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EXTREME VESTIBULO-OCULAR ADAPTATION INDUCED BY PROLONGED OPTICAL REVERSAL OF VISION

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SUMMARY

1. These experiments investigated plastic changes in the vestibulo-ocular reflex (VOR) of human subjects consequent to long-term optical reversal of vision during free head movement. Horizontal vision-reversal was produced by head-mounted dove prisms. Four normal adults were continuously exposed to these conditions during 2, 6, 7 and 27 days respectively.

2. A sinusoidal rotational stimulus, previously shown to be non-habituating (1/6 Hz; 60°/sec amplitude), was used to test the VOR in the dark at frequent intervals both during the period of vision-reversal and an equal period after return to normal vision. D.c. electro-oculography (EOG) was used to record eye movement, taking care to avoid changes of EOG gain due to light/dark adaptation of the retina.

3. All subjects showed substantial reduction of VOR gain (eye velocity/head velocity) during the first 2 days of vision-reversal. The 6-, 7- and 27-day subjects showed further reduction of gain which reached a low plateau at about 25% the normal value by the end of one week. At this time the attenuation of some EOG records was so marked as to defy extraction of a meaningful sinusoidal signal.

4. After removal of the prisms VOR gain recovered along a time course which approximated that of the original adaptive attenuation.

5. In the 27-day experiment large changes of phase developed in the VOR during the second week of vision-reversal. These changes generally progressed in a lagging sense, to reach 130° phase lag relative to normal by the beginning of the third week. Accompanying this was a considerable restoration of gain from 25 to 50% the normal value. These adapted conditions, which approximate functional reversal of the reflex, were then maintained steady, even overnight, until return to normal vision on the 28th day.

6. Thereafter, whereas VOR phase returned to near-normal in 2 hr, restoration of gain occupied a further 2–3 weeks.

7. There was a highly systematic relation between instantaneous gain and phase, even during periods of widely fluctuating change associated with transition from one steady state to another. During such transition there was a tendency for directional preponderance to occur in the VOR.

8. All the observed changes were highly specific to the plane of vision-reversal, no VOR changes being observed in the sagittal plane.

9. VOR changes were *adaptive*, in the sense that they were always goal-directed towards the requirements of retinal image stabilization during head movement. They were *plastic* to the extent that there was extensive and retained remodelling of the reflex towards this goal.

10. It is inferred that all the observed changes in gain and phase are compatible with a simple neural network employing known vestibulo-ocular projections *via* brainstem and cerebellar pathways, providing that the reversed visual tracking task can produce plastic modulation of efficacy in the cerebellar pathway and that this pathway exhibits a dynamic characteristic producing moderate phase lead in a sinusoidal signal at 1/6 Hz.

INTRODUCTION

A previous study (Gonshor & Melvill Jones, 1976) led to the conclusion that short durations of attempted visual fixation on a mirror-reversed image of the surroundings during sinusoidal head and body rotation, led to progressive and retained adaptive decline of the vestibulo-ocular-response (VOR) measured in the dark. The present experiments examine effects upon the VOR of prolonged vision-reversal during naturally occurring head movements.

The previous method of adaptive stimulation, in which subjects were rotationally oscillated on a 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, thus establishing horizontal reversal of the visual field whilst permitting direct forward vision with free head and body movement. The same non-adaptive sinusoidal stimulus as before was used to test intermittently the VOR in the dark. Brief communications on preliminary results have been reported previously (Gonshor & Melvill Jones, 1971, 1973; Melvill Jones & Gonshor, 1972, 1975).

METHODS

Dove-prism reversal of vision

The method of image reversal by means of the 'dove' prism is outlined in Fig. 1. With eyes and prism stationary relative to one another, movement of an object, O, from left to right leads to reversed movement of the virtual objects O′ and O″ due to total internal reflexion at the surface B. 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 a somewhat restricted visual field of approximately 60° solid angle in our experiment. With the prism-goggles fixed to the head, horizontal head rotation, 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. Orientation of the prisms was arranged to produce optical reversal in the 'horizontal', but not sagittal, plane of the skull. This conveniently allowed head rotation in the sagittal plane to be employed for within-subject control purposes.

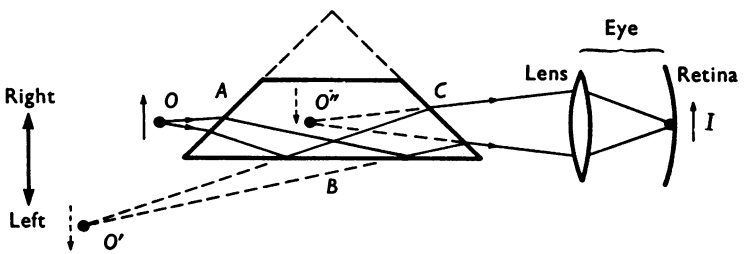

Fig. 1. Image reversal by the dove prism.

Experimental procedures

The main objective was to expose human subjects to long periods of natural head movement with horizontal prism-reversal of vision and periodically to examine the effect of this experience on the VOR by measuring its gain in the dark. VOR gain is here defined as compensatory eye angular velocity relative to the head (ω_e) ÷ head angular velocity relative to space (ω_h). Thus VOR gain is expressed below as the ratio (ω_e/ω_h). The main experiments were conducted on four adult subjects (three male and one female), ranging in age from 20 to 50 years, and free from vestibular and oculomotor disorders. The experiments were performed with the full understanding and consent of each subject. Additional subjects were employed in a series of preliminary trials (not described here) lasting up to 4 hr, in order to establish acceptable long-term conditions. Four main experiments were then conducted in series over periods of 4 (subject T.D.), 17 (A.G.), 25 (M.J.) and 49 (A.M.) days, with the durations of prism-reversal of vision extending over the waking hours of 2, 6, 7 and 27 days respectively.

Each active subject was first paired 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) the paired team was introduced to the experimental programme and the active subject fitted with prism goggles to establish comfort, exclusion of non-reversed vision, and acceptable binocular fusion. To avoid unintended optokinetic stimuli subjects' heads were held still by means of a dental bite-board during fitting.

Heavy stress was laid on the importance of rigorous continuity in wearing the goggles throughout the subjects' waking hours until their planned removal. Two standard control test sequences, detailed below, were run on D_1 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 min periods of such activity were alternated with 30 min periods of complete rest (supine, with head still) during the first 3–4 hr of the first day. Standard test sequences were performed 1, 3 and 6 hr after the prisms had been donned on D_2.

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 weekend, after careful briefing of his wife and family to ensure continuity of vision reversal during waking hours.

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 emphasized that without conscientious, 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 on subjects would be encouraged to range progressively more freely until by about D_4 they would venture outdoors for extended periods. During these periods walks would be taken 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 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 reversed vision the prism-goggles were worn until after the standard morning tests. They were then removed and normal locomotor activity resumed. Subsequent test sequences were then performed intermittently over a total duration similar to the period of maintained vision-reversal.

The standard test sequence

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

The rotational test stimulus, and the equipment employed have been fully described elsewhere (Gonshor & Melvill Jones, 1976). 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°/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. The

resulting eye movements were recorded by d.c. 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 & 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 & Malcolm, 1971). This was ensured by restricting durations of recording in the dark to less than 3 min, 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 test run. Head rotation was recorded as angular velocity from the turntable tachometer. The specific frequency, amplitude and duration of rotational movement were chosen because earlier experiments had shown they did not themselves lead to significant modification of the VOR (Gonshor & Melvill Jones, 1976).

Some 15–20 min 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 & 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

Fig. 2 reproduces an extract from records of head (i.e. turntable) and eye movement obtained from one subject during a control test in the dark prior to donning the reversing prisms. The bottom and top records give, respectively, head *angular velocity* relative to space, and the reflexly induced compensatory nystagmoid eye *displacement* registered relative to the head. The eyes were open behind blackout goggles. Bearing in mind these details, it can be seen that the eye movement was almost exactly compensatory in phase, with the maxima and minima of eye position lying close to midway between those of head angular velocity.

The relationship between these two traces was measured as described in detail previously (Gonshor & Melvill Jones, 1976). Briefly, curves of cumulative eye position (CEP) were constructed as in the middle trace of the Figure by extraction of quick phase eye movements and interpolation of slow phase movements during the 'saccadic' time-gaps (Meiry, 1966). From such CEP curves the gain, G, of the VOR was estimated, cycle by cycle, by calculating the ratio of peak eye angular velocity (ω_e max) to peak head angular velocity (ω_h max) so that

$$G = \omega_e \text{ max}/\omega_h \text{ max}$$

Mean values of these ratios were then obtained over each test run to yield the measured mean gain for the run. For example, the mean gain obtained in this way from the control run in Fig. 2 was 0·58 S.E. $= \pm 0{\cdot}017$, $n = 18$ cycles).

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 that response required for perfect ocular compensation. At 1/6 Hz the human compensatory response defined in this way would be expected to be a few degrees phase advanced due to normal semicircular canal and oculomotor dynamics (Hixson & Niven, 1962). The mean phase obtained from the control run represented in Fig. 2 was $+7{\cdot}2°$ (S.E. $\pm 0{\cdot}36$, $n = 18$).

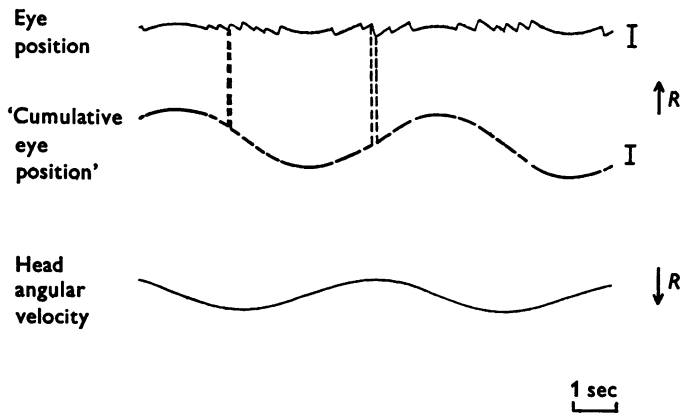

Fig. 2. Extracts from original records of eye position relative to the head (top trace) and head angular velocity relative to space (bottom trace). The middle trace of 'Cumulative eye position' (Meiry, 1966) consists of the sequential compensatory slow phase eye movements in the cycle with saccades (e.g. between dashed lines) omitted. In this Figure, as in all subsequent Figures, the stimulus is a sinusoidal oscillation at 1/6 Hz and 60°/sec velocity amplitude (peak-to-peak, 120°/sec). The eye calibrations, unless stated otherwise, always denote 20° displacement. *R* is right-going movement.

The objective was to obtain measured results from at least 10 cycles near the middle bracket of the standard 20 cycle test run. When less than five measurable cycles were available no mean was recorded (see intermittent portion of the curve in Fig. 6*B*). The following description of results is divided into two sections on medium-term and long-term effects resulting from less than a week, and more than a week of continuous vision-reversal respectively.

Medium-term effects

Fig. 3 shows examples of original records from the first subject (T.D.). 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.

The top trace shows the usual pattern of compensatory horizontal ocular nystagmus obtained on D_1 with eyes open (vestibular + optokinetic = $V+O$) *before* donning the reversing prisms. From CEP curves the mean VOR gain of this test run was 0·92 (S.E. $\pm$ 0·007, n = 18 cycles), typical of a normal response with eyes open. The second record from the

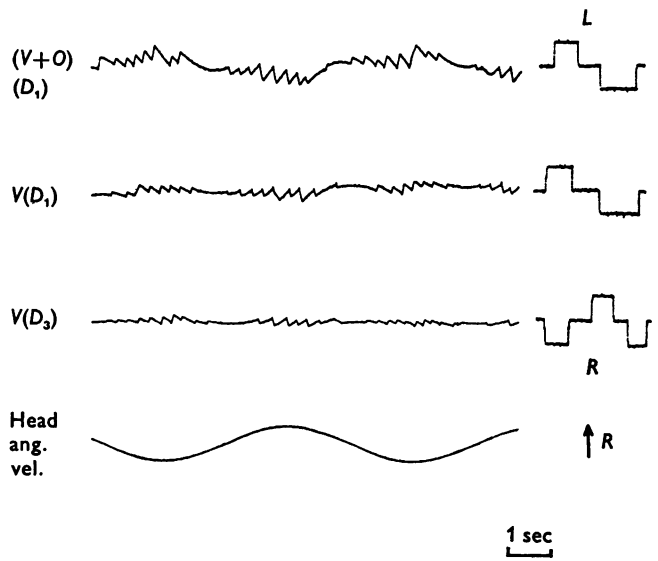

Fig. 3. Extracts from original records of eye movement (top three traces) during the standard rotation stimulus (bottom trace). $V+O$ = vestibular + optokinetic stimulation (i.e. with eyes open in the light). V = vestibular stimulation only (i.e. in the dark). D_n = nth day of experiment. Calibrations show 20° displacement either side of centre. L and R = left- and right-going movement. These letters are used to denote similar conditions in subsequent figures.

top (V, D_1) is taken from a control run in the dark on D_1, when only the vestibular input (V) to the oculomotor system is active. Comparison of smooth phase slopes (proportional to eye angular velocity) in this record with those in the top one illustrates the gain reduction of about one third of that normally expected on removal of vision in these circumstances (mean gain of this run was 0·61, S.E. $\pm$ 0·006, n = 18). The third record is an extract from the final test run on D_3 at the end of nearly 2 days exposure to the influence of vision-reversal, again recorded without vision. The additional highly significant ($P \ll 0{\cdot}001$) 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, n = 18) or about 50 % of the value obtained during the control run without vision (V, D_1).

Fig. 4 shows the cycle by cycle results obtained from subject T.D. throughout the 4-day experiment, each point giving the measured VOR gain from a single cycle. The three control tests (◐), two performed on

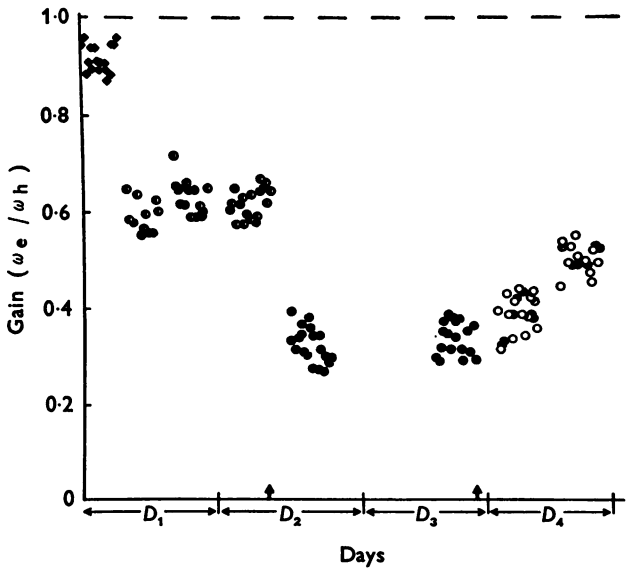

Fig. 4. Collected results for one subject over the 4-day experiment. The ordinate gives vestibulo-ocular reflex gain, defined as eye angular velocity/head angular velocity = ω_e/ω_h, determined from records as in Fig. 2. The vertical arrows on the abscissa represent the start (on D_2) and termination (on D_3) of maintained vision reversal. Each point gives the gain for one cycle before (◐), during (●), and after completing (○) the period of maintained vision reversal. These three sets of results were obtained in the dark. ◆ = responses obtained in the light with normal vision. All these symbols denote similar conditions in subsequent Figures unless otherwise stated.

D_1 and one on D_2, yielded consistent results which were closely similar to those described in another article for normal subjects in these circumstances (Gonshor & Melvill Jones, 1976). However, after donning the prisms (first vertical arrow on the abscissa) during the morning of D_2, the VOR gain, tested 6 hr later (●) was consistently about half the control value. A similar consistently attenuated VOR was found towards the end of D_3. Then, after removal of the prisms (second vertical arrow on the abscissa) two tests on D_4 (○) yielded results indicating progressive re-

covery of gain from beginning to end of the day. However, even after 20 hr of normal activity without vision reversal there was still a considerable and highly significant degree of retained attenuation. Unfortunately, this subject was not available after D_4 and consequently could not be followed to the point of full recovery. Nevertheless, this first medium-term experiment clearly indicates that the planned experimental procedure was feasible and likely to cause at least twice the relative gain

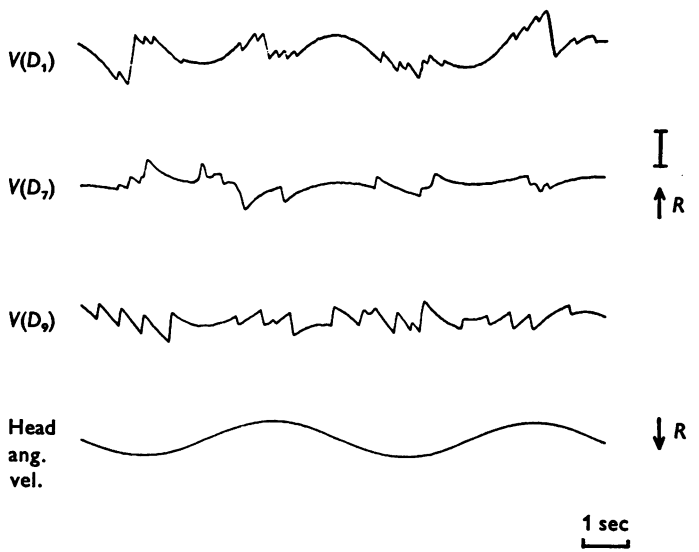

Fig. 5. Records from the 17-day experiment (subject A.G.). From above down these were obtained before (D_1), on the last day of (D_7) and 2 days after completion of (D_9), the period of maintained vision reversal.

attenuation seen in the earlier short-term experiments (Gonshor & Melvill Jones, 1976). The closed diamonds in the top left corner of Fig. 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 Fig. 3. They show that with normal vision the gain of response is in these circumstances close to one.

Original records from the second medium-term experiment (subject A.G.) are shown in Fig. 5. The top and bottom records of eye movement show vestibulo-ocular response (V) without vision during runs before (D_1), and two days after completing (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 a test run on the final day of vision reversal, shows

a greatly diminished mean gain of 0·16, S.E. ± 0·013, which represents about twice the percentage reduction seen in the previous subject's results in Fig. 4.

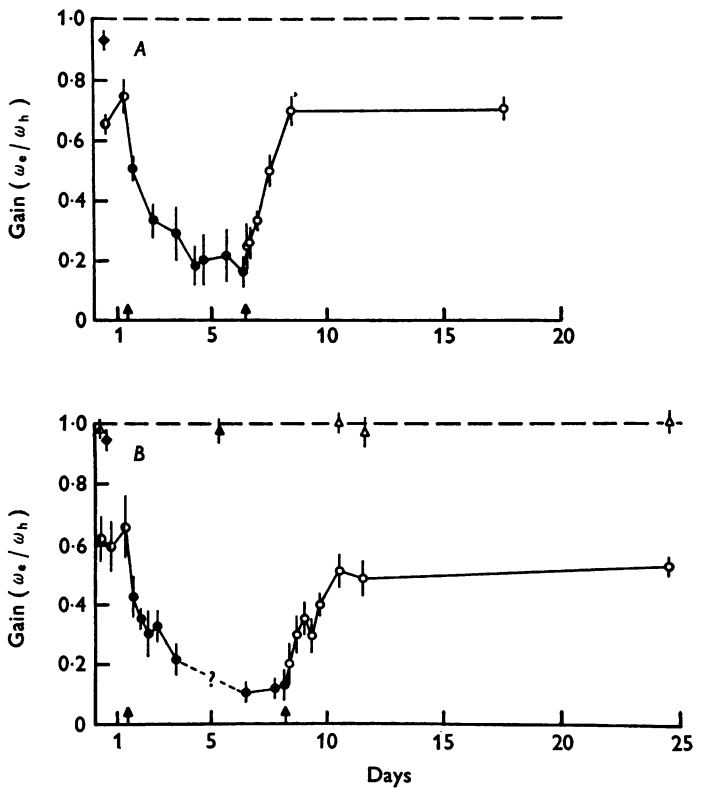

Fig. 6. Changes of mean VOR gain throughout (*A*) the 17-day and (*B*) the 24-day experiments. Numbers on the abscissae give the *end* of sequential experimental days. Vertical bars give one standard deviation of individual values (S.D.). In *B* the triangles give mean VOR gain in the sagittal plane recorded in the dark. The question mark indicates a period when low gain and changing patterns of response made meaningful analysis impossible (see *V*, D_6 in Fig. 7).

Fig. 6*A* and *B* show the changes of mean VOR gain plotted against time in days throughout the experiments of A.G. and M.J. respectively. Each point gives the mean value of all measurable estimates obtained from each complete test run. Vertical bars give 1 S.D. of the individual values. Ordinates, abscissae and symbols are similar to those in Fig. 4. Note that abscissal numbers indicate the *ends* of the corresponding days into the experiment. During the first 2 days of vision reversal there was a striking

similarity of gain attenuation in these two curves and the data in Fig. 4. Thereafter, both curves of Fig. 6 continued to decline, although at a progressively decreasing rate, to reach plateau values which were 75–80 % attenuated relative to control gains. After removal of the prisms, gain recovery occurred progressively over the following 2–3 days, eventually reaching the control value in A.G., but not apparently in M.J.

The dashed line with a question mark in Fig. 6*B* indicates a period when it was not considered feasible to make valid measurements of gain in the required minimum of five complete cycles. At first this difficulty was attributed simply to the very low signal-to-noise ratio found in

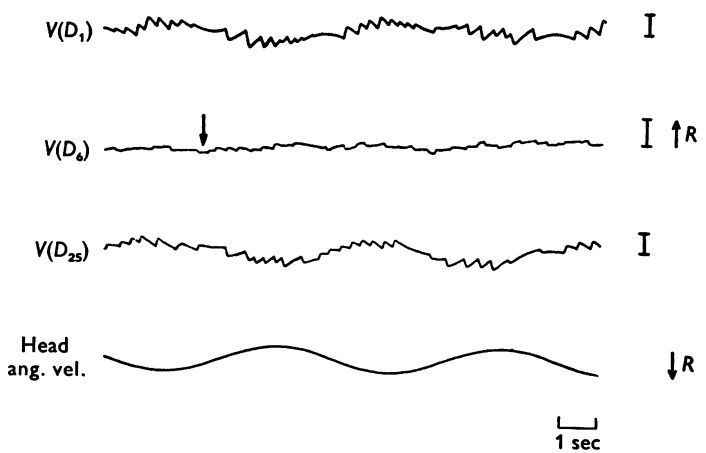

Fig. 7. Records from the 25-day experiment (subject M.J.). $V(D_6)$ is a record from the 5th day of reversed vision, and illustrates the difficulty of analysis referred to in Fig. 6*B*. The arrow over this record points to a nystagmic 'turnover' which appears to be approximately reversed. This was the first occasion in which such a phenomenon was recognized.

traces such as the middle EOG record of Fig. 7. For example, the right half of this record appears to contain virtually no stimulus-dependent signal, despite the presence of well marked and apparently normal saccades. However, during this period, and also in some other unanalysed cycles of both subjects A.G. and M.J., there was a suspicion that an additional factor may have been at play causing gross fluctuations in the phase of response. The difficulty of asserting this suspicion is exemplified in the left half of the middle EOG record in Fig. 7. Not only is there gross attenuation of response, but at the arrow there is even a hint of its approximate reversal. The transient and changing nature of this phenomenon led us at this stage to disregard phase as a reliable response characteristic. As will be seen below, however, the recovery of

signal-to-noise ratio associated with long-term vision-reversal proved that phase changes do become a critical element in the later stages of adaptive change.

The triangles at the top of Fig. 6*B* give the mean gain of VOR in the dark, measured in the *sagittal* plane (V_s), from records of vertical eye movement such as those shown in Fig. 8. There were no changes in this sagittal response throughout the experiment, which demonstrates the important feature that adaptive changes were strictly confined to the plane of vison-reversal. This feature is also seen in the more extensive data of subject A.M. shown in Fig. 16. Of incidental interest is the fact that all

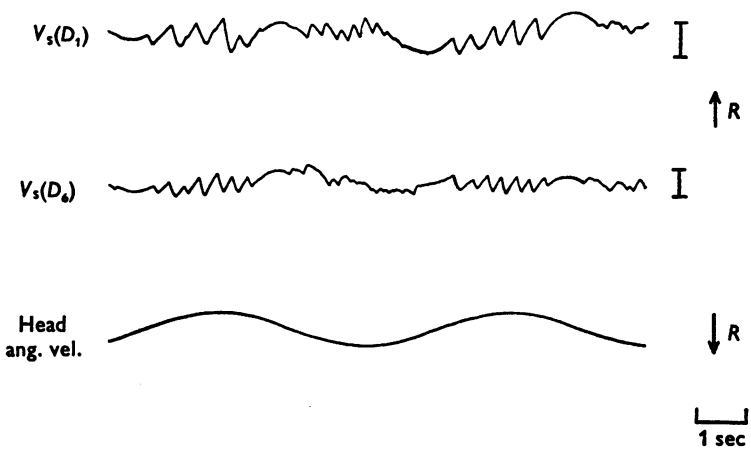

Fig. 8. Records of eye movement in the sagittal plane (V_s), with the head tilted at 90° on to the right shoulder. Hence eye movements towards the vertex are labelled *R*. $V_s(D_1)$ and $V_s(D_6)$ show responses obtained in the dark during a control run and a run on the 5th day of reversed vision respectively. There is no significant difference between the mean gains associated with these two runs.

sagittal tests yielded values of mean gain close to one, despite the fact that all such measurements were made in the dark. As in Fig. 4, the closed diamonds at the top left corners of Fig. 6*A* and *B* give the mean 'horizontal' gains obtained from each subject whilst looking at the surroundings with eyes open and before donning the prisms.

Long-term effects

The three medium-term experiments of T.D., A.G. and M.J. demonstrated a need for longer-term exposure to vision-reversal, in order to follow up the impression that more than mere attenuation of gain was at play in the adaptive process. For this a fourth subject (A.M.) undertook a 49-day experiment in which the reversing prisms were worn con-

tinuously for 27 days. Exactly the same procedures were employed as in the previous medium-term experiments.

Changes of gain observed during the first week 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 Fig. 9, in which each subject is denoted by a separate symbol. That subject A.M. (●) followed the same general pattern of adaptive changes 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 reversed vision.

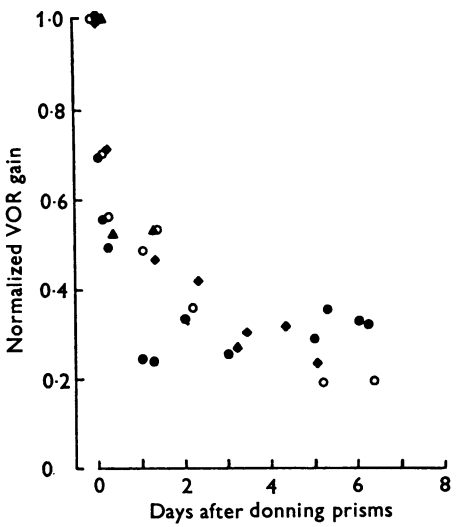

Fig. 9. Changes of normalized VOR gain during the first week of vision reversal in the 4-day (▲), 17-day (◆), 25-day (○), and 49-day (●) experiments. The abscissa represents real time after donning the prisms, each number denoting the end of a 24 hr period from 10.00 a.m. on one day to 10.00 a.m. on 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 long-term exposure of A.M. clarified our earlier suspicion that gain was not the only important adaptive parameter. Thus after an initial period of primarily gain reduction, there followed an extended period in which large changes of phase predominated. Fig. 10 illustrates this feature with a series of extracts from original records made during standard test runs on D_1 (control record before donning the prisms), D_3, D_7 and D_{18}. On D_3 there was considerable attenuation of gain without marked change of phase. On D_7 there was substantial development of phase lag without further change

of gain. On D_{18} this lag had become more marked, with the added feature that there was very considerable *recovery* of gain. The latter record illustrates the functionally important feature that this magnitude of phase-change amounts almost to overt reversal of the reflex response. Indeed, without the presence of the stimulus sinewave or the control trace of eye movement to indicate phase, it would not be easy to detect any abnormality other than somewhat reduced gain relative to the average control

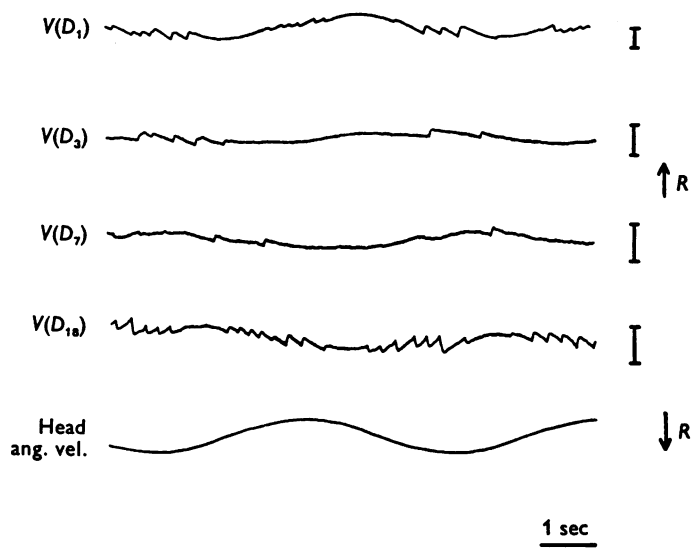

Fig. 10. Extracts of original records from subject A.M. in the 49-day experiment, showing the progressive development of phase lag in successive records of eye movement. On D_{18} the mean response phase was $-130°$ relative to the correct non-reversed compensatory response, i.e. $-137°$ relative to the mean control value (Table 1).

(note calibrations on the right of the Figure). 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 latter feature are considered important and will be discussed later.

Of considerable interest is the directional preponderance evident in D_3, not uncommonly found in records during the early stages of adaptation. The informational significance of this phenomenon is examined in Fig. 11. Here the top trace is an original record of 2 cycles from a response obtained

on D_6 from subject A.G. The nystagmus is asymmetric in that almost all saccades are to the right. This can be accounted for in terms of a d.c. bias of eye angular *velocity* (i.e. 'directional preponderance' in clinical terminology) to the left, as is apparent in the mean 'downwards' slope of the CEP curve shown below the original one. This phenomenon was commonly seen even though no subjects exhibited overt directional preponderance during control conditions.

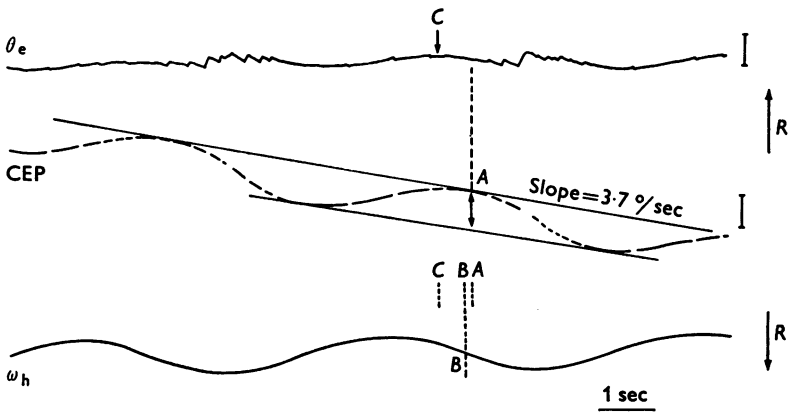

Fig. 11. Records obtained on D_6 from subject A.G., illustrating the velocity bias (directional preponderance) frequently seen during the transitional phase of adaptation. Also shown is the effect of this bias upon the measurement of response phase relative to that of the rotational stimulus. The middle CEP curve shows an angular velocity bias of 3·7°/sec. The real peak of the sinusoidal component of eye response is located at *A*, whereas the apparent peak in the original record is at *C*. *B* indicates the moment of zero head angular velocity. θ_e and ω_h represent eye position and head angular velocity respectively.

In addition to the inherent interest of the phenomenon it is important to appreciate that when directional preponderance is present the phase of response cannot be measured directly from the apparent 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, peaks of the sinusoidal component of response coincide with the apparent peak only after subtraction of the steady slope of drift; or what amounts to the same thing, at points of tangential contact (*A*) of the CEP curve with lines parallel to the mean drift. Thus the proper phase of the sinusoidal maximum of response is located at *A* in Fig. 11, rather than at *C*. *B* is marked in the Figure midway between peaks of sinusoidal head angular velocity to show the phase of peak eye displacement which would be associated with perfect compensation.

Relations between gain and phase. With the introduction of phase as a relevant variable it becomes advantageous to present the collective data for the whole long-term experiment as a three dimensional display showing simultaneous relations between gain, phase and time. Fig. 12 illustrates the overall results from subject A.M. presented in this format. The vertical ordinate gives VOR gain expressed as before. The abscissa gives time in

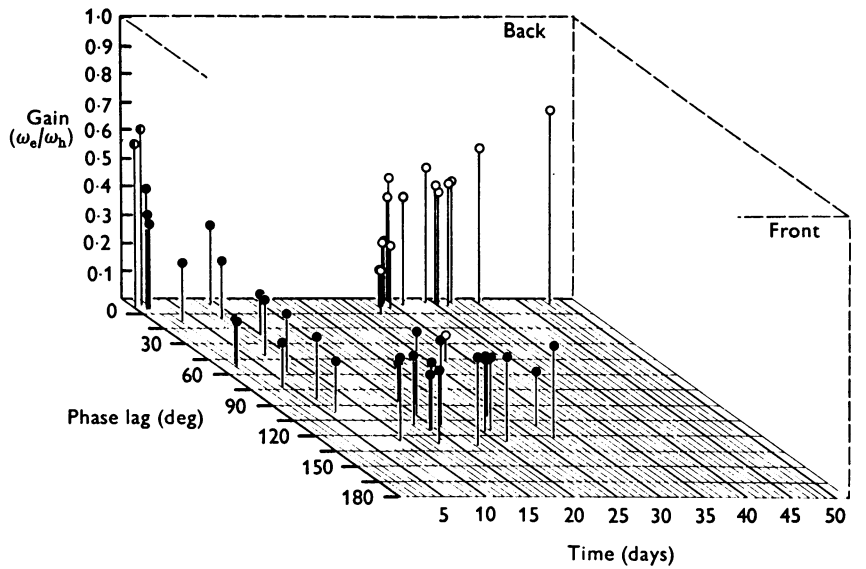

Fig. 12. 3-dimensional display of the simultaneous interactions amongst gain, phase and time throughout the 49-day experiment. Each point is the mean value for up to 20 cycles of a daily test run, and is placed according to both its mean gain and phase values. Note that 180° phase lag relative to the control response of +7° would represent reversal of the VOR. Symbols are as in Fig. 4. Numerical values and statistical characteristics of all points are given in Table 1.

days after commencing the experiment. The third, or z, axis gives the phase lag of the sinusoidal component 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. The lengths of the 'stalks' on which the points lie give the values of VOR gain on the same scale as the ordinate. Symbols are as in Figs. 4 and 6. Each point gives the mean values of gain and phase determined at a given time from a standard test run performed in the dark.

Six main stages can be characterized in the results of Fig. 12, four during the initial adaptation and two during recovery after return to normal vision.

(1) In the first 24–48 hr there were rapid and highly significant successive reductions of gain from the last control test on the morning of D_2 to the first test on D_3 ($P < 0{\cdot}001$ for differences between each of the five successive mean results over this period; see Table 1 results $2A$–$3A$ inclusive). Over this period the gain fell from a control value of 0·63 to a value on D_{3A} of 0·15, representing an attenuation of just over 75 %.

(2) Following this there was a 4–5 day period of fluctuating phase-change which progressed in a generally lagging direction. During this period there was no further consistent reduction of gain: indeed if anything there was a slight increase.

(3) Over the next 4–5 days, apart from two notable exceptions ($D_{10,B}$ and D_{11}, see Table 1 and Fig. 13), the phase moved considerably further in the lagging direction to reach a 'plateau' value around $-122°$ (i.e. approx 130° lagged relative to controls, see Table 1). Over the same period the gain climbed considerably to reach a plateau value of around 50 % of the mean control gain. These first three stages occupied approximately 2 weeks.

(4) During the second 2-week period of the vision-reversed experience the latter conditions remained relatively stable.

(5) Readaptation after removal of the prisms on D_{28} commenced rapidly. Before prism-removal the mean phase and gain were $-122°$ and 54 % of the control gain respectively. Then, during the first ½ hr after return to normal vision the mean phase reverted to $-76°$, although with a relatively high variability between individual cycles in the run (S.D. = 25°), as was associated with the middle range of phase values during the initial adaptation. In spite of this large variability, the new mean phase value is highly significantly smaller than the preceding value of $-122°$ ($P \ll 0{\cdot}001$). Over the same period the mean gain fell markedly to an all-time low of 0·09 (S.D. = 0·02) which is less than one third the preceding value ($P < 0{\cdot}001$) and only one seventh the original control value. These features are seen in the first open circle of Fig. 12. 1½ hr later the mean phase was restored to 0° whilst the gain had increased somewhat to 0·15 ($P \ll 0{\cdot}001$ for both these latter changes). Thus in the first 2 hr the phase characteristic was restored to near normal but the gain was not.

(6) From this moment on there was little further change of phase, apart from a tendency for it to become slightly advanced relative to normal (see Table 1 and Fig. 15*B*). However, in marked contrast to this rapid recovery of phase, the subsequent recovery of gain occupied a prolonged period of about 2 weeks, similar, that is, to the duration of the initial adaptation.

Fig. 13 shows extracts from original records taken during the recovery period. The top three traces are taken from standard test runs performed on the 28th day, (*A*) just before (last filled circle of Fig. 12), (*B*) ½ hr after

(first open circle of Fig. 12) and (*C*) 2 hr after removal of the prisms. Trace D_{49} is taken from the last record of the experiment to show the normal quality of the restored VOR, and for comparison with the transitional stages. The time scale of Fig. 12 is so compressed that it is often not possible to identify the exact sequence of events. Moreover, it would be too confusing to depict statistical reliability of results in such a Figure.

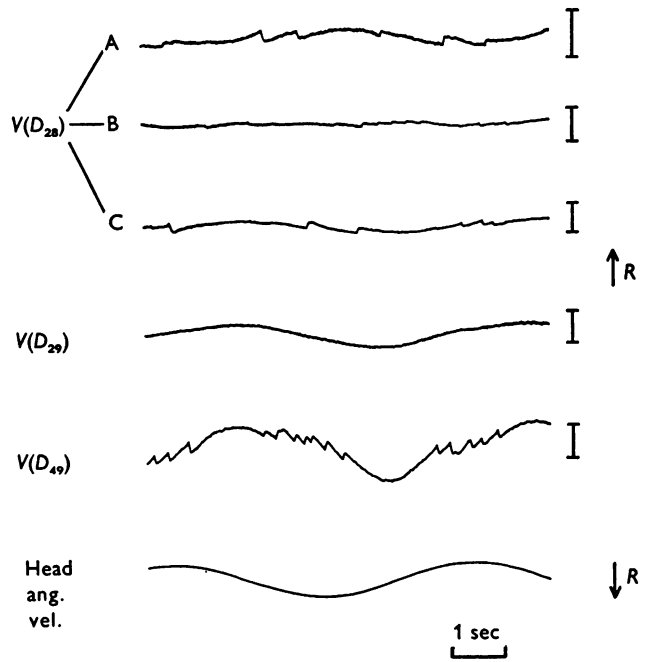

Fig. 13. Samples from original records illustrating the main characteristics of readaptation after removal of the prisms. The top three traces are from tests on D_{28}, (*A*) before, (*B*) ½ hr after, (*C*) 2 hr after prism removal. *V*, D_{29} is from a test 24 hr after removal. *V*, D_{49} was the final test of the complete experiment. All records obtained in the dark.

Consequently numerical values of the two means determining each point, together with their S.E.s and the number of individual estimates, are given in Table 1.

Statistical reliability of gain measurements is seen to be similar in this long-term subject to that found in the other three subjects, as depicted in Figs. 4 and 6 (note that the vertical bars in Fig. 6 give S.D.s whilst the numbers in Table 1 give S.E.s). As already mentioned, the reliability of mean estimates of *phase* varied widely. For example, whereas in control tests D_1 and D_{2A} the variability of individual values within a run was on

TABLE 1. Mean gain and phase from subject A.M. throughout the 49-day experiment. *A*, *B*, *C*, etc. denote test sequence in a day. 'Time' denotes the 'clock' hours when test runs commenced. Gain is given as mean scalar value of $\omega_{e\,max}/\omega_{h\,max}$, ± S.E. of the mean of (n) values. Phase values represent the degrees of phase advancement (+) or phase lag (−) with respect to perfect compensatory eye movement with normal vision. 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

Day	Time	Mean gain	Mean phase
1	10	0·581 ± 0·017 (18)	+7·2 ± 0·36 (18)
2*A*	11	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
3*A*	10	0·147 ± 0·009 (18)	−52·0 ± 8·26 (16)
3*B*	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)
7*A*	10	0·173 ± 0·011 (18)	−94·0 ± 3·99
B	17	0·198 ± 0·013 (14)	−83·0 ± 6·82
8*A*	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
10*A*	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
14*A*	10	0·259 ± 0·008 (19)	−128·0 ± 1·45
B	15	0·265 ± 0·009 (13)	−109·0 ± 4·43
15*A*	10	0·203 ± 0·013 (12)	−115·0 ± 4·83
B	15	0·242 ± 0·011 (18)	−115·0 ± 4·02
16*A*	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
18	11	0·312 ± 0·024 (17)	−130·0 ± 2·79
21	14	0·270 ± 0·031 (14)	−116·0 ± 3·88
22*A*	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
28*A*	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
29*A*	14	0·133 ± 0·005 (20)	+5·0 ± 2·92
B	18	0·233 ± 0·007 (16)	+6·0 ± 1·22
30*A*	10	0·223 ± 0·004 (18)	+9·0 ± 1·20
B	17	0·224 ± 0·005 (19)	+5·0 ± 1·45
31*A*	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

TABLE 1 (*cont.*)

Day	Time	Mean gain	Mean phase
35	11	0·482 ± 0·010 (10)	+10·0 ± 1·24
36*A*	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

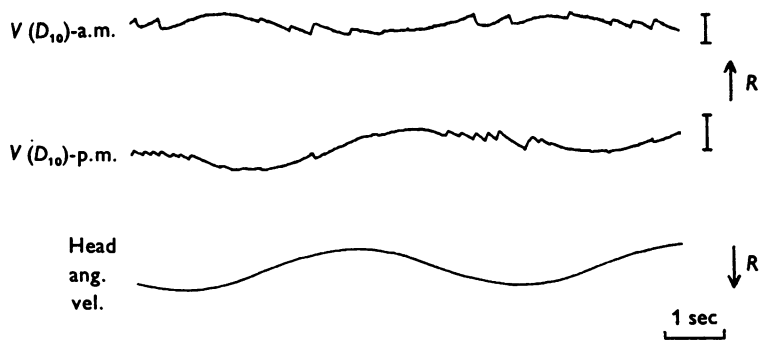

Fig. 14. Samples from morning and evening records on D_{10}. See also corresponding mean data in Fig. 12 and Table 1. Mean A.M. and P.M. response phases were −125 and +9° respectively.

the same order of magnitude as the accuracy of measurement (S.D. = 1·53 and 2·10° respectively), during the transitional period of adaptation (e.g. $D_3 - D_{11}$) there was more than a tenfold increase in this variability (mean S.D. over this period = 24°). Thereafter, except for occasional runs with high variability (e.g. D_{16A}), consistency within runs tended to improve; for example the mean S.D. from D_{18} to D_{28} was 11°, which is highly significantly less than the corresponding value of 24° during transition ($P < 0{\cdot}001$). After return to normal vision, except for the test made ½ hr after prism-removal (D_{28C}), consistency tended to improve further, quickly returning from D_{29B} onwards to levels similar to those seen on the original control days.

As mentioned earlier, a characteristic feature of transitional records was the marked fluctuations which occurred between successive mean values, especially those of phase. The most striking example of this fluctuation was seen on D_{10}, from which samples of morning and evening records are separately illustrated in Fig. 14. Here, the top record was obtained at 10.00 a.m. and shows a well defined 'reversed' pattern of response. The

bottom trace of eye movement was obtained at 5.00 p.m. and here the phase of response had reverted completely back to he initial control value, although the gain remained substantially (about 50 %) below the corresponding control value. Naturally, in this instance particular care was taken to review directional calibrations of head and eye records in case these may have been inadvertently reversed between morning and evening

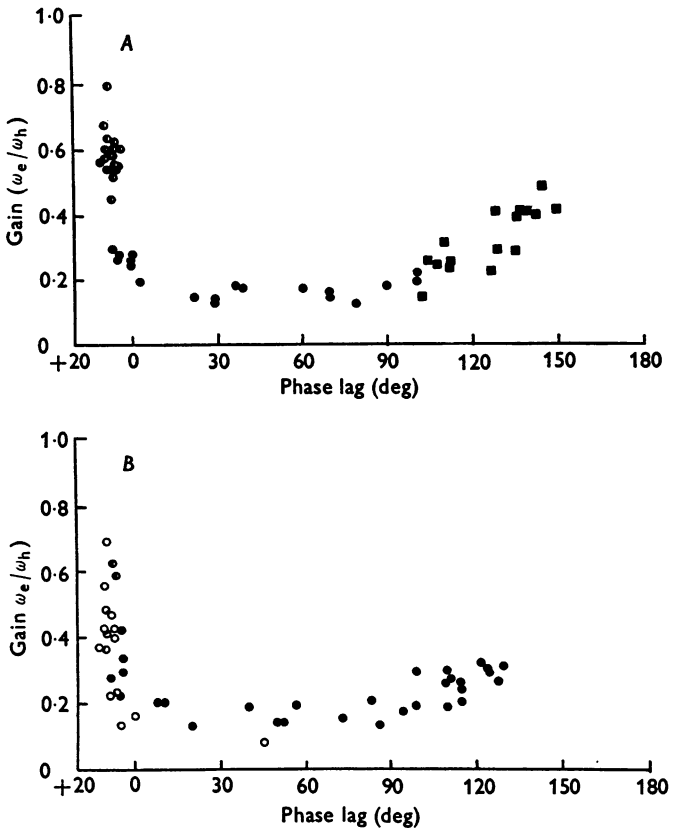

Fig. 15. Changes in VOR gain as a function of phase for (*A*) individual cycles in three chosen runs and (*B*) mean values for all experimental runs. (*A*) each point represents the phase and gain for *one cycle in a run* on D_1 (control – ◑), D_8 (●), and D_{18} (■). *B*, each point gives the *mean* values of gain and phase for an *entire run* before (◐), during (●), and after completing (○), the period of maintained reversal of vision.

sessions. Fortunately, this possibility is absolutely excluded by the fact that the mean phases of the morning and evening responses were −125° (S.E. = 2·23) and +9·0 (S.E. = 4·96) respectively, so that the magnitude of the difference between these means, namely 134°, is highly significantly less

than 180° ($P \ll 0{\cdot}001$). Consequently there can be no simple ambiguity of calibration direction and hence the observation must be a real one. Such extreme variability between tests within 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 possibility cannot of course be absolutely excluded, the fact that his whole day was under minute-to-minute observation by the full-time companion makes it unlikely.

The large fluctuations of results from moment-to-moment within a run and from one test run to the next, which seem to be characteristic of the transitional stage of adaptation, conceal a highly consistent relationship between gain and phase. Figs. 15*A* and *B* reveal this systematic relationship by projecting results on to the gain-phase plane of a three dimensional display such as Fig. 12, and hence removing the time variable.

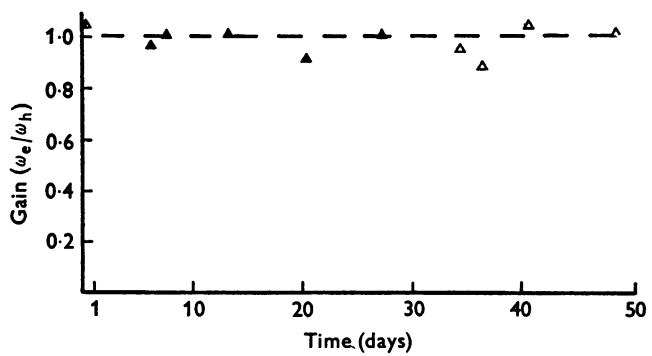

Fig. 16. Mean gain of 'vertical' eye movement response to rotational stimulation in the sagittal plane of the skull. (◭) before, (▲) during and (△) after completing, the period of maintained reversal of vision. See also Figs. 6*B* and 8.

Fig. 15*A* gives the individual *cycle by cycle* estimates of gain and phase obtained from three separate runs on D_1 (control; ◐), D_8 (●) and D_{18} (■). Of particular interest is the apparent continuity links between the three sets of data, suggesting that some physiological criteria were forcing a particular pattern of relationship between gain and phase, even when there was wide variability of these parameters with respect to time.

This conclusion is strongly supported by the data in Fig. 15*B* which plot the *mean* values of gain and phase obtained on individual days throughout the whole 7 week experiment, i.e. Fig. 15*B* shows a projection of the actual data in Fig. 12 on the gain-phase plane of that Figure. Symbols and numerical values in Fig. 15*B* are as in Fig. 12. The similarity of interdependence between the gain and phase in this plot and that of

Fig. 15*A* 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 (Davis & Melvill Jones, 1976).

Geometrical specificity. As with subject M.J., a number of 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. The triangles in Fig. 16 show that as in Fig. 6*B* the sagittal response remained unchanged throughout the experiment.

These results therefore confirm the earlier observation that the adaptive mechanism appears to be geometrically highly specific, and, moreover, that attenuation due to lack of arousal is most unlikely to have contributed significantly to the results.

DISCUSSION

These experiments extend the range of a previous study (Gonshor & Melvill Jones, 1976) which showed that short periods (8–16 min) of optically reversed visual tracking during sinusoidal head rotation leads to rapid attenuation of the VOR as tested in the dark. The *medium-term* results summarized in Fig. 9 of the present article confirm this general observation and contribute a number of additional new findings. First, free head movement with vision-reversal produces a similar effect to the strictly sinusoidal movements employed in the earlier experiments. Secondly, the daily level of VOR attenuation was consistently retained intact during each night; whereas in the previous short-term study in which subjects returned to normal vision after each daily experiment, substantial restoration of gain occurred from one day to the next. Thirdly, this retention allowed the magnitude of VOR decline to accumulate from day-to-day reaching a plateau value of about 75% attenuation over 5–7 days. This level of attenuation is about three times greater than the maximum corresponding value seen in the previous short-term experiments. Fourthly, after return to normal vision, recovery of VOR gain began almost immediately but took several days to reach completion.

What kind of processes could be responsible for these well defined characteristics of altered reflex function? It seems unlikely they were due to simple habituation resulting from repetitive vestibular stimulation, since the sinusoidal test stimulus employed was previously shown to be non-habituating (Gonshor & Melvill Jones, 1976) and the only other vestibular stimuli were due to natural movement. Moreover, there was no evidence of gain recovery during withdrawal of the stimulus at night, as would be expected from habituative attenuation. Rather it seems that, since alteration

of reflex function only occurred in the presence of a mismatched visual fixation stimulus and always in a manner suitable for resolution of that mismatch, these changes were truly adaptive to the requirements of retinal image stabilization during head movement. A similar conclusion has recently been drawn by Miles & Fuller (1974) who examined VOR changes in monkeys wearing magnifying or reducing spectacles.

The functional significance of phase changes

Change of gain was not the only form of adaptive alteration in the reflex. As mentioned in connexion with Fig. 8 of the medium-term experiments there was a suspicion that change of phase might prove to be at least as important as change of gain. The *long-term* experiment confirmed this suspicion by revealing the intriguing fact that, with extended durations of vision-reversal, the phase of oculomotor response became of central significance in establishing the final functional reorganization of the VOR. Thus, after an initial period of predominantly gain reduction there followed a period of about 10 days in which the phase of ocular response shifted extensively in a progressively lagging sense relative to the normal response, eventually reaching a value of around $-130°$ relative to normal after about 2 weeks of continuous vision-reversal. Thereafter the situation stabilized at around this phase value, with the gain climbing above its lowest value to about 50% of its normal control value. The important outcome, which is readily seen by comparing top and bottom eye movement records in Fig. 10, is that the new stable condition amounted to approximate reflex reversal. That this represents a general phenomenon is substantiated by similar observations in the intact cat (Melvill Jones & Davies, 1976).

This rather striking finding leads to the conclusion that the central neural mechanisms concerned are capable of far more than mere suppression of an adverse vestibular input to the oculomotor system. Rather, given time, the reflex vestibulo-ocular drive can effectively be reversed so that it then provides an input which becomes complimentary, rather than antagonistic, to the optically reversed input from the optokinetic system. Apparently the central networks are not only adaptive, but also plastic to the extent that the reversed optokinetic task brings about a high degree of retained remodelling in the VOR, the ultimate goal in these circumstances presumably being perfect VOR reversal.

Central mechanisms

The organized goal-directed nature of this remodelling encourages speculation on plausible central neural mechanisms. Turning first to the spinal cord for possible analogies, Holmqvist & Lundberg (1961) described

a system responsible for reflex reversal in the motor response to stimulation of flexor reflex afferents (FRA). FRA stimulation was shown to produce either flexor or extensor responses according to the differential distribution of supraspinal influences upon parallel excitatory and inhibitory interneuronal pathways converging on to single motoneurones at the segmental level. Could a similar mechanism operate in the VOR on the basis of known neuroanatomical connexions and physiological influences?

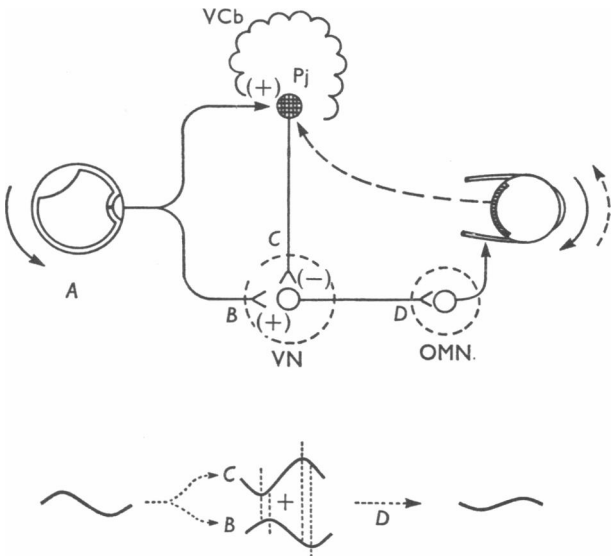

Fig. 17. Schematic diagram of a neural network capable of producing all the complex but systematic changes of gain and phase observed in these experiments, providing a short time constant 'lead' or 'forgetting' term is introduced in channel *C*. This term would produce the phase advancement of *C* relative to *B* shown below the diagram. *A* = primary afferent input. *B* and *C* = synaptic inputs to vestibular neurones (VN) via brainstem and cerebellar pathways respectively. *D* = projection from VN to oculomotor neurones (OMN). Pj = Purkinje cells in the vestibulo cerebellum (VCb). Dashed pathway indicates the visual influence on Pj in VCb. Normally ($B > C$) head rotation to the left would produce compensatory eye rotation to the right (continuous curved arrows). With $C > B$ the same stimulus would produce an approximately reversed ocular response (dashed curved arrow) by summation of sinewaves as indicated below the diagram. With $B \simeq C$, small changes of relative gain in *B* and *C* would produce large phase changes in *D*.

Vestibulo-cerebellar system. An approximate and neurologically plausible analogy is shown as a diagram in Fig. 17. Primary vestibular afferents from the canals innervate the vestibular nuclei *via* direct (*B*) projections which are excitatory to second order vestibular neurones (Precht & Shimazu,

1965). In addition primary vestibular afferents branch to innervate the vestibular cerebellum (Brodal & Høivik, 1964; Carpenter, Stein & Peter, 1972; Precht & Llinás, 1969) which, through Purkinje cell projections (Angaut & Brodal, 1967), brings inhibitory (or disfacilitatory) influences to bear (*C*) on vestibular neurones (*D*) (Baker, Precht & Llinás, 1972; Ito, Nisimaru & Yamamoto, 1973; Precht, 1972; Highstein, 1973) projecting to the oculomotor nuclei (Lorente de Nó, 1933; Szentágothai, 1950).

If, as in the spinal model referred to above, remote influences could change the relative efficacy of channels *B* and *C*, then this would provide a means of controlling VOR gain along the lines postulated by Ito (1970) before it was known that potentially suitable pathways (dashed line in Fig. 17) exist (Maekawa & Simpson, 1973). For example, with the influence of $B > C$ there would be a normal response in *D*. However, with progressive increase of relative effectiveness in *C* the VOR gain would progressively decline until $B = C$, when the over-all VOR gain would become zero. Of critical relevance to the present experimental findings is the fact that simple continuation of this trend would lead to the condition $C > B$, when the net effect would be *reversal* of the signal in *D*, relative to the primary afferent input generated by rotational stimulation of the canal. Thus the elementary network of Fig. 17, based on proven central pathways, could theoretically be made to produce both the attenuation seen in our short- and medium-term experiments and the reflex reversal which represents the goal towards which plastic changes of the long-term experiment appear to be directed.

A major limitation of this simple scheme is that it could not, as it stands, account for the complex approach to this apparent goal through the progressive changes of phase seen to occur in Fig. 12. However, as shown elsewhere (Davies & Melvill Jones, 1976) it is only necessary to introduce into channel *C* a simple 'lead' term (i.e. an 'adaptive' or 'forgetting' term) having a single time constant of about 1 sec, to account not only for the progressive change of phase but also the systematic inter-dependence of phase and gain seen in Fig. 15. Very briefly this is because such a 'lead' term would produce a frequency-dependent phase advancement in the inhibitory signal arriving at vestibular nuclei *via* channel *C*. If this is summed with the parallel excitatory input from channel *B* (as indicated below the diagram in Fig. 17) simple changes of relative gain in *B* and *C* could produce dependent changes of VOR gain and phase remarkably similar to those seen in Fig. 15 and hence also those in Fig. 12. The incorporation of such a 'forgetting' time constant in *C* seems not unreasonable since cerebellar cortical pathways abound with parallel inhibitory influences; for example, mossy fibre activation of Golgi cell inhibition of granule cells or alternatively granule cell activation of basket

and superficial stellate cell inhibition of Purkinje cells (Eccles, Ito & Szentágothai, 1967). It should be noted that this 'lead' term would presumably have to be attributed specifically to the new, rather than the normal, component in channel *C*, since in normal circumstances its influence does not appear to cause alteration of phase at *C* (Melvill Jones & Milsum, 1971) relative to the primary afferent input, *A* (Fernández & Goldberg, 1971). Alternatively it may be that the large phase changes in VOR found by Carpenter (1972) after cerebellectomy may in some as yet undefined way point to a normal contribution of channel *C* to establishment of normal phase relationships.

For reflex reversal to occur through the postulated network of Fig. 17 the inhibitory influence of *C* would have to play upon spontaneously active secondary neurones in channel *D*. Such spontaneous activity is certainly present in decerebrate cat vestibular nuclei (Melvill Jones & Milsum, 1970). Moreover, that such activity occurs normally is implied by findings of Precht, Shimazu & Markham (1966). They observed that after acute unilateral labyrinthectomy the spontaneous activity of ipsilateral Type I central vestibular neurones was initially reduced, presumably due to loss of the normally vigorous spontaneous afferent input (Goldberg & Fernández, 1971), and this was associated with continuous ocular nystagmus as described below. Subsequently, restoration of a normal steady-state in the VOR was associated with adaptive restoration of normal spontaneous levels of activity in these Type I neurones.

Directional preponderance. These latter observations also have an interesting bearing on the directional preponderance, or angular velocity bias, often seen in our subjects during transitional stages of adaptation (e.g. Fig. 11). Thus the immediate ipsilateral loss of central spontaneous activity seen by Precht *et al.* (1966) was associated with 'vestibular' nystagmus having a steady slow phase eye angular velocity, or velocity bias, directed towards the operated side. It seems reasonable to infer that the much less marked velocity bias seen in our experiments may have been associated with temporary inequality of adapting cerebellar influences on left and right pools of 'target' vestibular neurones. The 'velocity' nature of the resulting differential imbalance would be in accord with the velocity mode of informational content which predominates in neural signals at that level in the VOR (Melvill Jones & Milsum, 1971; Melvill Jones, 1972, 1974).

Visual influence. Returning to Fig. 17, what additional influences are available for bringing about the postulated modulation of efficacy in channel *C*? The short-term experiments in the present series (Gonshor & Melvill Jones, 1976) proved beyond reasonable doubt that the observed VOR attenuation was quite specifically due to attempting the reversed

visual tracking task during head rotation. Presumably both the attenuation and reflex-reversal of the medium- and long-term experiments described above were due to a similar combination of stimuli. Furthermore, other investigators have found that visual tracking during head rotation can be made to introduce changes in the vestibular system at a neuronal level, in the brain stem, at least on a short-term basis (Dichgans & Brandt, 1972; Henn, Young & Finley, 1974). Thus it seems certain that the visual tracking system is in some way capable of modifying the VOR. Various mechanisms would appear to be theoretically possible, acting for example through the media of mismatching between (i) a corollary discharge replicating the optokinetic oculomotor drive and the simultaneous oculomotor input from the vestibular system, (ii) ocular muscle afferents and vestibular afferents in the case of partially successful reversed tracking and (iii) optokinetic afferents due to retinal image movement and vestibular afferents due to head rotation. It does not seem possible from the current literature to conclude which mechanism predominates in which circumstances. However, there is strong evidence to indicate that retinal image movement can of itself influence the vestibulo-ocular system.

Thus, as suggested by Ito (1972), Maekawa & Simpson (1973) have shown that visual stimulation can modify, on a moment-to-moment basis, Purkinje cell activity in the vestibular cerebellum specifically *via* climbing fibre projections. Peculiarly, when the stimulus was a moving visual image on the retina, the induced climbing fibre input to Purkinje cells turned out to be contrary to that required for alteration of D in a manner suitable for the generation of following eye movements (Simpson & Alley, 1974). More recently Ghelarducci, Ito & Yagi (1975) have gone some way to resolving this apparent discrepancy by demonstrating in the rabbit that visual influence on vestibulo-cerebellar Purkinje cells is not restricted to climbing fibre input, at least insofar as so-called 'complex' spikes are diagnostic of such input. They have demonstrated that in addition to modulating complex spikes, moving visual stimuli also modulate simple spike activity in the same Purkinje cells, but predominantly in the *opposite* sense to the complex ones, and hence in the *appropriate* sense for assistance to visual tracking. Lisberger & Fuchs (1974) have also shown that some form of input from the visual fixation system reaches floccular Purkinje cells in the form of simple spikes in monkeys.

It is, however, most important to appreciate that although these specific observations at a neuronal level clearly demonstrate a functionally effective information pathway from the visual system to the vestibulo-cerebellar cortex, the neural influences thus far demonstrated are not suitable for causing the requisite maintained change of vestibular afferent efficacy in channel C, as postulated above. Rather, they are

suitable for continuous modulation of oculomotor drive according to the moment-to-moment requirements of retinal image movement. At this point in the argument, therefore, the question still remains open as to whether visual influence can bring about steady, retained, changes of gain in channel C, as would be required to account for our findings.

The most convincing evidence indicating that such changes do occur in the vestibulo-cerebellum derives from ablation experiments. Thus Takemori & Cohen (1974) have shown that cerebellar floccular lesions lead to loss of short-term modification of the VOR by means of visual fixation during calorically induced nystagmus. Of more direct relevance to our long-term findings, Robinson (1976) has found that the retained VOR attenuation which normally occurs in cats subjected to long-term (7–14 days) vision-reversal apparently does not occur after surgical removal of the vestibular cerebellum. Again, on a shorter-term basis (12 hr), Ito, Shiida, Yagi & Yamamoto (1974) demonstrated that specifically flocculectomy abolished such changes in the rabbit VOR as were induced by concurrent visual and vestibular stimuli, although Collewijn & Kleinschmidt (1975) did not find such changes in somewhat similar circumstances. Thus despite the lack of evidence at a neuronal level, it seems likely that somehow the visual communication pathway with the vestibulo-cerebellum is capable of altering the VOR (as measured in the absence of vision) in a manner corresponding to the postulated requirements in the network of Fig. 17. The nicety of such an arrangement would be that, contrary to the moment-to-moment neuronal modulation suitable for on-going visual tracking, it is only necessary to adjust the *steady-state* value of gain in C to achieve the observed retained changes in the complete vestibulo-ocular system. In this connexion Ghelarducci *et al.* (1975) have speculated on the possibility that visually evoked climbing fibre activity might be responsible for 'controlling the plastic modifiability of synaptic transmission from granule cells to Purkinje cells'.

Reticular formatiom. Could known characteristics of the reticular formation contribute to the observed changes of gain and phase in the present experiments? With regard to gain, it is well established that the reticular formation is concerned with the control of central arousal (Moruzzi & Magoun, 1949). Furthermore, numerous experiments have shown that vestibulo-ocular gain will decrease with lack of arousal (Wendt, 1951; Guedry & Lauver, 1961; Collins & Guedry, 1962), implicating the reticular formation as a potential source of VOR gain control. However, in the present experiments central arousal was maintained by mental arithmetic, as evidenced both by the lack of response decline in the short term experiments (Gonshor & Melvill Jones, 1976) and by the maintained 'sagittal' response of the present experiments.

With regard to phase it has been postulated that an important function of the reticular network's influence on the oculomotor nuclei may be to perform a mathematical integration on the velocity-dependent neural information flowing from vestibular to oculomotor nuclei (Robinson, 1971; Skavenski & Robinson, 1973). At the test frequency of 1/6 Hz used in our experiments, however, the postulated integrator would *normally* produce a substantial lag into the oculomotor output. Further participation of the reticular formation integrator due to adaptation could therefore hardly account for more than a fraction of the 130° lag seen in our long-term subject, and its inactivation could only produce phase advancement, which was not seen in the adapted state. Consequently it seems unlikely that alteration of these components in the reticular formation could be responsible for the adaptive and plastic changes described in results.

Further evidence that in the adapted state the reticular formation was performing its normal function comes from the observations that saccades were not changed dynamically (Gonshor, A. & Melvill Jones, G. unpublished), indicating no interference with the normal triggering and synchronization of saccade discharge described by Robinson (1964). In addition, the saccades were always appropriate in placement and direction for the smooth pursuit movements, even when the latter were effectively reversed, which in turn favours the view that the adaptive signal modification takes place 'upstream' of the reticular formation. Its components of smooth pursuit and saccadic input to the oculomotor system would then be driven in the same way as before VOR reversal, but with a modified incoming signal.

Functional advantage of VOR reversal

One may question the functional advantage of reflex reversal when simple VOR attenuation would suffice to leave an unimpeded reversed optokinetic response. However, the unimpeded optokinetic system, although accurate, has a strictly limited dynamic response, with an upper limit of frequency response at about 1 Hz (Melvill Jones & Drazin, 1962; Stark, Vossius & Young, 1962; Baarsma & Collewijn, 1974) and a maximum successful tracking velocity of around 25–30°/sec (Young, 1971). On the other hand normal head movements contain frequencies extending at least up to 5–7 Hz (Barnes, G. R., personal communication) and angular velocities of well over 100°/sec (Robinson, 1968). Consequently a functional VOR proves to be essential for clear vision during normal movement, since its frequency response extends at least up to 6–8 Hz (Benson, 1971) and its velocity capability up to well over 100°/sec (Malcolm & Melvill Jones, 1970).

Assuming that relatively normal head movements occurred in our subjects wearing the prism goggles, especially in the progressively more

adapted state, it clearly becomes desirable to reverse the VOR so that it may actively contribute once again to retinal stabilization of the reversed visual image.

The functional efficacy of doing so is probably reflected in the long-term psychological experiments of Kohler (1951, 1953, 1956, 1962; see also Kottenhoff, 1957*a* and *b* for an English summary of some of these experiments). Kohler exposed human subjects to prolonged periods of continuous dove-prism reversal with the aim of characterizing psychological adjustment to this bizarre situation. Particularly relevant to our physiological findings is the fact that *after about 2–3 weeks* (i.e. a duration similar to that required for VOR reversal) Kohler's subjects were able to perform complex visual-motor functions such as skiing, mountain and rock climbing, cycling and fencing. Although head movements were not measured, it seems unlikely these individuals could have achieved the necessary manoeuvrability without near-normal head movements, and in that case retinal image stabilization could not have been achieved without effective reversal of the vestibular drive to the oculomotor system.

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