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Plasticity in the Adult Vestibulo-Ocular Reflex Arc [and Discussion]

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Plasticity in the adult vestibulo-ocular reflex arc

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[Plate 1]

Human subjects with maintained reversal of their horizontal field of vision exhibit very substantial adaptive changes in their 'horizontal' vestibulo-ocular reflex (v.o.r.). Short durations (8 min) of vision reversal during natural head movement led to 20 % v.o.r. attenuation while long periods (4 weeks) eventually led to approximate reversal of the reflex. The reversed condition is approached by a complex, but highly systematic, series of changes in gain and phase of the reflex response relative to normal. Recovery after return to normal vision exhibits a similar duration, but different pattern, to that of the original adaptation. A chronic cat preparation with long-term optical reversal of vision has now been developed and shows similar adaptive and recovery changes at low test stimulus amplitudes, but different patterns of adaptive response at high amplitudes. An adaptive neural model employing known vestibulo-ocular pathways is proposed to account for these experimentally observed plastic changes. The model is used to predict the adapted response to patterns of stimulation extending beyond the range of experimental investigation.

Introduction

It is a remarkable fact that one can see with clear vision during the head movements incurred over the whole range of normal locomotor activity; for example while running over an irregular terrain. The ability to do so reflects upon the nicety of the several physiological mechanisms which together are responsible for ocular stabilization during head movement. This communication examines some aspects of these mechanisms, especially in the context of their maintained compatibility with one another due to adaptive interactions between them.

Consider first the ocular following of a moving visual target when the head is still. If one attempts to look at one's own hand while oscillating it over a small angle in front of the stationary head it quickly becomes blurred as the frequency of oscillation increases above 1–2 Hz. This relatively low frequency response of the visual tracking system must severely limit its contribution to retinal image stabilization during certain forms of normal locomotion, for example when running since the frequency of foot-fall and hence of head movement then lies predominantly in the range 3–4 Hz. If, however, the hand is held still and the head is rotationally oscillated about a vertical axis over a similar relative angular amplitude as before, then at least up to about 5 Hz the visual image remains clear. Introduction of the inertially dependent vestibulo-ocular reflex (v.o.r.) is largely responsible for this phenomenon, due in particular to its much higher frequency response (Benson 1971).

Nevertheless, the extended frequency response of the v.o.r. is not enough to ensure image stabilization over the higher frequency range. In order to avoid retinal image slip the gain of the reflex, expressed as compensatory eye angular velocity/head angular velocity, must remain close to a value of one. The clarity with which one sees the hand during head oscillation indicates that this condition is closely met, at least up to about 5 Hz. Indeed, the above reference

shows that the human v.o.r. exhibits approximately unity gain up to about 8 Hz, even in the absence of both vision and neck movement. The intriguing question then arises; how is unity gain maintained in this apparently open loop v.o.r. when operating at frequencies which are too high for a useful contribution from the closed loop visual tracking system? (To avoid confusion it should be mentioned that as frequency of head oscillation falls below about 1 Hz, the v.o.r. gain tends to fall below 1, for example to around 0.65 at $\frac{1}{6}$ Hz as determined in human experiments described below. But since precision *visual* tracking is possible at these lower frequencies the need for unity gain in the v.o.r. no longer exists.)

A clue to the above question is perhaps to be found in the results of psychological experiments designed to examine the subjective adaptation of humans to prolonged optical reversal of vision (Kohler 1956, 1962). One of the striking features of those experiments was that, given time (several weeks) subjects found they could engage in a wide range of sporting activities. Knowing the strict frequency response limitation to normal visual tracking, it struck the present author that in some way the v.o.r. of these adapted subjects must have become useful again, despite the fact that with reversed vision the *normal* v.o.r. response would be opposite to that required for reflex retinal image stabilization during head rotation. If this were true, then quite contrary to the above implication of an open loop characteristic, the v.o.r. must surely exhibit an enormous degree of flexibility, presumably due to some form of visual feedback tending always to modify the reflex towards successful minimization of retinal image slip during head movement. If such an influence was responsible for bringing about the extreme modification implied by the psychological experiments referred to above, then presumably with normal vision it would also be capable of maintaining unity gain at frequencies above the cut-off for visual tracking.

These arguments, although by no means 'watertight', seemed sufficiently provocative to initiate a series of human and animal experimental studies to investigate the adaptive influence of vision upon the vestibulo-ocular reflex system (Melvill Jones & Gonshor 1972, 1975; Gonshor & Melvill Jones 1969, 1971, 1976*a*, *b*; Melvill Jones & Davies 1976; Davies & Melvill Jones 1976). Selected findings from these studies are described and discussed below.

Methods

First it was necessary to establish a reliable method for measuring stimulus-response characteristics of the v.o.r. without the test stimulus itself modifying the reflex. The problem here centred round the wide range of literature suggesting that application of any rotational vestibular stimulus would itself lead to a form of habituation in the v.o.r. (Dodge 1923; Hood & Pfaltz 1954; Flurr & Mendel 1962; Collins 1964; Guedry 1965; Dix & Hood 1969). However, bearing in mind the introductory remarks implicating maintained v.o.r. gain during oscillatory head rotation in the adult human, the possibility arose that natural patterns of stimulation might be free of the habituating phenomenon.

To examine this possibility seven human subjects were each exposed to ten 2 min test runs of sinusoidal rotation about a vertical axis with 3 min rests between runs. This procedure was repeated on three consecutive days. All rotational stimuli and rest periods were conducted in the dark, the parameters of the standard sinusoidal test stimulus being $\frac{1}{6}$ Hz and 120°/s peak to peak (p.p.) angular velocity amplitude. These parameters were chosen both for practical reasons of feasibility and, more important, for the physiological reason that they lie within the

presumed range of natural head movement. With regard to the frequency of stimulation this presumption is based upon the following argument. First, over a limited frequency range of sinusoidal stimulation the mechanical components of the semicircular canal act as an integrating accelerometer the physiological response of which therefore registers instantaneous head angular velocity (Melvill Jones & Milsum 1971; Melvill Jones 1972). Secondly it has been shown by dimensional analysis over a wide range of animal species of differing size, that this limited frequency range of velocity transduction corresponds closely to the range of natural head movement likely to be associated with a species of any given size (Jones & Spells 1963; Melvill Jones 1974). Consequently, insofar as the lower frequency limit of velocity transduction in the human canal has been estimated at around $\frac{1}{10}$ Hz (Jones & Milsum 1965), the chosen test frequency of $\frac{1}{6}$ Hz may be presumed to stimulate the system in its natural mode of operation. With regard to amplitude, a peak stimulus velocity of 60°/s (i.e. half the test stimulus p.p. amplitude) may be assumed to lie within the range of natural movement on the grounds that much faster head angular velocities have been quoted in the literature (Hallpike & Hood 1953).

Since the results of this first experiment revealed no evidence of habituative attenuation over the three time scales of (i) a 2 min test run, (ii) the daily exposure of ten consecutive test runs, and (iii) the whole 3-day experiment (Gonshor & Melvill Jones 1969, 1976*a*), these parameters have been employed for test stimuli in all the subsequent human experiments. In this and subsequent experiments eye movements were recorded by d.c. electro-oculography (e.o.g.), care being taken to avoid errors introduced by changes of e.o.g. gain due to light-dark adaptation (Gonshor & Malcolm 1971).

In a second experiment (Gonshor & Melvill Jones 1976*a*) the same human subjects were exposed six months later to precisely the same 3-day sequence of *vestibular* stimuli, but during the majority of the oscillatory movement they attempted to fixate *visually* upon a *mirror-reversed* image of the scene surrounding the turntable. Since the mirror was fixed to the servo-driven turntable, the visual scene appeared to move relative to the subject at the same frequency and amplitude as the turntable, but in a direction opposite to that of the real world and hence opposite to the prevailing v.o.r. drive. The 1st, 6th and 11th test runs were conducted as before in the dark for the purpose of measuring v.o.r. charactersitics, whilst the 2nd–5th and 7th–10th runs inclusive were used for exposure to the reversed visual tracking task.

As described later, this short-term exposure to antagonistic inputs from the visual and vestibular sensory systems induced considerable, and temporarily retained, v.o.r. attenuation. Consequently, a third series of experiments was undertaken to examine long-term effects. For this, recourse was made to the goggle-mounted reversing (dove) prisms used in the psychological experiments referred to above. The prisms were mounted so as to reverse the horizontal, but not the vertical, fields of view. Subjects wore these goggles continuously during their waking hours for periods up to 27 days and their v.o.r. was tested intermittently in the dark over these periods and during equal periods after return to normal vision. Details of methods and procedures are described elsewhere (Gonshor & Melvill Jones 1976*b*), but it may be noted here that throughout each experiment subjects were required to engage in normal daily activities close to the limit of their current capability.

In view of the formidable degree of adaptive change observed in this long-term human study a corresponding animal programme has since been initiated, with the twofold objective of (i) investigating further the behavioural characteristics of the adapted reflex and (ii) interrogating neurophysiological mechanisms in a chronic animal preparation. For this, two cats have thus

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far been prepared with chronically implanted e.o.g. electrodes for recording eye movement and skull mounted fixtures for stereotaxic fixation of the head to a servo-driven turntable and precision location of a prism-carrying mask (figure 6). By using test stimuli similar, but not identical, to those employed for the humans, the v.o.r. of these animals has been examined over periods of continuous horizontal vision reversal extending up to 200 days. The methods and procedures employed in the animal experiments are detailed elsewhere (Melvill Jones & Davies 1976).

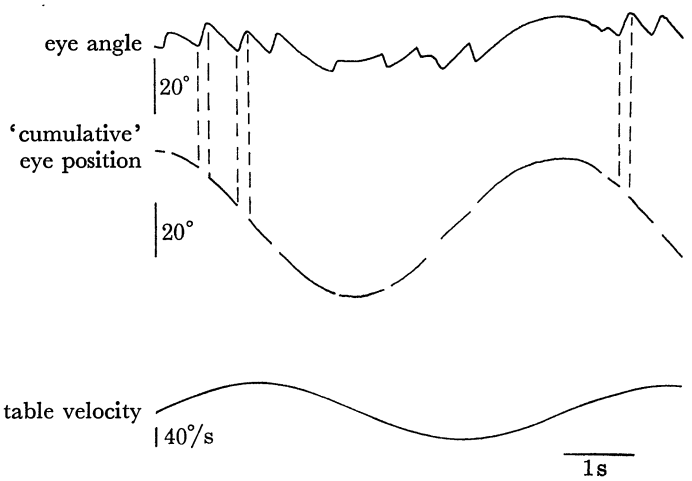

FIGURE 1. Construction of the curve of cumulative eye position. In all traces an upward movement is a right-going movement. (From Gonshor & Melvill Jones 1976*a*.)

RESULTS

(*a*) *Human experiments*

Figure 1 illustrates extracts from original records of normal reflexly driven eye movements obtained in the dark during sinusoidal rotation of a human subject. A typical nystagmoid pattern of reflexly driven compensatory eye movement is seen. From these records curves of cumulative eye position (c.e.p.) were assembled after the general method of Meiry (1966), to generate waveforms analogous to those which would have occurred if the compensatory response was not interspersed with quick phase return eye movements. C.e.p. curves were constructed by hand in the human experiments but with the aid of digital computation in the cat experiments. From such curves the gain and phase of the reflex response was computed by reference to the sinusoidal curve of rotational stimulation.

Mean gains obtained in this way from all subjects employed in the first two experiments are plotted in figure 2 as normalized values relative to the first mean control value. The abscissa is divided into the experimental durations of each of three consecutive days. The numbers 1–10 indicate the sequence of 2 min exposures to rotational movement. The upper set of points (●) illustrates the absence of any consistent trend of change in the v.o.r. gain over the whole 3 day control experiment. The lower curves (○—○) show the consistent daily attentuation of response found in the same subjects exposed to the same vestibular stimulus, when they were required to attempt visual tracking of the illuminated, mirror-reversed moving scene. The plotted points give the normalized mean v.o.r. gain obtained from the first, sixth and last runs which, as mentioned above, were recorded in the dark for this purpose. No measurements were made during the intervening runs when reversed visual tracking was underway. The combined

results clearly indicate a marked and statistically highly significant ($P \ll 0.001$) influence of this short-term reversed visual tracking task upon the gain of the v.o.r. as tested in the dark.

Much greater attenuation occurred in the long-term experiments, which exposed subjects to continuous vision reversal during all their waking hours. Figure 3 illustrates this feature by normalizing the combined data of four subjects obtained during the first week of exposure to the reversing prisms. In the first day there was rapid attenuation to about half the normal control gain, with subsequent continued decline to about one-quarter the normal value by the end of the week. It should be recalled that all these values were obtained from standard 2 min test runs conducted in the dark at $\frac{1}{6}$ Hz and 120°/s p.p. angular velocity amplitude with head fixed to the turntable. They therefore represent characteristics of eye movement induced by

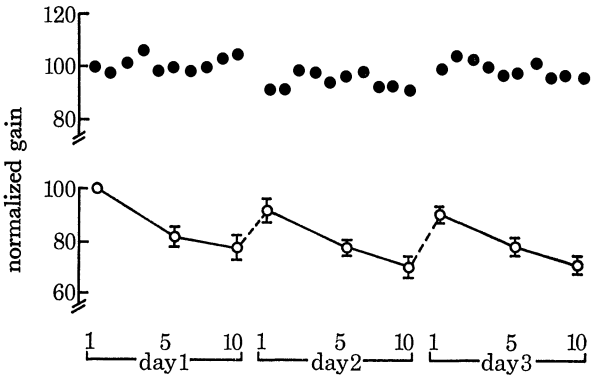

FIGURE 2. Combined results from the first (●) and second (○) set of human experiments, plotted as normalized vestibulo-ocular reflex (v.o.r.) gain against the temporal sequence of the 2 min test runs (1–5–10 in the abscissa) on 3 consecutive days. Gain is expressed as a percentage of the first day's mean control value. Each point gives the normalized mean value obtained in the dark from 7 individual subjects' means, each of which was derived from separate estimates made on several consecutive cycles of oscillation. Brackets show standard errors of the means ($n = 7$ subjects). (Composite data from Gonshor & Melvill Jones 1976*a*.)

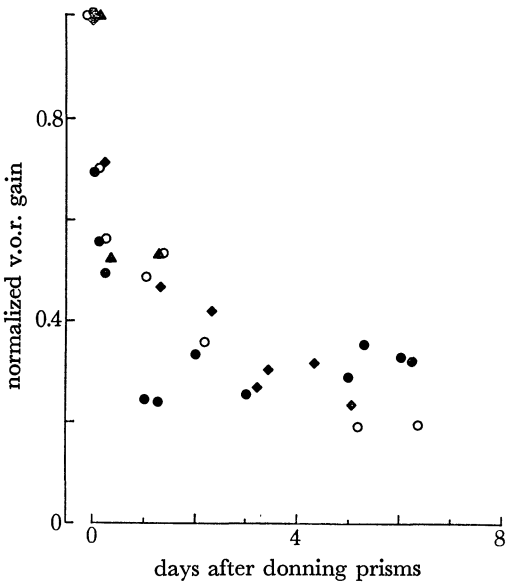

FIGURE 3. Normalized v.o.r. gain from four long term human subjects depicted over the first week of continuous vision reversal. Each point gives a mean obtained from approximately 10 consecutive stimulus cycles. (From Gonshor & Melvill Jones 1976*b*.)

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a purely vestibular stimulus; uninfluenced, that is by concurrent vision or neck movement. In practice, the most highly attenuated responses were often difficult to analyse, due not only to low signal to noise ratio but also to fluctuating modification of the phase of ocular response relative to the vestibular stimulus. The importance of this latter feature soon became clear as the longest human experiment of 27 days progressed into the second and third weeks. Figure 4 shows simultaneous plots of the gain and phase obtained from this subject throughout the whole of his experiment. Each point gives a mean value from around 10 estimates within a 2 min test run, with the gain normalized relative to the mean control value. As in figure 3 there was an initial rapid attenuation of gain, without significant deviation of phase from the normal control value of about +5 to +7° (Hixson & Niven 1962). However, as the gain curve began to flatten out marked, but violently fluctuating, changes of response phase began to occur,

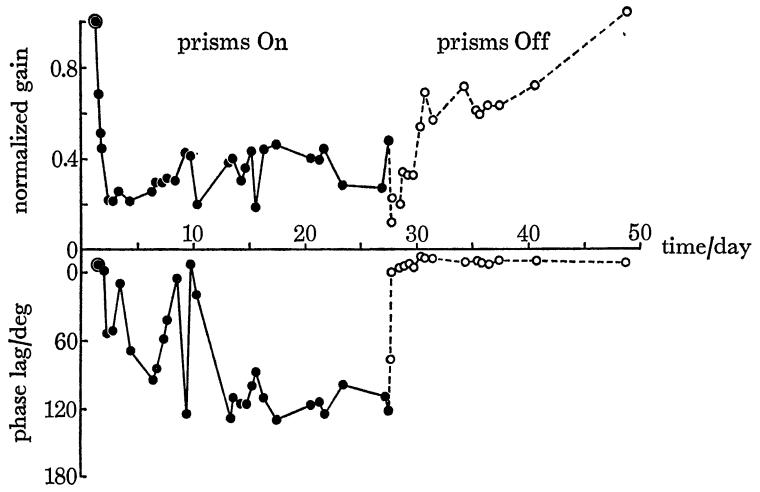

FIGURE 4. V.o.r. phase (lower curve) and normalized gain (upper curve) from one human subject exposed to continuous vision reversal for 27 days (●) and during readaptation after return to normal vision (○). Circled points ⊙ are mean control values obtained just before donning the reversing prisms. Phase is registered relative to that associated with perfect compensation using normal vision.

trending generally in the lagging direction. After about 2 weeks a new steady state was achieved in which the phase and gain settled at mean values of about (−) 125° and 0.45 respectively relative to this subject's control values. The important feature of this outcome is illustrated in figure 5, which compares a normal control response (upper trace of eye movement) with a response obtained on the morning of the 14th day after donning the prisms (lower trace of eye movement). The adapted response is close to being a reversed replica of the normal one, but in this instance was some 50° phase advanced relative to exact reversal, or alternatively 130° phase lagged relative to normal. An interesting additional feature is that the 'reversed' response includes saccadic quick phase repositioning eye movements which on quantitative characterization proved indistinguishable from corresponding normal quick phase movements. Apparently, the adaptive change brought about appropriate modification of the whole composite nystagmoid pattern of vestibulo-ocular response.

A particularly striking feature of the results is seen in the latter half of figure 4 (○), which represents the period of recovery after return to normal vision. Instead of a gradual, fluctuating return of phase to normal, this characteristic was rapidly restored in a matter of hours. In

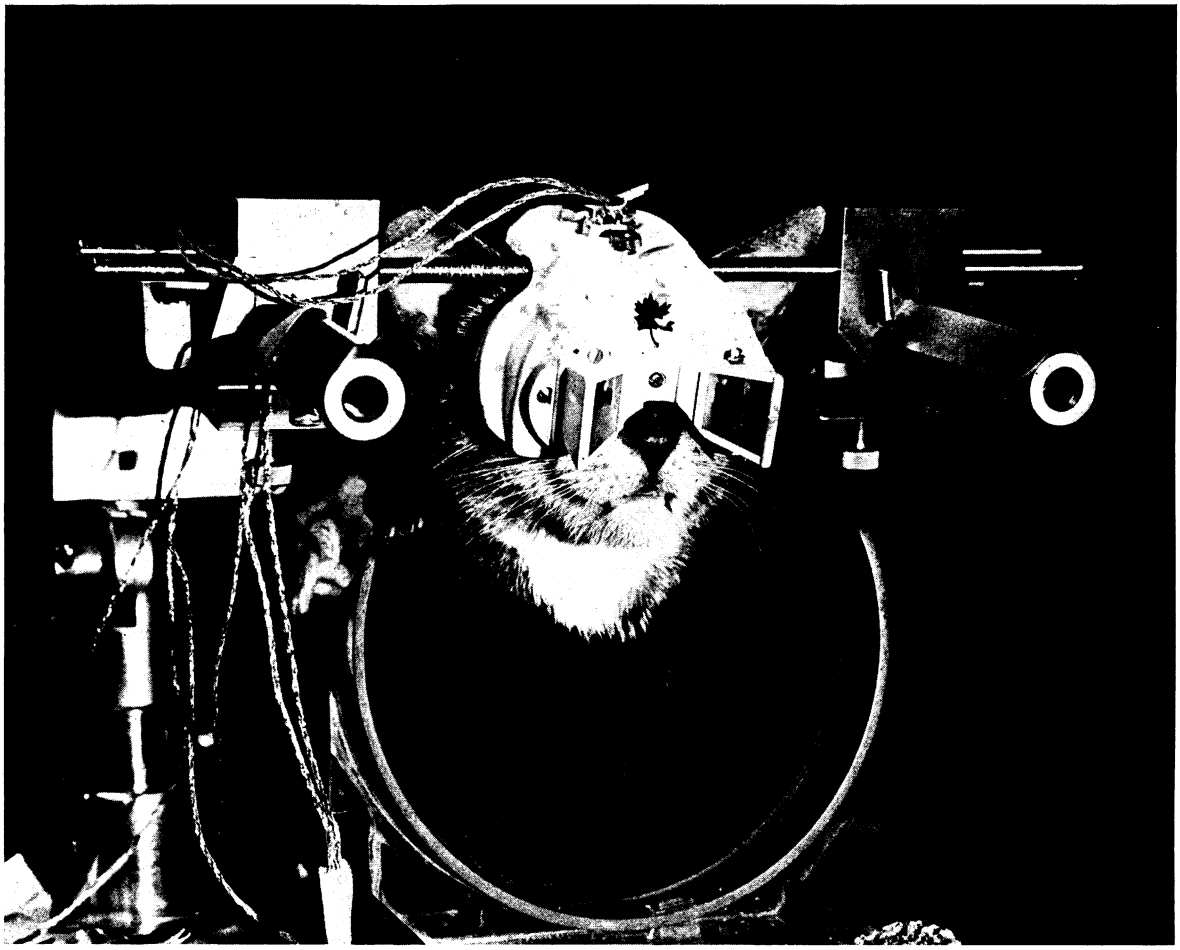

FIGURE 6. The chronic animal preparation wearing the prism-carrying mask with the head stereotaxically fixed to the turntable by means of an acrylic block fixed to the skull. The electrical leads are plugged into outlets from implanted d.c. electro-oculographic electrodes. (Photograph by Olga Panyszak)

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contrast to this after a short, but marked, transient attenuation the subsequent restoration of gain occupied about 2 weeks, a period similar to that of the original adaptation.

Subjectively the first week of the original adaptation was usually somewhat traumatic, both on account of moderate to severe nausea in the first few days and the continually frustrating experience of erroneous postural and locomotor control. Behaviourly these features were associated with loss of appetite and abnormal irritability. However, these behavioural anomalies became progressively less evident as physiological adaptation in the v.o.r. proceeded. Interestingly, during adaptive recovery after return to normal vision, appetite and ordinary locomotor control were only transiently affected, except for occasional 'blunders' of movement,

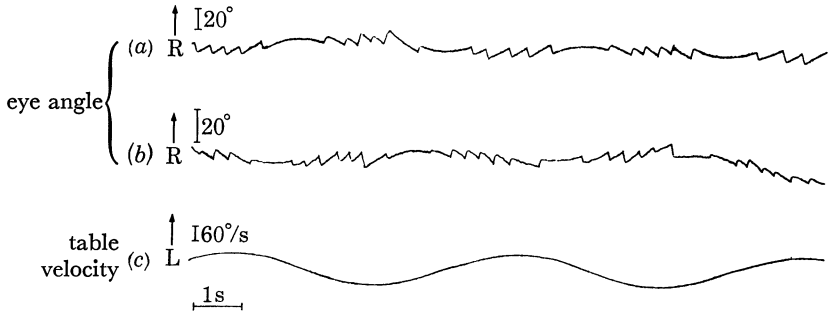

FIGURE 5. (*a*) Normal and (*b*) fully adapted nystagmoid responses obtained during test stimuli in the dark from the same long term human subject as in figure 4. The adapted response, which was recorded after 14 days of reversed vision, approximates a reversed replica of the normal one. Both records of eye movement are correctly phase related to the lower record (*c*) of stimulus angular *velocity*. (From Melvill Jones & Gonshor 1975.)

which occurred even up to 2–3 weeks after prism removal. Quantitative measures did however reveal more than transient impairment of postural control, both during the original adaptation and during recovery (Gonshor 1974). Indeed the dangers incurred by potentially erroneous movement control necessitated full-time monitoring of each subject's activities by another individual throughout the whole duration of each human experiment. This was especially important when subjects ventured outside the laboratory environment, as they were encouraged to do, for example by donation of theatre tickets and fully paid luxury restaurant meals.

(*b*) *Animal experiments*

Figure 6 illustrates the first chronic cat preparation with a close-fitting plastic mask carrying modified polystyrene dove prisms, the whole skull-mask assembly being stereotaxically fixed to the turntable. Figure 7 shows similar plots of normalized gain and phase (Melvill Jones & Davies 1975) to those of figure 4, except that test stimulus parameters were $\frac{1}{8}$ Hz at 8°/s p.p. amplitude and $\frac{1}{8}$ Hz at 17°/s p.p. amplitude for the adaptive and recovery periods respectively. Also the duration of maintained vision reversal was greatly prolonged compared with the human experiments. This accounts for the breaks in the abscissal time base which are introduced to allow inclusion of long term results while retaining the same time scale as that in figure 4. As in figure 4 each point gives a mean value computed from 10 consecutive cycles of rotational stimulation conducted in complete darkness. The first and second pairs of ringed circles give respectively control values and overall means obtained from five separate days close to the 200th day after donning the prisms.

The two sets of results in figures 4 and 7 show strong similarities. Thus, as in man, the cat

demonstrated a similar initial period of rapid gain reduction followed by a period of fluctuating change of phase which, after about 2 weeks, settled at a steady value not far removed from 180° relative to normal, and hence close to reflex reversal. Thereafter the gain progressively increased, much as in the human data, to reach an ultimate steady level of about 0.5 the normal control value. Also, after prism removal there was very rapid restoration of phase followed, after an initial sharp decline, by a gradual return of gain, as in the long term human experiment.

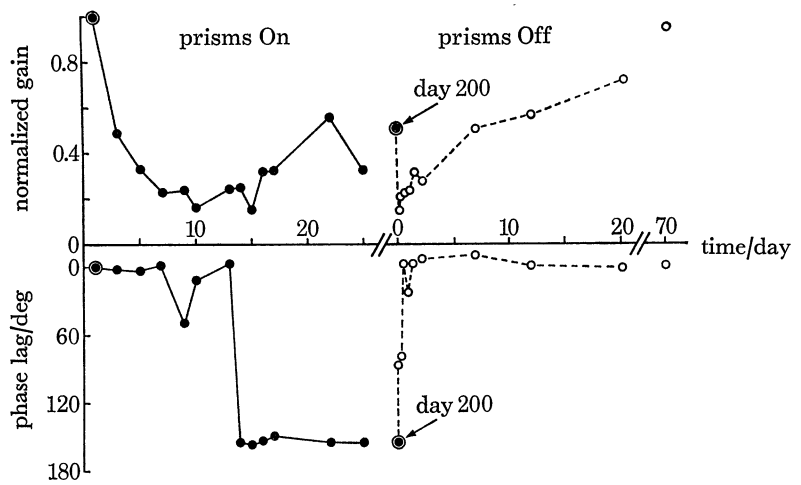

FIGURE 7. V.o.r. phase and normalized gain from one cat during (●) and after (○) 200 days of continuous vision reversal. The first and second pairs of ringed points (⊙) give respectively control values and overall means from 5 days (10 cycles per day) close to the 200th day of vision reversal. The adapting and recovering results were obtained with test stimuli of 1/8 Hz at 8°/s p.p. amplitude and 1/8 Hz at 17°/s p.p. amplitude respectively. Note the abscissal breaks which are included to permit the same time scale as in figure 4.

A second cat which is currently undergoing prism reversed adaptation shows similar changes. For example 70 days after donning the prisms its mean values of phase and normalized gain obtained from 10 computer analysed stimulus cycles of $\frac{1}{8}$ Hz and 17°/s p.p. amplitude were (—) 152° and 0.25 respectively.

Despite the general similarities between the adaptive patterns of man and cat, there are significant differences of detail. For example the cat demonstrates slower apparent rates of change in gain, sharper transition of phase and a considerably larger magnitude of adapted phase shift. These matters will be discussed later in the context of the possible central neural mechanisms involved.

There is however a major additional result which should be described here, manifest as a marked dependence of response upon stimulus amplitude (Melvill Jones & Davies 1976).

Figure 8 summarizes the main features of this phenomenon by plotting mean phase and mean gain (not normalized) against a wide range of stimulus amplitudes. Filled circles and continuous lines show results obtained after approximately 200 days vision reversal. Incidentally these were recorded on the same five days as those from which the '200 day' means of figure 7 were collated. The open circles and dashed lines show similar data obtained 70 days after removal of the reversing prisms from the plastic mask. The mask itself remained in place so as to retain unchanged the restricted field of view. The filled circles and continuous lines show that effective reflex reversal was restricted to the lower range of stimulus amplitudes, with the most effective adaptation being manifest at the lowest value. Over the upper amplitude range

v.o.r. phase progressively reverted back to normal with increasing stimulus amplitude. Except at the lowest stimulus amplitude the gain remained substantially subnormal despite this striking return of phase. In marked contrast, the recovered condition at 70 days after prism removal exhibited good linearity over the whole amplitude range, with the phase in particular firmly fixed at the normal compensatory value.

Behaviourly these cats performed more or less as expected, except that there have been no overt signs of nausea in that they never lost their appetite and never vomited. After initial fitting with the prism carrying mask their locomotor patterns were thoroughly disorganized, although the ultra-light-weight mask was remarkably well tolerated. Moreover, as in the humans, there was an unusually marked tendency to rest and sleep during the day, presumably due to the stressful situation. However, over roughly the same time course as their measured reflex adaptation, they became progressively more versatile in movement control, reaching the point where it was possible to jump from the ground up to a standard laboratory work bench and from there onto one's shoulder for normal feline caressing. Indeed, at the time of writing, given the opportunity to 'escape' into the building corridors, the second cat sets off at a gallop, negotiating awkward corners and unexpected obstacles with consummate skill.

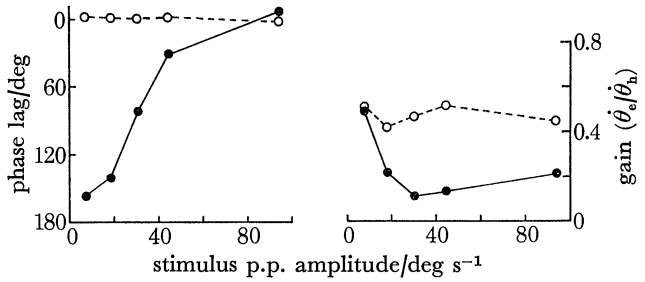

FIGURE 8. Dependence of the cat's adapted response (●) upon stimulus amplitude, each of these points being the mean of 50 (5 days of 10 cycles each) estimates near the 200th day of vision reversal. For comparison similar points (○) are plotted from 10 estimates each, made on the 70th day after removing the prisms but retaining the mask. All test stimuli were at $\frac{1}{8}$ Hz. θ_h and θ_e indicate head and eye angular velocities respectively. (Modified from Melvill Jones & Davies 1976.)

DISCUSSION

The first two short term human experiments demonstrated that, whereas repeated sinusoidal vestibular stimulation in the dark produced no modification of the measured v.o.r., a reversed visual tracking task superimposed on the same vestibular stimulus produced highly significant and temporarily retained reduction of gain. From this it may be concluded with fair confidence that it was the reversed visual tracking task which in some way produced the observed change in v.o.r. gain. The induced change would appear to be adaptive in the sense that the effect would tend to improve visual tracking by reduction of the opposing v.o.r.

The long term human and animal experiments indicate, however, that a much more versatile process is in operation than mere attenuation of gain. At least in appropriate circumstances, approximate reversal of the reflex was induced, with the added feature that such changes as occurred were retained from day to day until prism removal called for reversion to normal conditions. Even then, although the phase characteristic was quickly restored to normal, the

v.o.r. gain, after a marked but transient initial fall, required 2–3 weeks of normal vision for its full recovery. Evidently, a powerful form of adaptive plasticity is at play, apparently operating over both fast (hours) and slow (weeks) time courses, with the intriguing rider that these plastic changes occurred in the fully developed adult CNS. The ages of human and cat subjects ranged from 20–50 and 1–2 years respectively.

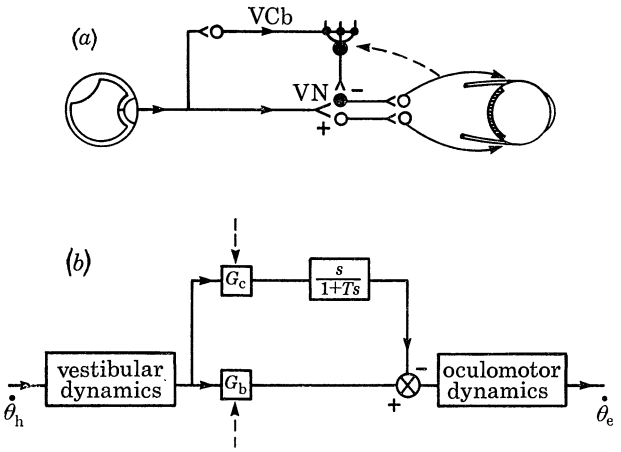

FIGURE 9. (*a*) Proposed neural network and (*b*) the corresponding informational model formulated to account for the observed plastic changes in the v.o.r., and to predict the frequency response of the adapting vestibulo-ocular system. VCb, vestibular cerebellum; VN, vestibular nucleus; G_c and G_b, neural gains in the cerebellar and brainstem pathways respectively; $(s/Ts+1)$, phase lead term in the cerebellar pathway. $\dot{\theta}_h$ and $\dot{\theta}_e$, head and eye angular velocities respectively. (From Davies & Melvill Jones 1976.)

(*a*) *Neural mechanisms*

What kind of central mechanisms could be responsible for these somewhat complex, but systematically goal-directed, adaptive changes? Rather surprisingly most of them can be accounted for reasonably well by the relatively simple neural network of figure 9*a* (Davies & Melvill Jones 1976), which employs only established central pathways. Referring to the figure, primary vestibular afferents are known to branch, projecting on the one hand directly to the brainstem to make monosynaptic excitatory connections with second order neurones in the vestibular nuclei (Precht & Shimazu 1965) and on the other hand to activate cortical Purkinje cells in the vestibular cerebellum via mossey fibre projections to the granule cell layer (Brodal & Høivik 1964; Precht & Llinás 1969). In turn, there are monosynaptic (inhibitory) Purkinje cell projections to vestibular interneurons which themselves project to the oculomotor nuclei (Angaut & Brodal 1967; Precht 1972). Thus, whereas the direct primary afferent influence ('B' pathway) provides an excitatory input to vestibulo-ocular interneurons, the indirect cerebellar pathway ('C') can almost simultaneously provide an inhibitory influence on those same interneurons. Therefore, providing it were possible to alter the relative efficacy of the direct and indirect pathways, the eventual output to the oculomotor system could theoretically be made to range from normal (predominant direct influence) to a reversed condition (predominant indirect influence), assuming a reasonably high spontaneous level of interneuronal activity in the vestibular nuclei (Melvill Jones & Milsum 1970, 1971).

Nevertheless, this simple scheme could not produce the remarkable progression of phase changes through which the final adaptive process was in fact approached, nor indeed the

incomplete phase reversal which apparently represents the fully adapted state, as manifest at the particular stimulus test frequency employed. It is however only necessary to introduce moderate phase *advancement* in the transcerebellar inhibitory signal relative to the direct excitatory one, for all the complex gain-phase behaviour depicted in figures 4 and 7 to be readily accountable, provided only that plastic changes of steady state gain can be induced in the B and C pathways. Such phase advancement in the C pathway might well result from the many parallel and recurrent inhibitory influences attributed to cerebellar networks (Eccles, Ito & Szentágothai 1967), since these would tend to manifest their effect as a 'forgetting' time constant, which would indeed constitute a systematic 'lead' term. On the basis of this possibility the information flow diagram of figure 9*b* has been proposed as a simplified working model of the adaptive neural system (Davies & Melvill Jones 1976). Peripheral vestibular (Melvill Jones 1972) and oculomotor (Skavenski & Robinson 1973) dynamics would be unlikely to contribute phase at the frequencies employed. The relevant system components are therefore identified as the gains of the direct brainstem (G_b) and indirect cerebellar (G_c) components and a phase-lead term ($s/Ts+1$) in the inhibitory transcerebellar pathway.

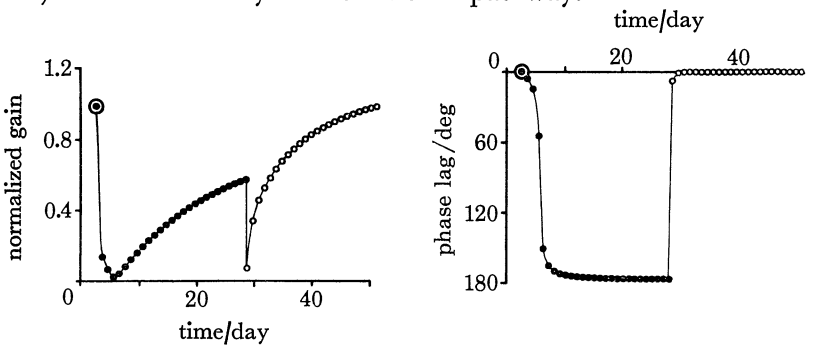

FIGURE 10. *Predicted* response of the adapting and recovering v.o.r., as if tested at 3 Hz on each day of the long term human experiment (cf. figure 4 in which results were *measured* at $\frac{1}{6}$ Hz). Each pair of points (gain and phase) was calculated by inserting into the model of figure 9*b* values for G_b and G_c estimated from the experimental data of Figure 4. In practice calculated regression curves through the original, somewhat scattered, estimates of G_b and G_c were used, which accounts for the smoothness of the predicted curves in the above figure.

(*b*) *Functional implications of the model*

Applying this model to the *human* data of figure 4, it has been possible to estimate the value of the 'forgetting' time constant T as approximately 1.3 s (Davies & Melvill Jones 1976). Using this value, hypothetical values of G_b and G_c were computed for each *measured* (i.e. at $\frac{1}{6}$ Hz) mean v.o.r. gain and phase combination of figure 4. From calculated curves fitting the resulting time plots of G_b and G_c (not shown here) it then became possible to predict by computation the v.o.r. gain and phase which would have occurred throughout the adaptive and recovery sequence at other test stimulus frequencies if the central network behaved according to the model.

Figure 10 shows one such idealized data set, redrawn from photographs of computer graphic curves, as calculated from assumed test stimuli of 3 Hz applied at daily intervals throughout the whole of the long term human experiment. Details of the computational methods are described in the previous reference. Several notable features emerge from these theoretical graphs, the smoothness of which is due to their being calculated from smooth curves fitted mathematically to the actual, somewhat scattered, estimates of G_b and G_c, deduced as

mentioned above from real experimental data. First the transition from normal phase to the adapted, phase-lagged, condition would have manifested itself much earlier if tested at 3 Hz than at $\frac{1}{6}$ Hz. Secondly the final adapted phase would have quickly settled to a steady value of about (−) 177°, which is much closer to true reversal (i.e. −180°) than the actual value of (−) 125° obtained for practical reasons at the much lower stimulus frequency of $\frac{1}{6}$ Hz. Thirdly, the final gain of the adapted (reversed) condition would be greater than the measured gain at $\frac{1}{6}$ Hz by a factor of about 1.4. All these features would be functionally advantageous to the task of maintaining a stable reversed retinal image during oscillatory head movement. A generalization thus emerges whereby the fully adapted state would have the property of becoming progressively more useful as the frequency of head oscillation increases. The theoretical implication is that, as the frequency of head movement increases above the frequency response of the visual tracking system, so the functional efficacy of the *adapted* v.o.r. would improve, perhaps even to the point of self-sufficiency when needed.

A number of differences were noted above in the results obtained from humans and cats. First, whereas the initial phase transition of figure 4 occurred rather gradually over a period of about 10 days, in the cat this transition was relatively rapid. Theoretically this difference could be largely accounted for by assigning a greater value of the C pathway time constant, T, to cat than man. In the model this would have a similar effect to that of increasing the stimulus frequency with T held constant; which produced the rapid phase transition seen in the theroretical high frequency response of the human system (figure 10). Secondly, successful adaptation in the cat was restricted to a much lower range of stimulus amplitude than in man. Possibly this could reflect a comparatively low capacity for informational transport in the newly adapted pathway of the cat; perhaps functionally associated with more effective head stabilisation in cat than man. Be that as it may, a simple capacity limit of this kind in the C pathway would also be compatible with the rather dramatic amplitude dependence of response seen in figure 9. Thirdly, the rate of adaptive change in gain appears to be slower in cat than man. In the model this would call for slower changes in the values of G_b and G_c.

(*c*) *Visual-vestibular interactions*

An essential feature of figure 9*b* is implied by the dashed arrows indicating influences capable of modifying the neural gains identified as G_b and G_c. What evidence is there to suggest that such modification could be induced by moving visual stimuli? First, it has recently been demonstrated by several groups of investigators that moving visual stimuli can be made to modify both complex (Maekawa & Simpson 1973; Simpson & Alley 1974) and simple (Lisberger & Fuchs 1974; Ghelarducci, Ito & Yagi 1975; Miles & Fuller 1975*a*), spike activity in vestibulo-cerebellar Purkinje cells. Furthermore, other workers have demonstrated that appropriate visual stimuli can modify presumed second order vestibular cell activity in the brain stem (Henn, Young & Finley 1974; Hassul, Cogdell & Kimm 1975) as well as modifying the subjective impression of whole body movement (Dichgans & Brandt 1972). Evidently, there are informational pathways projecting their influence from retinal and/or oculomotor sources to relevant central components of the v.o.r.

However, the influences described in the above references vary from moment to moment in accordance with the instantaneous direction and magnitude of the visual stimulus. In strict contrast to this the required influences in the adaptive model of figure 9*b* (dashed arrows at G_b and G_c) must be manifest as retained changes of scalar gain, independent of the instantaneous

direction of the visual stimulus. The possibility that such effects may occur in the vestibular cerebellum has been evidenced by ablation experiments, which have shown substantial modification of acquired adaptive changes in both cat (Robinson 1975) and rabbit (Ito, Shiida, Yagi & Yamamoto 1974).

(*d*) *Additional central mechanisms*

It should be emphasised that the adaptive network of figure 9 is intended to provide no more than a provisional working hypothesis. Indeed there are already indications that other central components may be involved. For example, Llinás, Walton, Hillman & Sotelo (1975) have very recently shown that long-term adaptation to unilateral labyrinthectomy is abolished by chemical lesion of the inferior olive. They suggest that 'compensation probably occurs through the olivary projections to fastigial and Deiter's nucleus, these in turn projecting to brainstem and spinal centres'. In this connection, however, the cautionary observation might be added that unilateral labyrinthectomy calls for extensive modification of vestibulo-*spinal* projections, whereas vision reversal does not. Again the reticular formation has long been associated with vestibulo-ocular activity (Lorente de Nó 1933; Szentágothai 1950). More recently its potential contribution to visual-vestibular interactions has been suggested by the finding of reticular neural units which respond both independently and jointly in association with both purely vestibular and purely oculomotor activity (Hassul *et al.* 1975).

Seen in the larger context of whole body movement, it may also be significant that neck afferents have now been found to converge with second order vestibular projections to the floccular lobe of the vestibular cerebellum (Wilson, Maeda, Franck & Schimazu 1975). Perhaps this new observation is in line with Miles & Fuller's view (1975*b*) that floccular Purkinje cells 'synthesise a true neuronal facsimile of track target velocity' from combined inputs of head, eye and retinal image movements. Clearly the relationships between these inputs would have to be modified to produce the new facsimile required for successful retinal stabilization of an optically reversed visual image during head movement.

(*e*) *Normal functional role of the adaptive system*

Returning to the introductory theme, one might well question the relevance in natural life of an adaptive process which is capable of inducing reflex reversal. Perhaps in reality this experimental paradigm is extenuating to its limits an adaptive capability which is ordinarily used to maintain a required value of v.o.r. gain and phase throughout life. At frequencies of head movement above the upper frequency limits of visual tracking, precision maintenance of unity gain is necessary for clear vision. Seen in this light one might expect that the adaptive capability revealed in these vision reversed experiments would readily correct for artificial changes of *optical* gain introduced for example by wearing telescopic spectacles. Following this reasoning Miles & Fuller (1974) fitted monkeys with magnifying, or reducing, spectacles and found that these animals did indeed quickly adjust their v.o.r. gain towards the goal of automatic elimination of retinal image slip during head movement. More recently Gauthier & Robinson (1975) have shown that similar plastic v.o.r. gain adjustment occurs in human subjects wearing magnifying spectacles, with the added feature that these subjects manifested modified psychophysical experience during forced rotation.

In conclusion the evidence that some kind of visually induced modification of steady state gain is operative in central components of the vestibulo-ocular system seems sufficiently strong

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to call for speculation upon potential plastic processes which could conceivably be at play. Possible mechanisms such as changed efficacy in established synaptic connections, altered distributions of synaptic terminals and even modified distribution of informational flow at points of axonal branching (van Essen 1973) come to mind. At this stage however it would seem rash to speculate further on the question of how visually evoked neural signals might activate such processes at the cellular level in this neuronal system.

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Discussion

R. L. Gregory (*M.R.C. Brain and Perception Laboratory, Department of Anatomy, University of Bristol*).

Experiments on adaptation of human vision to optical inversion given by prisms and telescopes, by G. M. Stratton in 1896 and more recently by Ivo Kohler at Innsbruck, show radical correction to reversal after a few days. It may occur suddenly, often 'switched' by added touch information, or by improbable perceptions such as rain 'falling' upwards. Adaptive correction may develop for specific situations or tasks, and correction is not always of the entire scene. For example, Kohler reported, for lateral reversal, seeing people on the correct sides of a road, though the buttons on the ladies' coats were on the wrong side. The implication is that he had developed adaptation to the positions of people while avoiding them while walking; but there was not the manual experience of the coat butttons to give adaptation. He also reported (private communication) that after successive adaptation to inverting prisms, when his secretary accidentally flicked his nose with a pencil, his visual world immediately switched upside down. Evidently the nose stimulation indicated that the prisms were in place – setting up a previously developed but now inappropriate set of corrections.

Such rapid reversible changes are surely not compatible with cell migration as the basis of this kind of plasticity. It seems, rather, that visual codes are modified: perhaps much as adding 'not' to a sentence changes the entire meaning with small physical modification. If this is so, we need to find the codes by which brain activity represents perception and controls behaviour. If, though, the analogy to symbols of language is just, we can hardly expect to find simple relationships between neural activity and perception or behaviour. The relations cannot be known before the neural codes for perception are discovered.

G. Melvill Jones. Early in the design of these experiments we were fortunate to have Ivo Kohler visit our laboratory and hence had the privilege of being made aware at first hand of the observations quoted by Dr Gregory. However, as Dr Kohler was quick to concede, it is important to discriminate between subjective phenomena associated with conscious perception and objective sensory-motor reflexes acting at a subconscious, involuntary, level. The experiments described in the present communication specifically concentrated on *one measurable brainstem sensory-motor reflex* in a paradigm deemed likely to uncover an otherwise covert potential for its plastic modifiability. Seen in this context the systematic nature of the changes observed encouraged the search for a simple but plausible explanation using contemporary knowledge of relevant neural pathways and their known physiological characteristics. Bearing in mind the extensive contemporary literature demonstrating that synaptic modifiability is ubiquitous throughout the nervous system (see, for example, Schmitt *et al.* 1976) it seemed reasonable to offer the interim working hypothesis as summarized in figure 9, despite its inclusion of synaptic modifiability. Of course, as emphasized before, this is viewed as no more than a 'stepping stone' and no doubt much more is really at play; perhaps for example the ability to make sudden 'switches' along the lines suggested by Dr Gregory's speculative comments. It would however seem hard to imagine that sudden switching could alone account for smooth, gradual adaptive changes of the kind realized in the present experimental findings of figures 3, 4 and 7, and idealized from recorded data as in figure 10.

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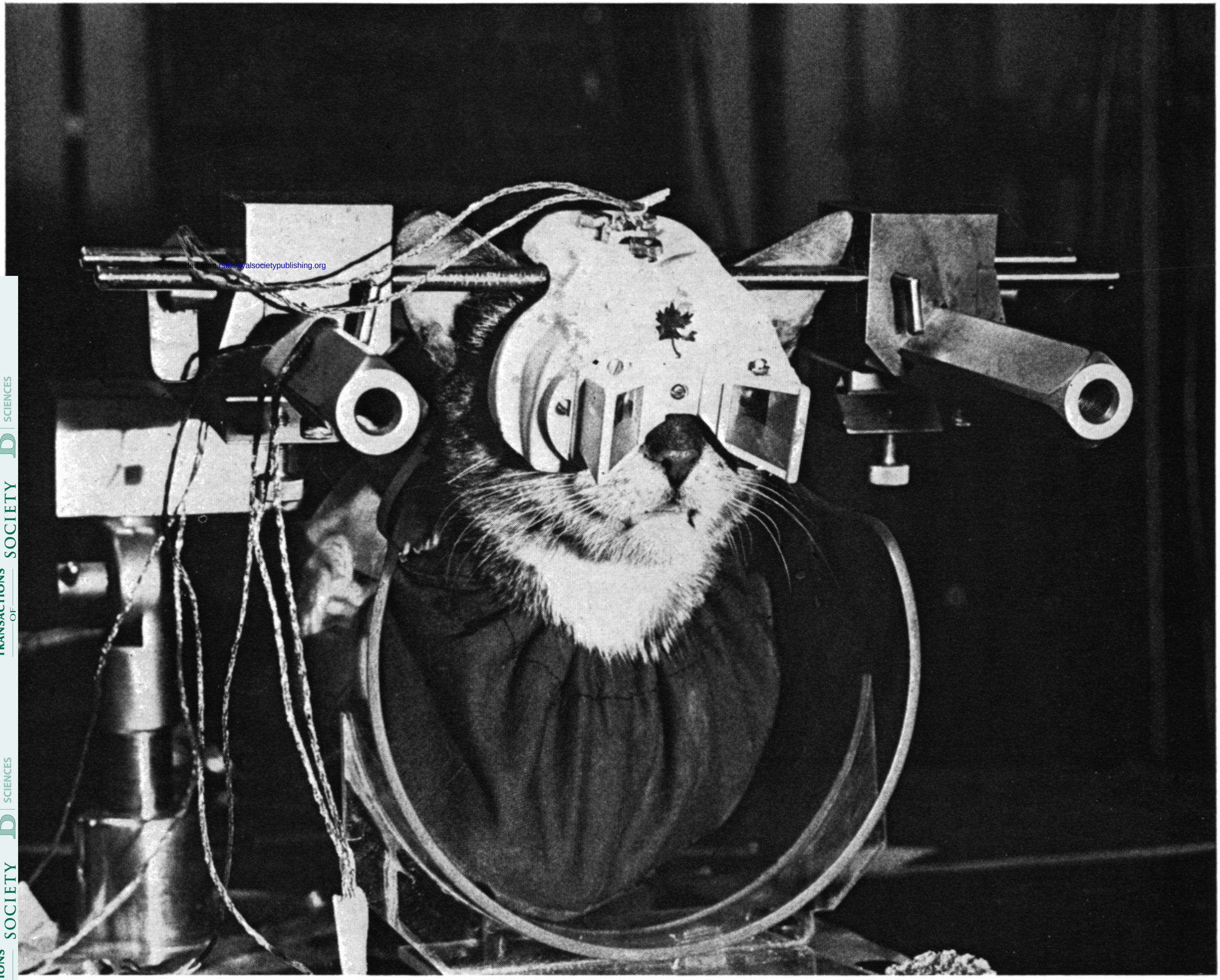

FIGURE 6. The chronic animal preparation wearing the prism-carrying mask with the head stereotaxically fixed to the turntable by means of an acrylic block fixed to the skull. The electrical leads are plugged into outlets from implanted d.c. electro-oculographic electrodes. (Photograph by Olga Panyszak)

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