complete reversal from normal compensation. The tests at 0.16 Hz resulted in a final plateauing of the output at a gain of 0.3 and a phase lag of 130°. The present head oscillations at 0.5 Hz seem to indicate that a complete 180° reversal of phase is taking place, as well as an increased gain from that seen at 0.16 Hz. As the frequency of head

oscillation increases through 0.5 to 1.5 Hz, (Fig. 9b) the gain of this reversed response decreases. Since the gain of canal output increases with the rise in frequency (Benson, 1970; Fernández and Goldberg, 1971), it is likely that the attenuated disynaptic pathway begins to boost its gain with respect to the reversing pathway from the cerebellum. This would lead to a final output that is decreasing in gain. If in addition, the pathway through the cerebellum has a lower frequency cutoff than the basic disynaptic reflex, one would expect to reach a frequency where the output would be a product of the disynaptic pathway alone. Evidence supporting this postulate comes from Figure 9b.

Thus at 2 Hz the phase has returned to its normal compensatory position, at which it remains even with increasing frequency. Gain, on the other hand, increases with frequency at a rate which closely parallels that of the control tests in Figure 9a. The important consideration that emerges is that this gain increase must be due almost entirely to inherent properties within the vestibulo-ocular reflex, since the optokinetic gain declines steadily as the frequency increases past 0.5 Hz, falling almost 80% in the 2 to 3 Hz range (Fig. 13). It is of added interest that at this frequency range one may be seeing the greatest attenuation level of the disynaptic pathway; that is, a gain value of about 0.18.

It therefore seems clear that even in test situations where utilization of all normal stabilization mechanisms is permitted, a marked functional deficit is manifest in the subject's inability to

produce the desired fixed visual image on the retina. The added intriguing feature is the indication of frequency dependence in the pathways that produce the output response to the reversed environment.

The functional changes discussed in the article have focused on those systems directly affecting the oculomotor system. In a subsequent article an analysis will be made of overall bodily readjustments to the reversed environment, focusing specifically on postural and perceptual readjustment.

CHAPTER 7

ADJUSTMENTS IN POSTURAL EQUILIBRIUM AND VISUAL PERCEPTION ASSOCIATED WITH CHANGES IN THE VESTIBULO-OCULAR REFLEX, INDUCED BY PROLONGED VISION REVERSAL IN MAN

SUMMARY

1. This investigation is concerned with the adjustments in postural equilibrium and perception associated with long-term vision reversal.

2. The prism-induced vision reversal lasted 6, 7, and 27 days during experiments of 17, 25, and 49 days respectively. Daily tests included walking and standing, with eyes open, on rails of 0.75 and 2.25 in. widths, and standing with eyes closed on 2.25 in. wide rail. Measurements of performance were compared for tests before, during, and after vision reversal. Subjective reports of perceptual change and observations of subject behavior were noted at all times.

3. The walking tests proved to be the most sensitive indicator of improved performance capability during and after vision reversal, and together with subjective reports and observations of the subject, make it clear that vision reversal has caused definite functional deficits in overall postural equilibrium and locomotor capability.

INTRODUCTION

A series of recent articles has detailed the results of experiments on long-term adaptability in the vestibulo-ocular reflex arc (Gonshor and Melvill Jones, 1974a, b, c; Gonshor, 1974a). The two latter articles covered the most extensive series of experiments, in which subjects were exposed to prismatically-reversed vision for prolonged time periods, lasting up to 27 days. Results of daily test sessions showed the following. Vestibulo-ocular reflex response, in the dark, to low frequency oscillatory rotation (1/6 Hz, and 60°/sec velocity amplitude), underwent profound changes, amounting to a functional reversal of the reflex (Gonshor and Melvill Jones, 1974c). In addition, the subject incurred functional deficits due to the changed vestibulo-ocular reflex. In separate tests, the subject produced active head oscillation at both steady state (1.75 and 3 Hz) and continuously changing frequencies, whilst attempting fixation. Even in this situation, where utilization of all normal stabilization mechanisms is permitted, the subject showed an inability to produce the desired fixed visual image on the retina (Gonshor, 1974a).

The functional changes discussed above focused on the area most directly affected by a vestibulo-ocular reflex change; that is, the oculomotor system. However, it became apparent that in a situation where subjects were required to make voluntary, whole-body readjustments to cope with vision reversal, there was a case for analysing the postural and perceptual changes coincident with the requirements

of the new environment. These latter changes are discussed in the present article.

METHODS

1. Postural Equilibrium

The most extensive experiments on long-term vision reversal lasted 17, 25 and 49 days, during which vision reversal lasted 6, 7 and 27 days respectively. The reversal was brought about by means of "dove" prisms, which permit reversal of vision in only one plane of rotation: in this case, the horizontal plane. A detailed account of their action has been given previously (Gonshor and Melvill Jones, 1974c).

The prisms were fitted onto goggles, which the subject was required to wear during all waking hours of what will hereafter be called "vision reversal" days. Control tests were held on the first day (D_1) and a portion of the second day (D_2). At least one test session was then held almost every day during the vision reversal, and post-vision reversal periods. On the days of initiation (D_2) and termination (D_{28}) of vision reversal, 4 test sessions were held, in order to record any rapid alterations of response due to change in the visual environment. Between tests the subject was allowed complete freedom of movement, such as walking and climbing. Supervision of the subject was provided at all times.

The postural equilibrium tests were an integral part of each

complete test session. The postural tests chosen for the present experiments are known generally as the "Quantitative Ataxia Test Battery", or QATB (Graybiel and Fregly, 1966), and have been used in situations where subjects are exposed for long periods to rotatory environments, involving unusual vestibular stimulation. The QATB has now also been used extensively in the clinical sphere to measure the disturbance in postural equilibrium as a consequence of labyrinthine pathology.

All of the tests were performed on "rails" of various heights and widths. Both a long and short version of the test are available (Graybiel and Fregly, 1966), and due to time limitations in the present experiments, the short version was chosen (Appendix). The most helpful aspect of this test battery was the large statistical information already accumulated (Fregly and Graybiel, 1968, 1970; Fregly, Smith and Graybiel, 1972). Tests have been made on well over 1000 individuals of all ages, and ranging from astronauts to oto-neurological patients. With such a large statistical population on hand, one can view the progress of the present subjects in the perspective of a quantitatively analysed continuum of human vestibular function. All subjects in the present experiments were free of any vestibular dysfunction.

2. Perception and Visual-Motor Coordination

Throughout the experiments, subjects were asked to make subjective

reports on any perceptual changes that might be taking place, as well as assessing their overall visual-motor coordination. At the same time observations were made of their overall behavior, with particular emphasis on postural equilibrium and locomotion.

RESULTS

1. Postural Equilibrium

(a) Walking Test - Eyes Open

The walking tests, with eyes open were administered during the 17, 25 and 49 day experiments, and proved to be the most sensitive of the equilibrium tests in indicating performance capability. Figure 1 is a measure of the number of steps taken in a test run as a function of the days in the experiment. The vertical arrows on the abscissa enclose the period of vision reversal. Each point represents the sum of the steps in the best 3 out of 5 trials constituting a test with the maximum for each trial being 5 steps. The tests consisted of walking heal-to-toe, and with eyes open, on a 0.75 in. (circles) and 2.25 in. wide rail (triangles). The subject in Figure 1a was a 20 year old female. A perfect score was obtained during the pre-vision reversal tests on the 2.25 in. rail, with a close to perfect score on the 0.75 in. rail. However, immediately upon donning the prisms the scores for both rails decrease dramatically to "0". Note that the prisms are worn during the tests in the vision reversal period. From this initial

low score there was a systematic increase in performance capability during the remainder of the vision reversal period, reaching values on the final day of vision reversal up to 50% (2.25 in. rail) and 25% (0.75 in. rail) of their pre-vision reversal level. In the post-vision reversal stage, the return to normal is almost immediate for the 2.25 in. rail test, reaching pre-vision reversal values within one hour of prism removal. However, for the 0.75 in. rail the return is much slower, requiring at least 3 days to reach the pre-vision reversal level.

(Fig. 1 near here)

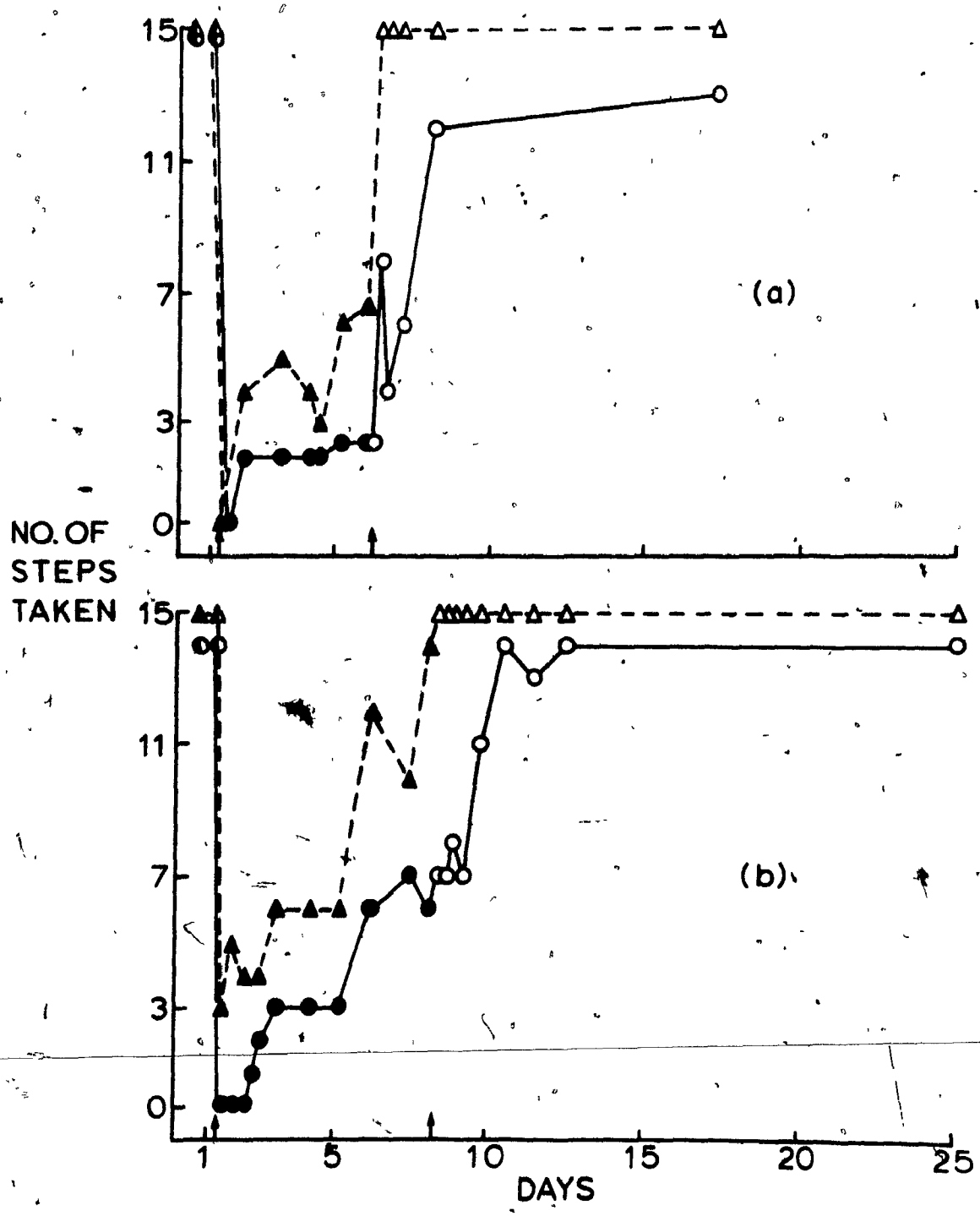
Similar results were obtained from tests performed during the 25 day experiment on a 50 year old male subject, shown in Figure 1b. The systematic increase in score with vision reversal is higher in this experiment than in the previous one, with values on the final day of vision reversal being 90% (2.25 in. rail) and 50% (0.75 in. rail) of pre-vision reversal levels. This higher level can be accounted for in part by the increase in the number of vision reversal days (one) in this experiment. Upon removal of the prisms the return to normal is immediate on the 2.25 in. rail, but again requires a 3 day period on the 0.75 in. rail.

(Fig. 2 near here)

The walking tests in the 49 day experiment (Fig. 2) were again very similar to those of the 2 previous experiments. The subject,

Fig. 1.

Scores of performance capability, measured during walking tests, with eyes open, as a function of the (a) 17 day and, (b) 25 day experiments. Tests were performed on a 0.75 in. wide rail before (◐), during (●), and after (○) vision reversal, with identical tests on a 2.25 in. wide rail (triangles). Each point represents the sum of the steps in the best 3 out of 5 trials constituting a test, with the maximum trial score equaling 5 steps. The vertical arrows on the abscissas enclose the periods of vision reversal.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NO. OF STEPS TAKEN
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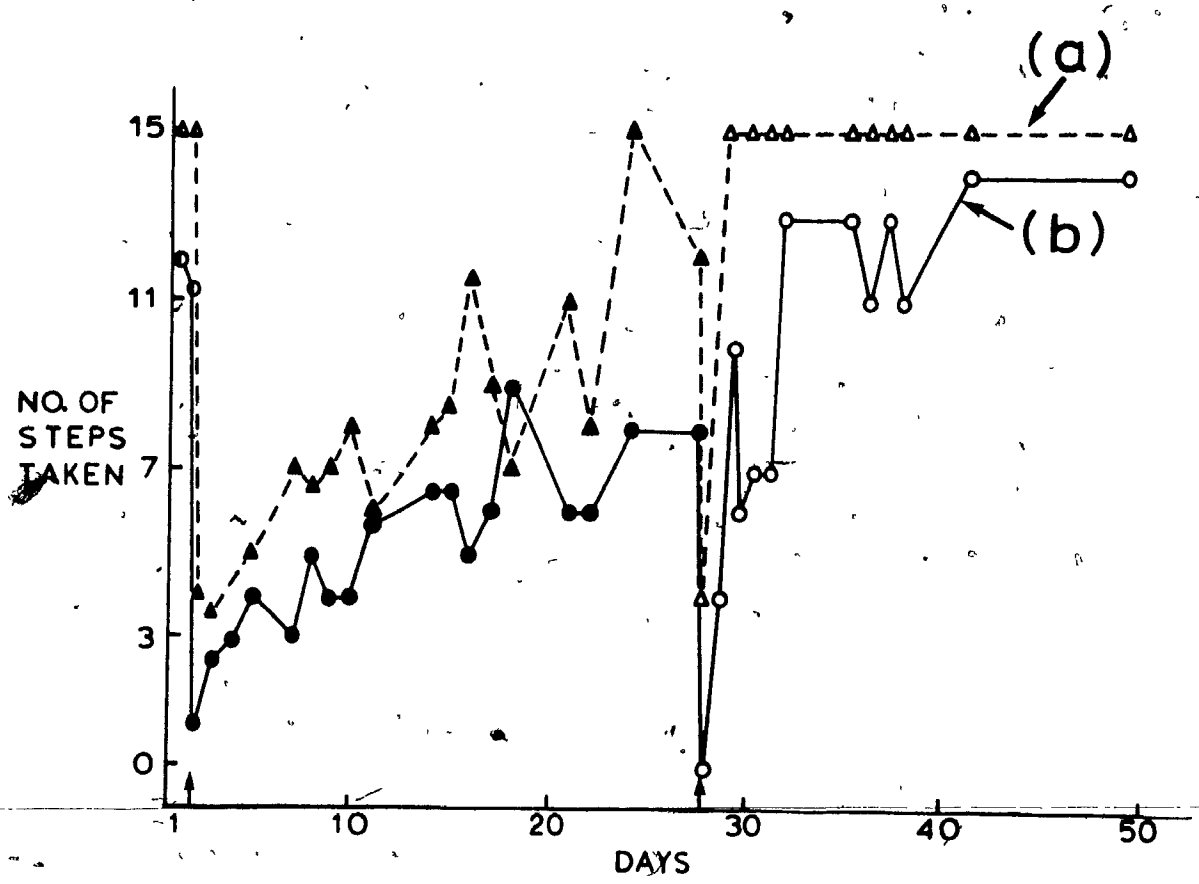
20
25
DAYS

Fig. 2.

Walking tests, with eyes open, in the 49 day experiments. (a) The 2.25 in. wide rail. (b) The 0.75 in. wide rail. Ordinates and symbols are as in Fig. 1.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DAYS

a 30 year old male, underwent 27 days of vision reversal; almost 3 weeks more than the 7 days of the 25 day experiment. Again there is the initial deficit upon donning the prisms, with a subsequent systematic increase in performance capability during the period of vision reversal, to the extent that on the 2.25 in. wide rail the subject achieves a performance value equal to the pre-vision reversal standards during a test in the 3rd week of vision reversal. The performance values on the final day of vision reversal are 85% (2.25 in. rail), and 70% (0.75 in. rail) of pre-vision reversal values, the 70% being the highest value achieved on the 0.75 in. rail during vision reversal in any of the 3 experiments.

The changes in performance on the 0.75 and 2.25 in. rails in the post-vision reversal period of the 49 day experiment differed from those in the two previous experiments, in that performance immediately after prism removal decreases dramatically to levels that equal the lowest values encountered during vision reversal. This is followed by a swift return to normal on the 2.25 in. rail (Fig. 2a) but, as in previous experiments, a more prolonged return to normal for the 0.75 in. rail tests. Scores on the latter took 5 days to return to pre-vision reversal control values (Fig. 2b). The overall increase in performance capability in the post-vision reversal period above that of pre-vision reversal levels (Fig. 2b) is most likely due to the effect of practice (Graybiel and Fregly, 1966).

(Fig. 3 near here)

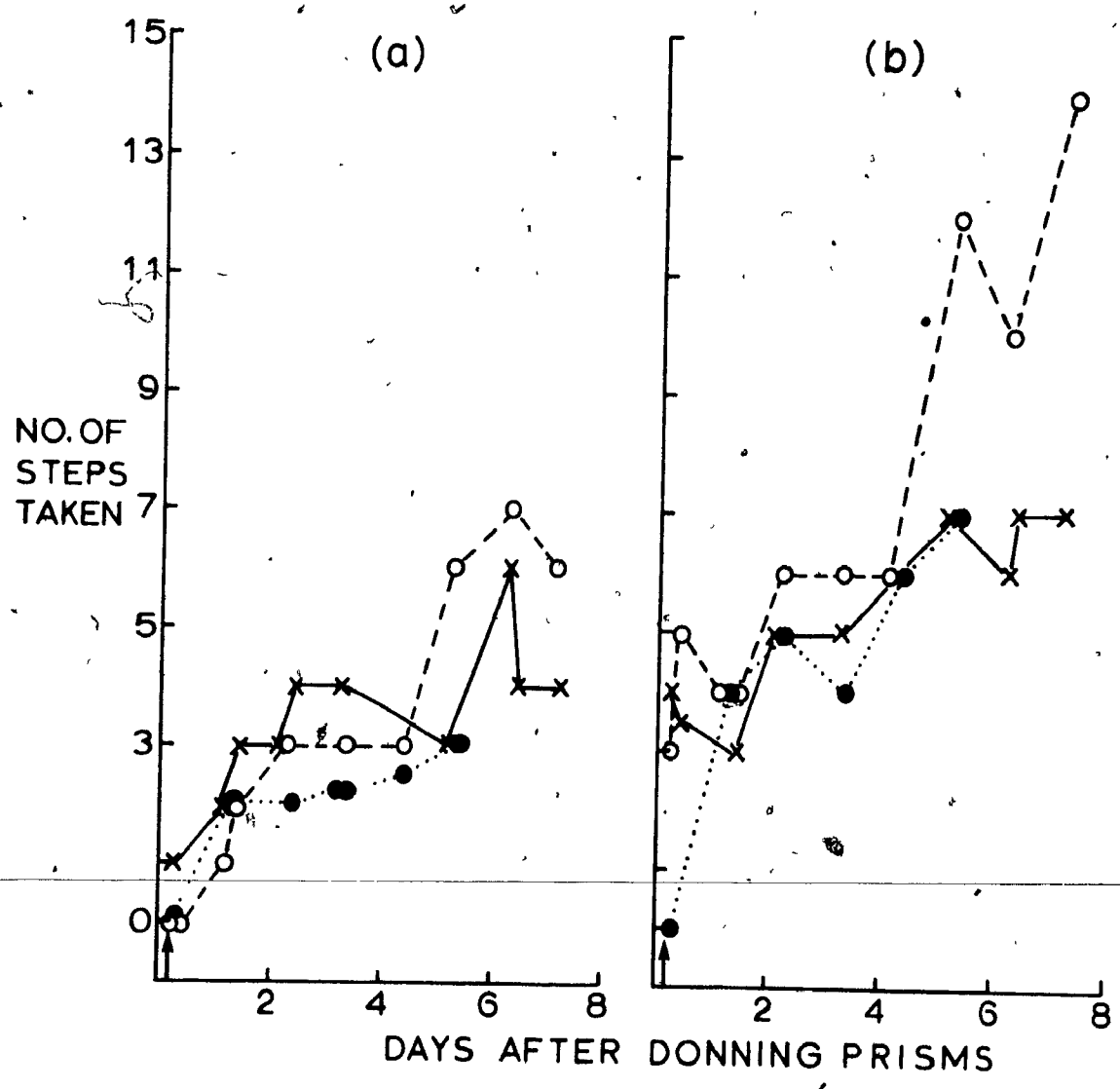
Combined results for the walking tests in the 3 experiments are seen in Figures 3 and 4. Figure 3 measures performance capability as a function of the days of vision reversal in the 17 day (●), 25 day (○), and 49 day (x) experiments. The ordinate is as in Figures 1 and 2, and the abscissa denotes the time in days after donning the prisms (↑), each number denoting the end of a 24 hour period. Each point again represents the sum of the steps in the best 3 out 5 trials constituting a test. The results for the 0.75in. wide rail tests, in Figure 3a, show clearly that the slope of increase in performance is quite similar for all 3 subjects during the first week of vision reversal. This increase progresses still further in the 49 day experiment (Fig. 2b). A similar result can be seen for the 2.25 in. wide rail tests in Figure 3b, although the point scatter is much more pronounced. Nevertheless the high degree of overlap in these values shows that not only is the increased performance capability a real phenomenon, but that it follows a definite time course, dependent on very specific neural readjustments to the new environment.

(Fig. 4 near here)

The combined results in the post-vision reversal period for the 0.75in. wide rail are shown in Figure 4. In this case the abscissa denotes time in days after removal of the prisms (↑), with

Fig. 3.

Combined results for the walking tests in the 17 (●), 25 (○), and 49 day (x) experiments, giving the total number of steps taken in tests on the (a) 0.75 in. and (b) 2.25 in. wide rails as a function of days after donning the prisms. Each day number denotes the end of a 24 hour period. The vertical arrows represent the start of vision reversal. Description of points as in Fig. 1.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NO. OF STEPS TAKEN
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8
DAYS AFTER DONNING PRISMS

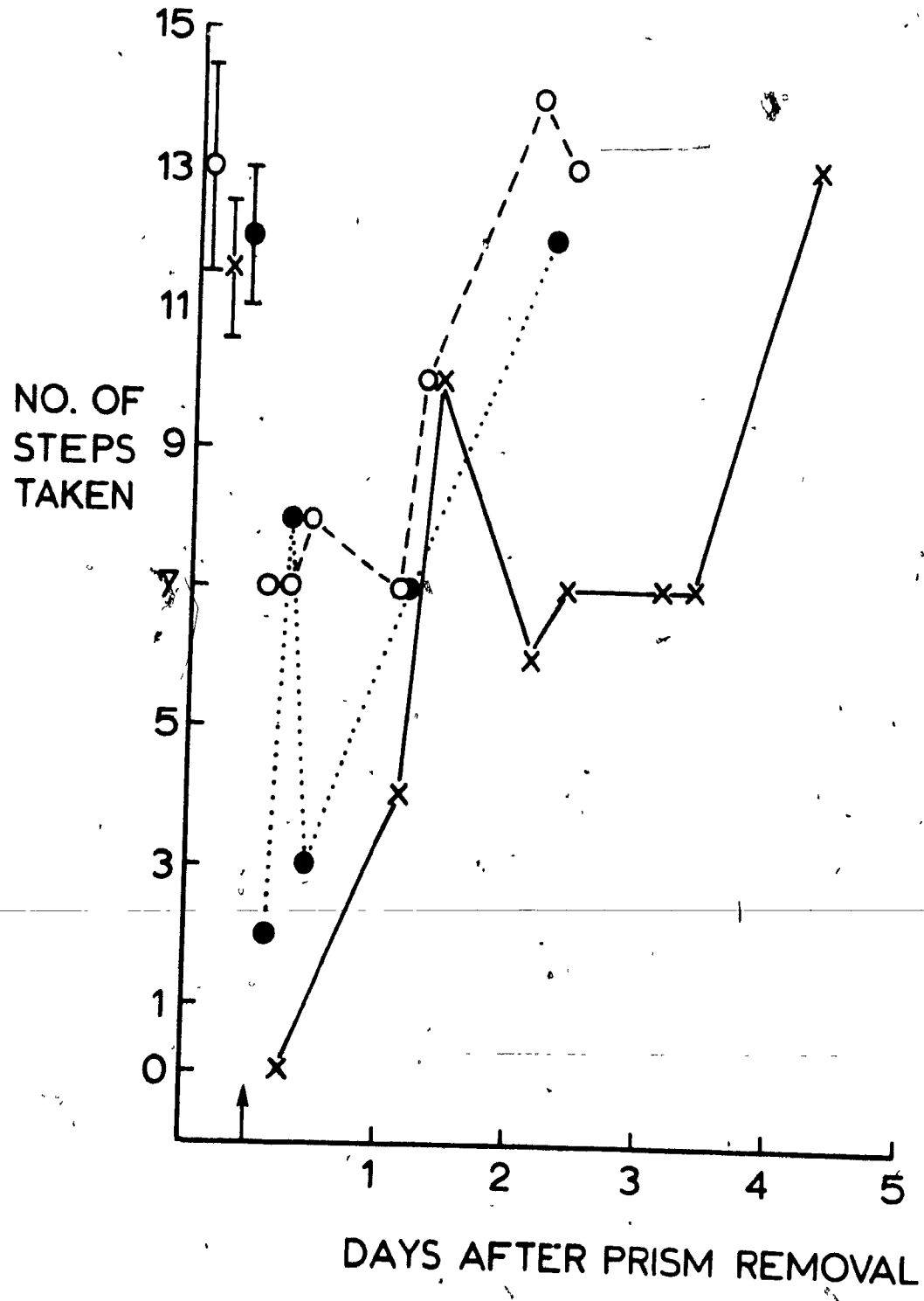
each number being the end of a 24 hour period. Pre-vision reversal control values for the walking tests are also shown, each point representing the mean of 10 tests, and the bars denoting 2 standard deviations (S.D.s) either side of the mean. Values for the 17 day (●) and 25 day (○) experiments return to normal along a similar time course, reaching control levels by the 3rd day. It should be noted that the vision reversal time for both these experiments was quite similar, being 6 and 7 days respectively. The return to normal for the 49 day experiment is more prolonged, taking at least 5 days. This is due in part to the initial low level of performance on the first post-vision reversal day (Fig. 2b) together with the fact that vision reversal in this case extended for up to 4 weeks. In general, however the return to normal during the period of post-vision reversal appears definitely to lie along a very defined course, as did the increase in performance during vision reversal, (Fig. 3), indicating a high degree of specificity in whatever change is taking place in the nervous system.

(b) Standing Tests

Standing tests were performed during the three long-term experiments on both the 0.75 in. and 2.25 in. wide rails, with eyes open or closed. The final values obtained consist of the 3 best scores out of 5 trials, with 180 sec. being a perfect score.

Fig. 4.

Combined results for the walking tests in the 17 (●), 25 (○), and 49 day (x) experiments, giving the total number of steps taken in tests on the 0.75 in. wide rail as a function of the days after prism removal. Prevision reversal points are the means of ten tests, and the bars represent 2 standard deviations either side of the mean. The vertical arrow represents the end of vision reversal. Description of points as in Fig. 1.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NO. OF STEPS TAKEN
1
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3
4
5
DAYS AFTER PRISM REMOVAL

(Fig. 5 near here)

(i) Eyes Open: Figures 5 and 6 show the capability of subjects in the 3 experiments to stand with eyes open on the 0.75 in. (circles) and 2.25 in. (triangles) wide rails. The ordinate denotes the standing time scores (sec) as a function of the days in the 17 (Fig. 5a), 25 (Fig. 5b), and 49 day (Fig. 6) experiments. The vertical arrows enclose the periods of vision reversal.

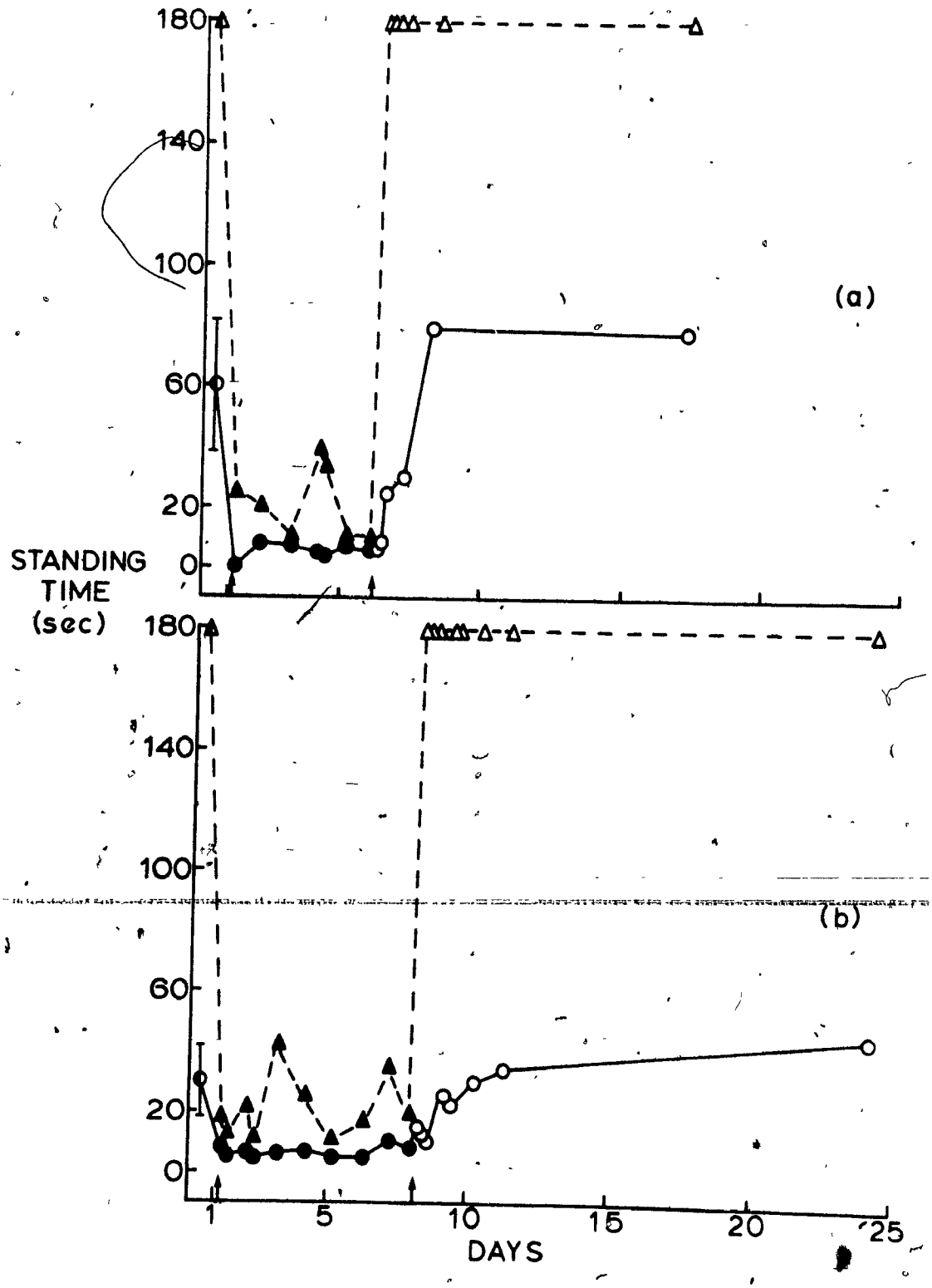
(Fig. 6 near here)

Perfect scores were obtained quite easily by all subjects in the pre-vision reversal trials on the 2.25 in. rail. However the start of vision reversal produced an almost immediate drop of more than 80% in the score. From then on there was no consistent change in score, even after 27 days of reversal in the final experiment (Fig. 6). Removal of the prisms produced an immediate return to normal in the 17- and 25 day experiments, and a return within 24 hours in the 49 day experiment.

On the 0.75 in. wide rail, pre-vision reversal control scores were only 20 to 30% of those obtained on the 2.25 rail, even after numerous practice sessions. Initiation of vision reversal again produced an immediate drop in the score, with almost no change at all during the remaining days of reversal. Upon removal of the prisms, a much more gradual return to normal took place, lasting three days

Fig. 5.

Scores of performance capability, measured during standing tests, with eyes open, as a function of the (a) 17, and (b) 25 day experiments. Tests were performed on a 0.75 in. wide rail before (◐), during (●), and after (○) vision reversal, with identical tests on a 2.25 in. wide rail (triangles). Each point represents the best 3 out of 5 trials constituting a test, with the maximum trial score equaling 60 seconds. The points in the before-vision reversal period are the means of 10 tests, with the bars representing 2 standard deviations either side of the mean. The vertical arrows enclose the periods of vision reversal.


180
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STANDING TIME (sec)
(a)
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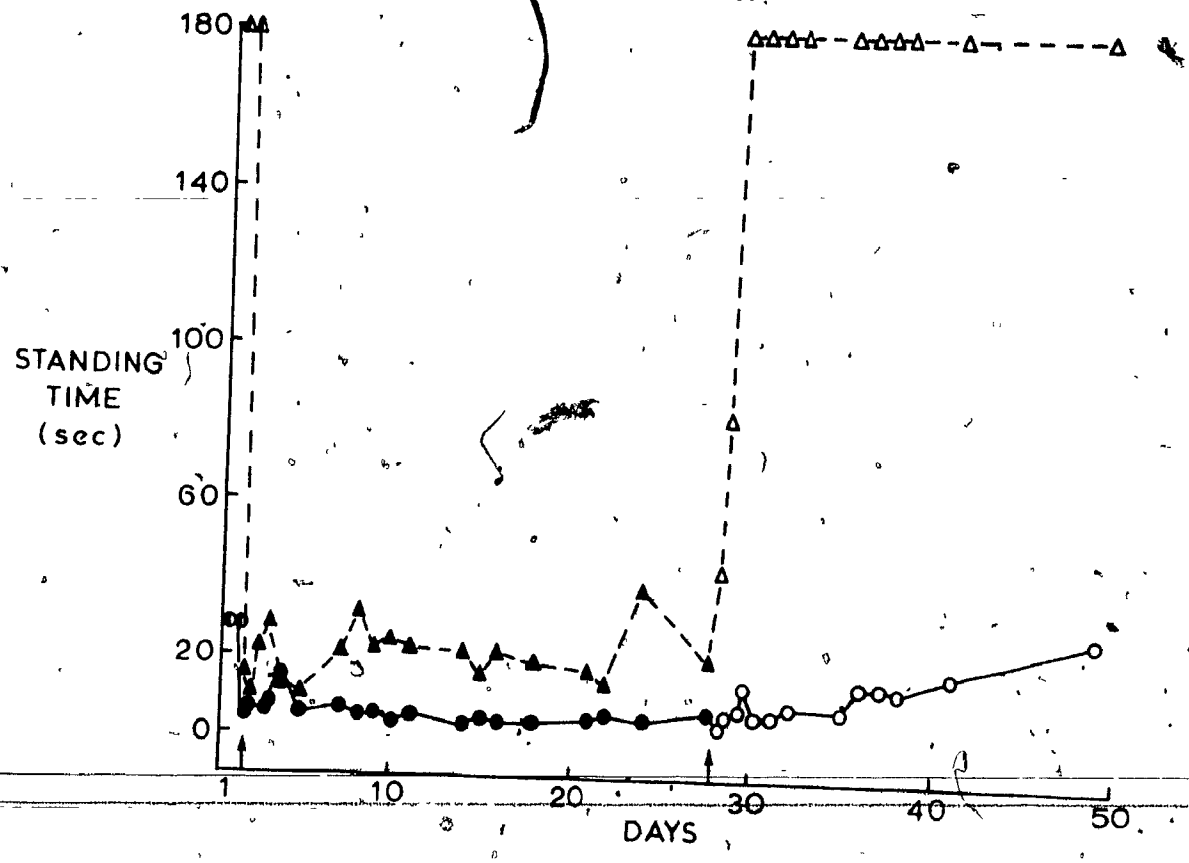
25
DAYS

Fig. 6.

Scores of performance capability measured during standing tests, with eyes open, as a function of the 49 day experiment. Description as in Fig. 5.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DAYS

in 17 and 25 day experiments and almost 3 weeks in the 49 day experiment. A practice effect is probably responsible for the high values in the post-vision reversal period of the 17 and 25 day experiments.

(Fig. 7 near here)

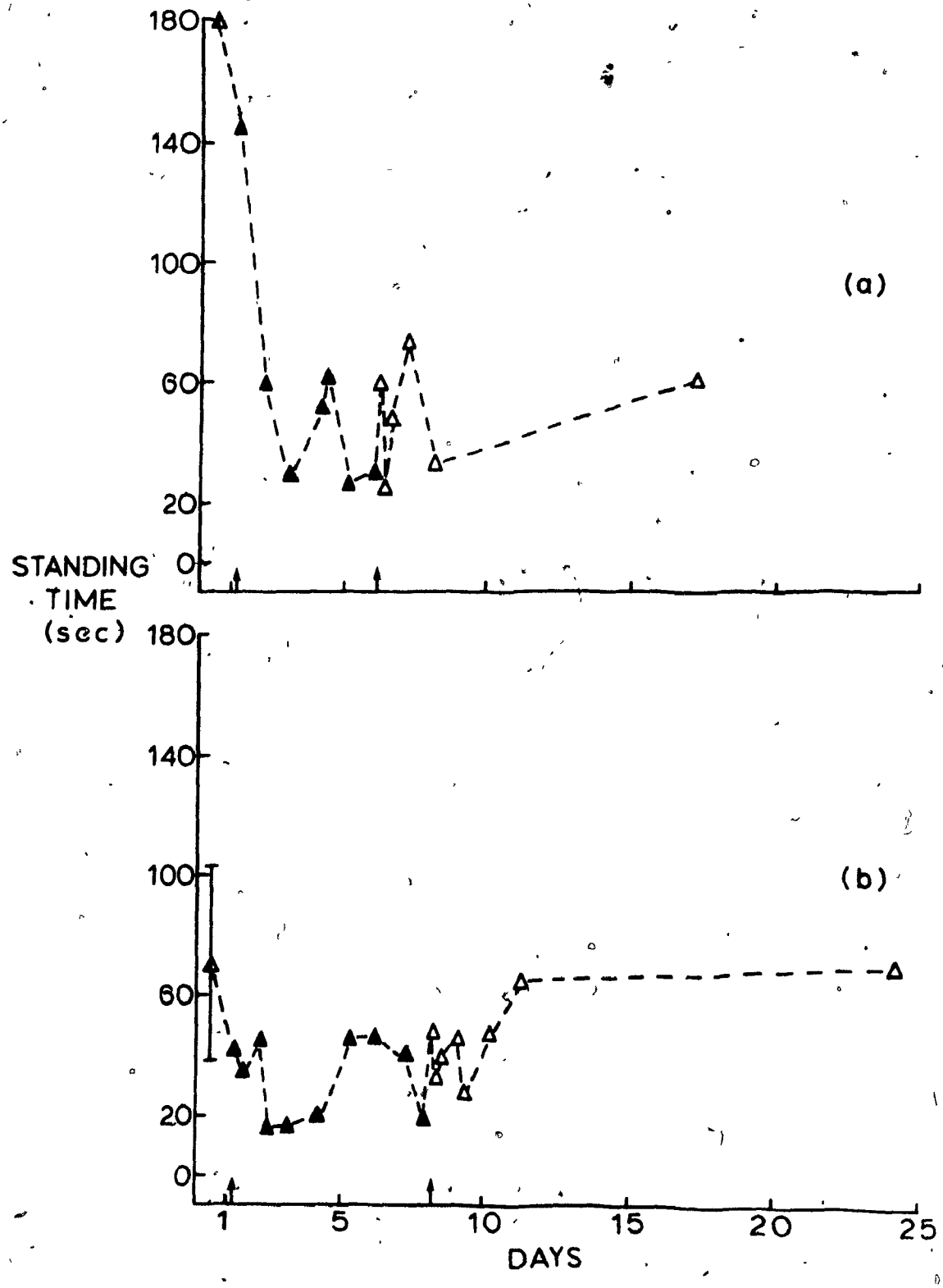
(Fig. 8 near here)

(ii) Eyes Closed: The standing tests, with eyes closed, in the short version of the QATB, are performed only on the 2.25 in. wide rail. Results of these tests are shown in Figures 7 and 8. All coordinates are as in Figure 5. In the pre-vision reversal trials only the subject in the 17 day experiment consistently attained the 180 sec. perfect score. The mean control scores for subjects in the 25 and 49 day experiments were significantly lower, at 70 and 90 secs respectively (bar shows 2 S.D.s about the mean). Values fell to their lowest levels within 48 hours of the start of vision reversal in both the 17 and 25 day experiments and in less than 24 hours during the 49 day experiment (Fig. 8), indicating a slightly lower rate of decrease in the eyes closed than in the eyes open condition. The scores for the remaining reversal days, although undergoing some fluctuations, did not show any consistent overall change.

The improvements after removal of the prisms followed an interesting pattern. In the 17 and 49 day experiments, improved

Fig. 7.

Scores of performance capability, measured during standing tests, with eyes closed, as a function of the (a) 17, and (b) 25 day experiments. Remainder of description as in Fig. 5.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(a)
STANDING TIME (sec)
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(b)
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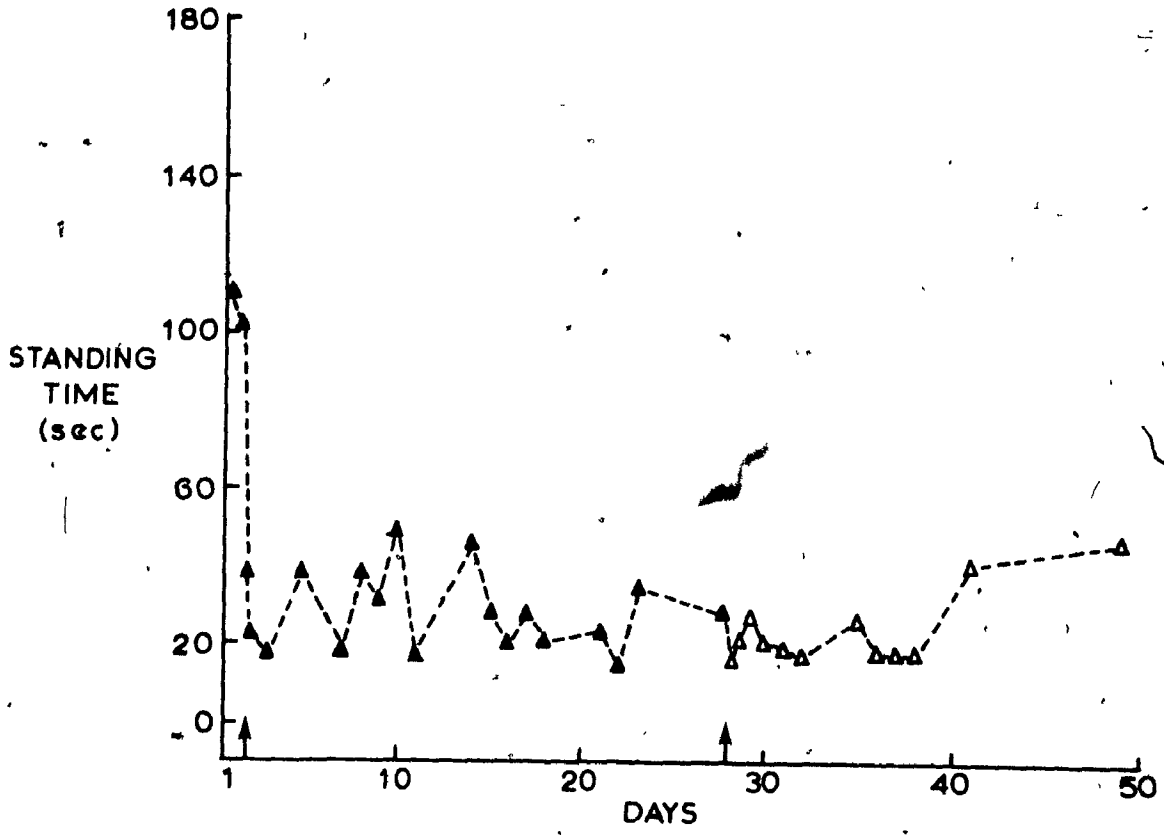
25
DAYS

Fig. 8.

Scores of performance capability, measured during standing tests, with eyes closed, in the 49 day experiment. Remainder of description as in Fig. 5.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STANDING TIME (sec)
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DAYS

performance was quite limited and erratic, with the feature that even up to the last testing day the scores remained at levels almost as low as those encountered during vision reversal. In the 25 day experiment the score returned to normal after 4 days, although the improvement was also quite erratic. However, the absolute increase in score was no greater than in the other two experiments, the return to normal being due to a low control value in the pre-vision reversal trials. The eyes closed therefore proved more sensitive to the influences of prolonged rotation.

2. Perception And Visual-Motor Coordination: Subjective Reports and Observations

In most of the previous studies on long-term adaptation (Guedry, Kennedy, Harris and Graybiel, 1964; Graybiel, Kennedy, Knoblock, Guedry, Mertz, McLeod, Colehour, Miller and Fregly, 1965; Guedry, 1974), objective testing has been augmented by subjective reports of the subjects, together with observation of their overall visual-motor coordination. In fact, observation and subjective reports have played the dominant role in many of the psychological experiments concerned with visual reversal (Kohler, 1962; Taylor, 1962), and its effect on perception.

Although the main interest in the present experiments was to study the effect of vision reversal on the vestibulo-ocular reflex, subjective reports and observations were carried out, as means of providing any extra information on what the responsible underlying physiological processes might be.

(a) General Observations

Some of the subjective reports and observations have already been described elsewhere (Gonshor and Melvill Jones, 1974c). Briefly, all subjects suffered from varying degrees of nausea in the first days of vision reversal. This was coupled with overall lethargy and fatigue. During this time all the senses acquired an increased sensitivity. One subject reported that both hearing and smell were greatly accentuated. It is interesting that this was coupled with a loss of appetite that accompanied the overall feeling of nausea.

A consistent finding during this period, in all subjects, was the mild sensations of rotation experienced upon retiring for the night or resting, with eyes closed, in a supine position. The sensation was most often about the body's long axis and took various forms, from to-and-fro swaying, to very transient feelings of uni-directional acceleration. In one case it took the form of an uncontrollable "... involuntary motion, with the world going round and round." One subject described the sensation as similar to "... going to bed after having just a bit too much alcohol." This sensation continued occurring even into the 4th week of reversal in the 49 day experiment. These sensations often were sufficient to wake the subject in the middle of the night, and in one instance a subject reported that these sensations were associated with objective eye movements. The following morning there would be an unpleasant

overall feeling; that is, a residual nausea coupled with considerable fatique. One subject likened the feeling to a "... mild influenza attack."

The conflict between the reversed visual system and the remaining senses manifested itself in numerous ways. For example, while riding in a car that was making a turn to the right, the subject sees himself turning left but feels the centrifugal force acting to the left rather than to the right. Although one normally generates programmed muscular activity to tilt against the force, the strong visual impression of turning to the left leads, in this case, to initiation of muscular activity to the left. Therefore, the muscular programs now increase the tilt produced by the centrifugal force itself, and the subject experiences the sensation of "... being forced by an 'iron hand' into the left side of car as it went around the corner."

Another strange feature encountered whilst turning in a car, was a peculiar sensation of "... turning in a straight line." With eyes shut, the subject felt clearly that the car was turning, say, to the left (the true direction). However, upon opening the eyes, the subject "saw" that the car was turning right. The cancelling of these sensory inputs produced a sensation of 'zero turn"!

On a day when objective tests had shown his vestibulo-ocular gain to be very low, one subject went on a shopping excursion, and whilst sitting in a parked car, looked at the surrounding outside world; in this case a parking lot. Upon rotating the head very slowly in the

horizontal plane, the outside world seemed to oscillate relative to space. Similar sensations were encountered by all subjects in the first few days of vision reversal. However with continuation of the reversal, all three subjects began to report that vision was becoming "clearer" with the prisms on. So much so, that reports from one subject on the final day of vision reversal in the 25 day experiment were to the effect that, clarity of vision with the prisms on had improved to the extent of making it easier now to see the outside world whilst moving with the goggles on, than with them off

(b) Postural Equilibrium And Locomotion

In the first days of vision reversal locomotory activity underwent severe disruption. Subjects made very slow and deliberate movements, often utilizing a shuffling locomotion reminiscent of that seen in Parkinsonians. When making a turn subjects would go through a series of stop and start manoeuvres; first, stopping and moving the head in a to-and-fro "hunting" fashion toward the target seen through the prisms, and then moving the rest of the body in the supposed direction of the target. In this manner turning was accomplished; but very slowly. If the subject attempted to turn a corner in one continuous walking motion, the lack of visual-motor coordination resulted in some interesting body contortions. For example, upon attempting a left turn, the subject's head would begin to move right, following the reversed visual surround. At the same time the torso would continue moving straight ahead, so that the

head and torso were now heading away from each other at an increasing angle. Sensing this discrepancy one leg would now be moved in the direction of head motion, causing a crossover of the legs and loss of balance, not to mention disorientation and frustration on the part of the subject. Since these manoeuvres can be very dangerous, it is advisable that anyone undertaking a vision reversal experiment, make provision for constant supervision of the subject.

After the first 3 to 5 days, subjects became increasingly adept at negotiating straight corridors, as well as turning corners, without stopping. However, the "hunting" movements of the head during locomotion did not disappear completely, even after 4 weeks of vision reversal in the 49 day experiment.

In the first several hours after removing the prisms subjects exhibited a wide-stanced shuffling gait when walking, requiring assistance so as not to bump into walls. When turning a corner subjects often began to move in the opposite direction to the intended turn, in a manner much like that described for the first days of vision reversal. By the end of the first day the subjects were manifesting an increasingly proficient walking capability. Subjects commented at this time that, in their opinion, locomotory activity was now back to normal. However, up to 3 days after termination of vision reversal two subjects reported that the act of walking along a corridor in a straight line required conscious effort. In fact, one of these subjects was actually observed holding onto the wall as he negotiated a curve in a corridor.

During walking tests (0.75 in. rail) on the first day after prism removal, all subjects complained that they were unable to walk because "... the world is shaking." One subject noted further that unlike the normal case of balancing, where the head is kept steady in space while the body moves under it, in the tests on the day of prism removal the head tended to automatically move in the same direction as the body. Two subjects, attempting to walk on the 0.75 in. rail with eyes open, noted that even a slight movement of the head, say to the left, produced a violent movement of the world to the left, and then to the right. That is, an initial movement of the world in the wrong direction. On the first post-day this caused immediate imbalance. On the second day, the movement of the outside world was still present and in the opposite direction, but covering only half the distance of the previous day. This phenomenon persisted into the third day.

Finally even after one week post-vision reversal the subject in the 49 day experiment reported mild vertigo during rapid head movement, and a blurring of objects in the visual surround with even moderate head oscillation.

DISCUSSION

Postural Equilibrium Tests

In previous articles it was shown that long-term vision reversal has a profound effect on vestibulo-ocular function (Gonshor and

Melvill Jones, 1974c; Gonshor, 1974a), producing large changes in the gain and phase of vestibulo-ocular response, as well as functional impairment of visual fixation.

It seems clear from the present results that functional deficits are also incurred in whole body balance, or postural equilibrium.

The following is a brief discussion of some interesting features arising from the results.

(1) The walking tests with eyes open, when compared to the standing tests, have shown themselves to be a far more sensitive indicator of the changes taking place in performance capability. Furthermore, inclusion in the present experiments of two additional tests (stand, and walk, with eyes open on the 2.25 in. wide rail), to supplement the regular 3 tests comprising the short version of the Quantitative Ataxia Test Battery (see Appendix), has highlighted the importance of using a test battery that includes rail sizes that can statistically separate individuals in a large test population on the basis of their ability to maintain postural equilibrium. Wide gradation of rail widths is available in the long version of the Ataxia Test Battery (Graybiel and Fregly, 1966), but the latter is quite cumbersome and time consuming. For the latter reasons, a short version was devised by these same authors (Graybiel and Fregly, 1966). This short version includes tests on a 0.75 in. wide rail, which most subjects find difficult to balance on, but can still master. The 0.75 in. rail has been found to be a good indicator of postural

equilibrium in their tests.

In the present experiments, it was initially believed that the 0.75 in. wide rail would prove too difficult a challenge for the subjects, and for that reason duplicate tests were added on the 2.25 in. rail. The results show clearly that the subjects were capable of balancing on the 0.75 in. wide rail, and that this rail was, in the final analysis, the most sensitive guage of improving capability, registering changes that were not detected on the 2.25 in. wide rail.

(2) The improvements seen in performance capability after vision reversal are similar to results obtained from a recent series of Skylab orbiting space missions (Homick, Reschke and Miller, 1974). In the 2nd, 3rd and 4th flights, crewman were exposed to weightlessness for 28, 59 and 84 days respectively. In the pre and post-flight periods, they were tested on a modified version of the quantitative ataxia test battery (Graybiel and Fregly, 1966). The tests consisted of standing with eyes open and closed either on rails of various widths, or on the floor (the latter only in the 28 day mission). The post-flight data indicated moderate decrements in postural equilibrium in the eyes open tests for only 3 of the 9 crewmen. In the eyes closed condition all crewmen showed a considerable decrease in ability to maintain balance, with recovery taking up to 2 weeks.

The zero "g" condition encountered in the space environment probably causes functional alterations in the interaction of vestibular, visual and kinesthetic mechanisms, much like those

observed in the present experiment, so that functional impairment was to be expected. However, it seems that by not utilising some form of walking test, Homick et al (1974) have omitted what the present experiments have shown to be the most sensitive indicator of functional impairment. Inclusion of the walking test in future flights may allow for a more precise indication of overall impairment, as well as time course of recovery.

In addition to these objective tests, subjective reports and observation of the astronauts has shown that in the post-flight period they experience an almost identical shuffling gait, inability to turn corners, and vertigo during the first several days.

(3) A complete ataxia test battery has been performed on several groups of normal subjects who were rotated for 12 day in a slow rotation room or SRR (Graybiel et al, 1965). Comparison of pre, and immediate post-tests on the rails, showed in all instances a severe decline in performance, with recovery in 24 to 72 hours for all save the standing, eyes closed test. In fact, walking and standing with eyes open tests had actually improved, leading the authors to conclude that non-visually influenced standing, eyes closed, was more sensitive to the influences of prolonged rotation. Similar results were obtained with subjects undergoing a day of severe sea conditions off the Canadian coast (Graybiel and Fregly, 1966).

Apart from Skylab, the experiments in the SRR are probably the closest parallel of the present experiments, in that both cases involve functional rearrangements during the stimulus condition so

as to optimize for the new environment. This leaves the subject with a functional impairment when returned to the normal environment.

This being the case, our results follow a very similar pattern. The walking tests do prove to be a sensitive measure of improving performance during vision reversal. Note that no balance tests were performed during rotation in the SRR. In the post-vision reversal period of the present experiments, performance on the walking tests returned to normal within 3 to 5 days (1 to 3 days for the SRR), whereas the performance in the standing, eyes closed, test stayed very low; in some cases up to the last day of post-testing, weeks later.

The fairly rapid return to normal performance in the post-tests, with eyes open, is probably due in great part to the stabilizing role played by active visual fixation. With eyes closed, one is left with a bilateral vestibular mechanism that is attempting to readjust to normal. The varying rates of recovery of this bilateral system could account for an imbalance in its posture control, just as it probably is responsible for the "directional preponderance" in nystagmus (Gonshor and Melvill Jones, 1974c).

(4) In the first test of walking with eyes open (0.75 in. and 2.25 in. wide rails - Fig. 2), after removing the prisms, one sees a dramatic drop in performance. This result could be explained by the fact that in this case normal vision is incompatible with a functionally reversed vestibulo-ocular response (Gonshor and Melvill Jones, 1974c); this incompatibility being quite similar to what is

experienced in the initial period after donning the prisms. But this low performance improves very significantly by the next test, one hour later. Tests of vestibulo-ocular reflex recovery (Gonshor and Melvill Jones, 1974c) showed that phase returned in a matter of hours to its normal relationship, whilst gain took much longer. Therefore the reversed response is present in only the first one or two tests, accounting for the initial decrease seen in Figures 2a and b.

Possible Mechanisms

In previous experiments (Gonshor and Melvill Jones, 1974c; Gonshor 1974a)it was proposed that cerebellar modification of the basic disynaptic vestibulo-ocular reflex arc could be responsible for the large changes observed in vestibulo-ocular response. In searching for possible centers that could play a role in the changes of postural equilibrium, one must again view the cerebellum as a prime candidate. It has been established for many years (Pollock and Davis, 1927; Mussen, 1934; Hess, 1940), that one main function of the cerebellum is to coordinate labyrinthine with other postural reflexes so as to maintain normal postural equilibrium and locomotory activity. Disturbance of postural equilibrium and righting reflexes can be brought about by lesioning the fastigial nuclei (Moruzzi and Pompeiano, 1957a), the response having its origin in the vermis and moving to the pons via the inferior peduncle (Moruzzi and Pompeiano, 1957b). Many cerebellar fibers move down the vestibular

nuclei either directly (Jansen and Brodal, 1958; Walberg and Jansen, 1964) or by way of the cerebellar nuclei (Brodal, Pompeiano, and Walberg, 1962), and from there vestibulo-spinal pathways lead to all levels of the spinal cord, with afferent information returning by way of the spinocerebellar tracts (Lundberg and Oscarsson, 1962). This strong connection with the spinal cord, the vestibular system, as well as the thalamus, red nucleus and reticular formation, gives the cerebellum a powerful position for the control of postural equilibrium.

In addition to the cerebellum, recent experimental evidence indicates that the spinal cord itself possesses great capacity for change. Lundberg and his colleagues (1966; 1967) have shown that inhibitory interneurones in well known reflex arcs receive input from more than one primary afferent path as well as from descending pathways, so that every segmental pathway between primary afferent fibers and motoneurones receives convergent input from descending and other afferent systems. These recently discovered patterns of input convergence, cross-connections, and feedback allow one to conceive of a spinal cord that can radically alter its control of flexor and extensor muscles, if not reverse its input to these muscles entirely. Furthermore, this alteration could be brought about by a combination of inputs from the vestibular, cerebellar, and reticular systems, as well as from muscle, skin, and joint receptors.

Therefore, experiments such as the present vision reversal, the Skylab space missions, or the SRR, all expose subjects to a

change in the normal interrelationship of kinesthetic, visual and vestibular inputs. Further neurophysiological experimentation will be necessary to determine if and how the spinal cord and cerebellum play a role in the modification of postural response.

CHAPTER 8

CONCLUSIONS

CONCLUSIONS

In the Introduction chapter a series of questions were put forth as the problem formulation for this thesis. In this concluding chapter what remains is to assess the degree to which these questions have been answered by the present experiments, and to provide a final overview of the entire study as a possible basis for future research.

It seems that this thesis is a good example of how a very specific topic in the initial stage can, in the end, develop into a general and perhaps more basic conception of what underlying principles and mechanisms are involved.

The initial experiment, concerning habituation to oscillatory rotation in the dark, had its gestation in the specific realm of applied aviation experiments. The observation that vestibular response declines during unidirectional rotations, such as those experienced in the flight environment, led to the question of whether this would appear with "natural", sinusoidal stimulation. Why sinusoidal? It seemed that at least in the human, observation alone shows that a good part of one's head motion is of a sinusoidal nature. This observational information is borne out by the action of the vestibular end organ, which responds most effectively to transient input, and less so to those of a steady state nature, the latter created by unidirectional rotations. The fact that there were no changes in

vestibular response to the sinusoidal stimulation, cannot however rule out the possibility that we are merely looking at an already habituated response, the latter occurring in childhood. Not withstanding the inherent experimental difficulties, it might therefore be of interest to conduct formal experiments in very young subjects to determine if a higher vestibulo-ocular gain does in fact exist at that early stage of life, and if response changes do occur during oscillatory stimulation per se. The results of such experimentation may show that adult man's vestibular response is inexorably set after what has been called the critical learning time. Such a critical point has been shown to exist in the monkey visual system, where lack of patterned vision during the first 7 months of life leads to significant and permanent loss of normal visual capability even if patterned vision is permitted after that period (Riesen, 1950).

The importance of the habituation brought on by conflicting visual and vestibular stimuli in the mirror-reversed vision experiment (Chapter 4), lay not so much in the discovery that the vestibulo-ocular response to the previously non-habituating sinusoidal stimulus could now be attenuated, but rather in the formulation of a more basic concept of physiological capability. Namely, that the results obtained constitute a neurological remodelling of relevant elements in order to meet the new stimulus-response optimisation criteria, no matter how radical the required change. In that light,

the definition of habituation, as attenuation in response to long-term repetitive stimulus, must be broadened accordingly to encompass the more general concept of optimisation.

The long-term vision reversal experiments provided the necessary condition for radical change, and the resulting changes went far beyond mere attenuation of the vestibulo-ocular response, leading instead to the required optimisation; that of a functional reversal of the vestibulo-ocular reflex, with accompanying optimisation of postural equilibrium, perception, and visual-motor coordination. However, the change in vestibulo-ocular response was not just to a simple high gain, though reversed reflex, but rather to a much more complex, and yet stereotyped, pattern of change in gain and phase of vestibulo-ocular reflex relative to stimulus condition.

To elucidate the nature of these stereotyped changes, some tentative proposals have been made as to possible mechanisms at the neuro-physiological level, which could be responsible. A tentative model would consist of the well known disynaptic vestibulo-ocular reflex arc (Szentágothai, 1950) as the primary pathway, the secondary path running via the vestibulo-cerebellar-vestibular nuclei relay (Brodal, Pompeiano and Walberg, 1962; Precht and Baker, 1972), and possessing an inhibitory influence on the vestibular signals to the oculomotor nuclei (Precht and Baker, 1972). The necessary visual influence could be provided by a retinal-cerebellar pathway recently found to exist in rabbits (Maekawa and Simpson, 1972; 1973). The retinal stimulation has very recently been shown to cause short latency membrane potential

changes in the Purkinje cells of the flocculo-nodular node of the cerebellum (Ito et al, 1974a, b).

It seems, therefore, that apart from the short "hard wired" connections such as the vestibulo-ocular reflex arc, there are additional central elements, such as the secondary pathway above, that may be capable of directing a high degree of goal-directed plasticity when functionally required.

The present experiments have established that given an appropriate goal-directed need for change, the human central nervous system is capable of phenomenal change, even at the level of the simple two synapse reflex arc. This change is accompanied by functional impairments of visual fixation and postural equilibrium as well as fatigue, lack of motivation and malaise, and acute disorientation. The adaptative changes also run a long and stereotyped course of a month or more, with a similar period of time for the readaptation to normal after vision removal is terminated.

Future animal experiments will hopefully begin to examine what mechanisms in the central nervous system are responsible for the dramatic reorganisation of neural elements that must in turn be the cause of the habituating process established in this thesis. It would be of great interest to determine what pathways are involved in the response changes, what drive is needed to force the process to its limit. Perhaps such experimentation will lead to an understanding of the basic time course of a general habituating process in the central nervous system.

As a final remark, some applied considerations are apropos. The recent Skylab astronauts, as well as pilots and seamen, have often suffered the malaise and nausea that comprise the motion sickness syndrome, the latter being responsible for impairment of performance and motivation. The time course of their symptoms is very similar to the induced motion sickness of vision reversal. The prism-reversal may provide a simple and inexpensive method upon which to base the assessment of the time course, the degree of impaired function, and the value of therapy in the treatment of the side effects of the habituating process. In the case of astronauts the prisms may be a useful tool in the habituating of individual whilst still on the ground, therefore increasing the valuable working time of the man in space. Intriguing results from recent experiments employing vision reversal (Taylor, 1962) have shown that by wearing reversing goggles for only selected periods of the day one can eventually reach a point of normal motor performance and visual perception in both the reversed and non-reversed environment. Could such training be applied to astronauts, so as to allow them to perform with the least amount of side effects both on earth and in their space environment?

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APPENDIX

"Quantitative Ataxia Test Battery"

Test Battery (Short Version)

All the tests were performed with shoes on. Males wore flat leather soled shoes, and the female subjects wore thin-soled flat shoes. Prior to testing, all subjects were given the following instructions.

Instructions

Test Sequence:

(a) Walking with eyes open (E/O) on a 0.75 in. wide rail (8 ft. long)

(b) Standing with eyes open on a 0.75 in. wide rail (")

(c) Standing with eyes closed (E/C) on a 2.25 in. wide rail (")

(d) Walking with eyes open on a 2.25 in. wide rail (")

(e) Standing with eyes open on a 2.25 in. wide rail (")

(Note: (d) and (e) were added to tests not included in the original Pensacola tests. The rest of the instruction and procedure are identical.)

Body Position For All Tests:

a. Body erect or nearly erect

b. Arms folded against chest

c. Feet in heel-to-toe position (H/T)

d. Feet tandemly aligned

Scoring: The best 3 out of 5 trials constitutes the scoring procedure.

a. Walk H/T Test - The first 2 steps, which are necessary for positioning on the rail, are not scored. A trial begins when the third step is taken.

b. Stand E/O Test --Timing begins as soon as correct position on the rail is assumed.

c. Stand E/C Test - You may take unlimited time for positioning yourself on the rail, first with your eyes open. Timing will begin as soon as you close your eyes. Examiner will observe your eyes carefully, so that signalling the examiner is unnecessary.

General:

As there does not appear to be any single "best method", you must develop (rapidly) your own techniques. You may position your head up or down and/or forward or backward; you may lean forward or backward slightly if you do not prefer a perfectly erect position; between trials, alternation of the feet is permissible; you may place more weight on your front foot than on your rear foot or vice versa, or you may distribute your weight equally. However, a stooping position should be avoided.

Scoring Procedures

As with the Long Version, after subjects read instructions the examiner demonstrated all procedures and answered all questions raised about the performance procedures. Examiner gave two or three demonstrations

of standing on each of the two rails. The scoring procedures were as follows:

Walk H/T Test

a. Each correct step is scored as one (step).

b. Maximum trial score equals five (steps).

c. Maximum test score equals fifteen (steps), the sum of the three best trials.

Stand E/O Test

a. Timing, to the nearest second, begins when subject assumes correct and balanced position on the rail, and timing ends at 60 seconds, or when subject violates his position, or falls off the rail.

b. Maximum trial score equals 60 (seconds).

c. Maximum test score equals 180 (seconds), the sum of the three best trials.

Stand E/C Test

a. Timing begins as soon as positioned subject closes his eyes, and timing ends at 60 seconds or when subject violates his position, or opened his eyes, or falls off the rail.

b. Maximum trial score equals 60 (seconds).

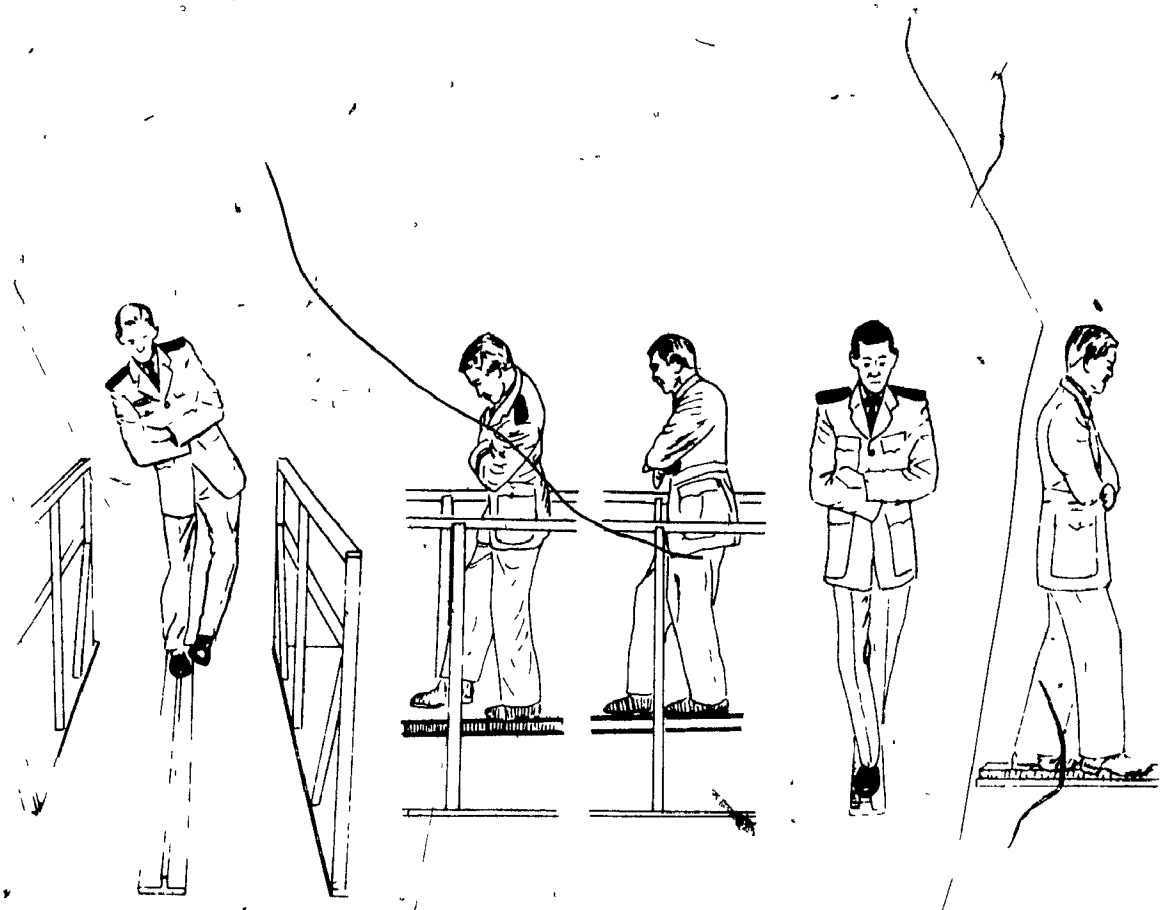
c. Maximum test score equals 180 (seconds), the sum of the three best trials.

A representation of the test battery - short version (from Graybiel and Fregly, 1966).

a. and b. - walk H/T Test (on 0.75 in. wide rail).

c. - Stand E/O Test (on 0.75 wide rail).

d. and e. Stand E/C Test (on 2.25 in. wide rail).



A B C D E