SENSORY INTERACTIONS IN BALANCE AND EYE MOVEMENT CONTROL

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ABSTRACT

Eye and head movements were recorded during angular/linear motion of the head or neck. Four areas of sensory-motor interaction in human balance control were studied.

In the **cervico-vestibular** section, eye movements elicited by neck torsion were shown to be weak in normal subjects but considerably enhanced in labyrinthine defective patients, in whom they may partly compensate for the lack of the vestibulo-ocular reflex.

In the **vestibulo-cervical** section, experiments showed a diminished ability of patients with absent vestibular function to stabilize the head in space during trunk motion. Other experiments found vestibular abnormalities in patients with cervical dystonia (Spasmodic Torticollis) which could not be explained by the abnormal head posture per se; it was concluded that the vestibular system contributes to human head posture and that the hitherto unexplained neural processes provoking Spasmodic Torticollis interfere with vestibular signals.

Under the **otolith-canal** interaction section, experiments showed that slow phase eye movements of high velocity can be elicited in response to combined angular-linear acceleration, obtained by placing the head eccentrically in an ordinary "Barany" rotating chair. The possibility that the procedure could become a clinically useful test of otolith function was preliminary studied in oto-neurological patients.

The section on **otolith-visual** interaction examines slow phase eye movements in response to lateral linear acceleration of the head. In the presence of visual fixation these responses are strong and compensate for head motion at very short latency, allowing the eyes to maintain fixation on stationary objects. In the dark responses are weak and inappropriate for visual stabilization. The experiments combining angular acceleration or

visual stimulation with linear acceleration suggest that, in order to generate functionally meaningful eye movements, otolith-ocular responses are highly dependent on interaction with other sensory stimuli.

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PREFACE

The work presented in this thesis could not have been achieved without the help and support of many people and institutions with a common interest in understanding normal and abnormal balance mechanisms; detailed and much deserved gratitude cannot be expressed in a short preface so that a special acknowledgement section has been included.

Most of the work included was being published in specialized journals as the various steps in the research programm were being completed; those papers are an integral part of this thesis and are presented as apendices at the end of this volume. However, it is only now, when the different chapters are presented together, that the author's original intention of exploring some relatively neglected areas of sensory interaction in balance control consolidates and becomes meaningful. The General Introduction tries, above all, to recreate that sense of unity in the work and make a case for the need of studies concerning the interaction amongst different sensory inputs contributing to balance and eye movement control. Chapters I to IV deal with the specific experimental work which constitutes the main body of the thesis; however, each particular experiment will be much more meaningful if the general sense of unity inspiring the work is kept alive in our minds.

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GENERAL INTRODUCTION

Traditionally, the sense of balance has been linked to the vestibular receptors housed in the labyrinth, the semicircular canals and the otolith organs the saccule and the utricule. This emphasis is reflected in the fact that a disproportionate amount of balance research has been concerned exclusively with semicircular canal function and to a lesser extent that of otolith function. Furthermore, in the examination of the vertiginous or unsteady patient there has been an assumption that adequate measures of disorder may be derived from caloric or rotational tests which are confined to the activity of the lateral semicircular canals. Not infrequently, however, the results of these tests are normal suggesting that the cause of the balance problem may lie elsewhere (Brandt and Daroff, 1980; Hood, 1986).

Control of balance and, in fact, that of eye movements depends on sensory information provided not only by the vestibular receptors but also on proprioceptive and visual signals. The information provided by these senses summates at various levels in the central nervous system so that a multi-sensory representation of the dynamic relation between head, eyes and body position and gravitational and spatial coordinates is achieved (Dichgans et al, 1973; Henn et al, 1974; Buttner and Buettner, 1978; Wilson et al, 1975; Precht, 1976; Peterson et al, 1981; Mergner et al, 1981). This interaction amongst various sensory inputs subserves higher order perceptual functions, such as spatial orientation, and it also generates motor responses stabilising the head and body in space, in the case of the postural system, and stabilising images on the retina, in the case of the ocular-motor system. With certain notable exceptions, namely the work of such classic authors as Magnus and De Klejn (Magnus, 1924), little consideration has been given in the

past to the role played by non-vestibular information in normal and abnormal balance control.

The convergence of these various sensory signals at various levels of the neural axis, however, can hardly be unexpected since multisensory stimulation is the rule during natural interaction of any animal with the environment. Normal head movements, for example, activate the semicircular canals but, in addition, there is simultaneous stimulation of neck proprioceptive and visual afferents. Concurrent input from the otolith organs, signalling translational components during head motion, may also be present. The addition of the cervical, visual and/or otolith signals may have significant effects on the ocular response originating from the canals and, conceivably, this might also be different in health or disease. These and other aspects of sensory interaction in human balance control have been the primary concern of the studies described in this thesis.

In more recent years the topic has attracted increasing attention. The demonstration, for example, that the vestibular-ocular reflex (VOR) is not subserved by rigidly wired connections, but rather by a plastic, modifiable system has had considerable impact (Melvill Jones, 1985). In normal circumstances, the VOR generates eye movements in the opposite direction to those of the head with a gain close to unity (gain= peak eye velocity/peak head velocity), which allows for clear vision during head movements. However, long term exposure to telescopic or optically reversing goggles has shown that the output of the VOR can be dramatically changed (Gonshor and Melvill Jones, 1971; 1976). The nature of this change is adaptive to the new situation in that if the subject wears magnifying glasses (which would require more compensatory eye movement for the same head movement) the gain of the VOR increases and viceversa. Clearly, visual information (in this example

slippage of images on the retina during head movements) is able to modify the efficiency of the vestibular system and considerable effort has been devoted in an attempt to identify the structures and/or mechanisms responsible for its development (Robinson, 1976; reviewed in Miles and Lisberger, 1981).

Other plastic changes recently described involve the neck-eye loop. In the normal monkey, eye movements elicited by cervical stimulation (cervico-ocular reflex, COR) are negligible but, following bilateral labyrinthectomy, gradually become more powerful and generate significant compensatory eye movements during normal head motion (Dichgans et al, 1973). Although this finding has subsequently been confirmed in the cat (Baker et al, 1982) doubts remain about its occurrence in man and on the functional significance of the COR in the compensation process of patients with loss of vestibular function. Chapter I in this thesis, on Cervico-Vestibular Interaction, will describe experiments aimed at clarifying the development and possible role of plastic changes in the COR after bilateral vestibular loss, a matter which clearly has theoretical as well as clinical implications.

Related to the problem of how the vestibular system modifies the cervico-ocular loop is the question of vestibular influence upon neck tonus and head movement. In animals, stimulation of the vestibular end-organ elicits not only ocular reactions but also postural adjustments, particularly of the neck, which contribute to maintain head stability (reviewed in Wilson and Melvill Jones, 1979). Although there have been some indications that this might also be the case in humans, the matter deserves further investigation particularly in the clinical context. A particular case in point is that of spasmodic torticollis, a neurological disorder characterised by abnormal head posture in which a "vestibular hypothesis" as to its origin has been formulated as early as 1929 (Barre, 1929), but never re-examined with modern

techniques of vestibular research. In chapter II, on Vestibulo-Cervical Interaction, the results of experiments assessing head stability in patients with absent vestibular function will be described. This will be followed by a quantitative assessment of vestibulo-ocular and vestibulo-spinal function in patients with spasmodic torticollis.

In chapter III experiments carried out to assess the effect of interactive semicircular canal-otolith stimulation on eye movements compensatory to head motion will be presented. The influence of the otoliths in generating slow phase eye movements during combined linear and angular stimuli has been demonstrated in the past by rotating subjects around the longitudinal axis of the body at an angle of either 90° ("barbecue-spit rotation") or less ("vertical off-axis rotation") with respect to the gravity vector (reviewed in Benson, 1974 and Barnes, 1980). However, such paradigms involve prolonged rotation at constant angular velocity whereas it was felt that a study combining otolith-canal interaction during transient head motion, such as those more likely to be encountered during every day life, was needed.

Interaction of visual and vestibular signals has been one of the most fruitful areas of eye movement research in recent years (reviewed in Henn et al, 1980). Vestibularly and visually elicited slow phase eye movements are in continuous interaction as illustrated by the fact that, in combination, they provide near perfect retinal stability during the whole range of normal head movements: the relatively poor response of the VOR at low frequencies of rotation finds a perfect complement in the optokinetic system, the optimun efficiency of which is precisely at low frequencies. Further need of visuo-vestibular interdependence arises as a result of the fact that the axis of rotation of the eyes and head are not coincident. This anatomical fact

dictates that the angle which the eyes will have to travel in the orbit during natural head turns will depend not only on the angle travelled by the head but also on the distance from the eye to the object of interest (Collewijn et al, 1982). Such information, of course, can only be specified by the visual system. However, the particular area of visuo-vestibular interaction which has had a more direct impact at the clinical level is that of VOR suppression. The integrity of VOR suppression mechanisms, which allow a subject to fixate an object which rotates together with his head by cancelling vestibular eye movements, is now routinely assessed in eye movement and balance clinics and has considerable value in the differential diagnosis of central and peripheral vestibular lesions (Hood and Korres, 1979; Halmagyi and Gresty, 1979).

For various reasons (not least the considerable technical problem of generating controlled linear acceleration), however, the study of visuo-vestibular interaction in the otolith system has been neglected in spite of the fact that simple geometrical considerations would indicate that the otolith-ocular reflex might be profoundly affected by visual input (Barnes, 1980). Since parallel lines meet at infinity, compensatory eye movements in response to linear head displacements are only necessary whilst viewing a nearby object but not whilst fixating a target in the distance. Clinical observations on the enhancing effect of near vision and convergence on some otolith related (tilt sensitive) nystagmus also supports this view (Fisher et al, 1983). In chapter IV, on Otolith-Visual Interaction, eye movements in response to linear acceleration in the dark and in the presence of visual fixation of nearby targets will be reported. Also, in chapters III and IV, an effort will be made to develop the experimental situations used, into tests of clinical function of the otolith.

This thesis was to some extent inspired by the difficulties in understanding the patient with unsteadiness and by the paucity of test procedures capable of providing information on non-semicircular canal aspects of balance control. The aim of this thesis has been to attempt some form of integration of at least some of the many facets of balance control outlined above. In general terms the thesis will explore the following:

i) ways in which ocular responses from different sensory origins interact with each other (eg otolith function in the absence/presence of concurrent visual stimulation, chapter IV; semicircular canal function in the presence/absence of concurrent otolith stimulation, chapter III),

ii) clinical conditions in which primary involvement of a sensory-motor set leads to secondary changes in others (eg cervico-proprioceptive control of eye movements in patients with absent vestibular function, chapter I),

iii) postural mechanisms in cases of abnormal sensory input (vestibular control of head posture, chapter II).

The different areas covered in this thesis are cervico-vestibular and vestibulo-cervical interaction, otolith-canal interaction and otolith-visual interaction. For convenience, more detailed consideration and review of these topics will be given by way of introduction to the relevant chapter, together with the experimental strategy adopted.

CHAPTER I

CERVICO-VESTIBULAR INTERACTION

REVIEW AND INTRODUCTION

In the course of most natural head movements, the head moves with respect to the trunk so stimulating vestibular and cervical receptors simultaneously. It has long been known that these sensory signals interact during stabilisation of posture and gaze and this is reflected in the fact that there are numerous anatomical sites in the CNS where convergence between neck and vestibular signals occur (see references below).

The nuchal sensory input relevant to balance control originates in the first three cervical segments (McCouch et al, 1951). Experimental damage or anaesthesia to the dorsal roots in these segments lead to gait disturbance, ataxia and, less consistently, nystagmus in several species (Cohen, 1961; Biemond and de Jong, 1969; de Jong et al, 1977). The cervical muscles are rich in spindles and these have an unusually complex organization, with two to six spindles linked in tandem and parallel groupings (Richmonds and Adams, 1979). Although no definitive explanation for this particular organization has been given, it is known that the spindle high density does not occur as a compensation for a difference in transductive function: the basic properties and dynamic indices for neck primary and secondary endings are similar to those found in spindles elsewhere (Richmonds and Abrahams, 1979). It is believed that the relative importance of the main muscle mass in generating tonic neck reflexes is less than that of the tissue close to intervertebral joints (McCouch et al, 1951), which consists of connective tissue and short muscles. Golgi tendon organs are also numerous in neck perivertebral muscles.

At least three neural structures show significant cervico-vestibular modulation: the vestibular nuclei, the cerebellum and the cerebral cortex. Perhaps the primary and most important site for such neural convergence is the vestibular nucleus where vestibulo-spinal neurons are strongly modulated by neck stimulation. Static (otolith) units have been shown to summate linearly with neck input during lateral tilt (Boyle and Pompeiano, 1981). During dynamic conditions, both the labyrinthine and the cervical input encode angular velocity signals (Rubin et al, 1975; Anastasopoulus and Mergner, 1982), with some vestibular nucleus units showing a synergistic pattern of interaction whereas in others this interaction is antagonistic.

Presumed or positively identified vestibulo-ocular units with cervical modulation are less numerous and display a much weaker sensitivity to neck stimulation than vestibulo-spinal neurons (Rubin et al, 1977; Anastasopoulus and Mergner, 1982). A short latency route (less than 3 ms) from cervical dorsal roots to vestibular neurones projecting to the abducens nucleus has been demonstrated in electrical stimulation experiments (Hikosaka and Maeda, 1973), however, the type of signals travelling in this fast pathway during natural neck stimulation is not known.

The areas of the cerebellum of significance in balance control are the vestibulo-cerebellum, involved in the generation and control of slow phase eye movements, and the vermis-anterior lobe, which participates in vestibulo-spinal control (Ito, 1974). Both of these areas receive projections from vestibular and cervical receptors. Vestibular signals to the vestibulo-cerebellum are carried both by mossy and climbing fibers and they comprise primary and secondary vestibular fibres (Precht, 1976). Interestingly, a large proportion of Purkinje cells are sensitive to rotation in more than one axis, inputs arising from several canals and the otolith receptors (Blanks et al, 1975a,b). Nuchal input reaches the vestibulo-cerebellum via mossy and

climbing fibers, at latencies of 3 and 8-10 ms, respectively (Wilson et al, 1975). Cervico-vestibular convergence in the vermal cortex, particularly the anterior lobe (lobe V), has been demonstrated for undefined units recruited by electrical stimulation of the vestibular nerve (Bertholz and Llinas, 1974) and for static (macular) units (Denoth et al, 1979). The cervical input reaches the vermal cortex at a latency of 8 ms (mossy fibers) and 20 ms (climbing fibers). Since this area of the cerebellum does not receive primary or secondary vestibular fibers, it is believed that vestibular signals found here are relayed from reticular structures such as the lateral reticular and pontine tegmental nuclei (Ladpli and Brodal, 1968; Bertholz and Llinas, 1974).

Single units studies in the anterior suprasylvian cortex of the cat have shown that essentially the same type of interaction present in the vestibular nuclei, ie velocity coded vestibular and cervical signals with both substractive and additive patterns, is present at the cortical level (Becker et al, 1979). It is believed that this cortical representation of neck-vestibular interaction underlies conscious perception of trunk and head rotation (Mergner et al, 1981; 1983).

One of the functions of the cervical input is to inform about the relative position of the head with respect to the trunk and, thereby, about the location of visual objects with respect to body-centred spatial coordinates (Mergner et al, 1981; 1983; Biguer et al, 1988). In animals, cervical proprioceptors are an important source of postural reflexes acting on the neck and the limbs, aiding the orientation of the head with respect to the trunk and the limbs with respect to the head (Magnus,1924; Roberts, 1978; Wilson, 1984). In humans these so called "tonic neck reflexes" are not easily obtainable except in the infant during the first weeks of life and in some patients with decerebrate rigidity. Recent studies seem to show a modest

modulation of EMG activity in the limbs related to neck position or stimulation in normal subjects (Nashner and Wolfson, 1974; Rossi et al, 1987; Aiello et al, 1988); however its functional significance is not clear. Additionally in animals, specially those with laterally placed eyes, neck stimulation is able to generate eye movements of sufficient magnitude to complement the role of vestibular and visually elicited eye movements in gaze control (Magnus, 1924; de Kleyn, 1918; 1922; Suzuki, 1972; Gresty, 1976; Fuller, 1980). As it will be described in more detail in the following section, this has not yet been definitely established in man.

THE CERVICO-OCULAR REFLEX IN NORMAL SUBJECTS AND IN PATIENTS WITH ABSENT VESTIBULAR FUNCTION

Most active head movements occurring in every-day life are step or ramp movements, normally associated with eye movements as part of a strategy designed to shift gaze in space in response to visual (Bizzi et al, 1971) or auditory stimuli (Whittington et al, 1981). This type of eye-head co-ordination consists of an initial fast offset of the eyes in the direction of the object of interest (refoveating saccade), followed, after a few milliseconds, by a head movement in the same direction. During this head movement fixation upon the target is supported by the vestibulo-ocular reflex (VOR), which induces a compensatory slow eye movement in the opposite direction to that of the head. Although the initial anticompensatory saccade was originally thought to be visually elicited there have been more recent suggestions that, at least in certain circumstances, it may be generated by way of the VOR (Barnes, 1979; Roucoux et al, 1981) its function being to contribute to target acquisition in the direction of the ongoing head movement.

Patients with absent vestibular function typically suffer from imbalance and oscillopsia. The latter results from loss of the VOR and manifests itself as a disturbing illusion of movement of the environment (Bender, 1965). Some patients, however, are much less disabled than others and this can be attributed to the development of a number of compensatory mechanisms which take over the stabilizing role of the slow component of the VOR (Kasai and Zee, 1978). Prominent among these is the cervico-ocular reflex (COR) which, although virtually non-existent in normal monkeys, has been shown in labyrinthectomized animals to become increasingly instrumental in restoring the slow compensatory eye movements which accompany active head movements

(Dichgans et al, 1973). To date, however, information is lacking on the relevance of these findings to the possible role the COR might play in other circumstances such as gaze transference.

The existence of a COR in man has been recognized since Barany's early observations (Barany, 1918) but its function remains a matter of some controversy. This may be attributed in part to the technical difficulty of examining the reflex in isolation which involves restraining the head in space while rotating the trunk. Surprisingly, the limited studies available using this technique have, without exception, been confined to the effects of sinusoidal trunk rotation. This selective interest in the dynamic components of the COR contrasts with the early observations of Barany (1906; 1918), Magnus (1924), DeKleyn (1918), and Frenzel (1928) who invariably included investigations searching for tonic deviation of the eyes on sustained neck torsion.

The results of recent studies of the neck-eye reflexes in humans with absent vestibular function are by no means as clear cut as those in the monkey. Only one of two patients studied by Barnes (1979) had an enhanced COR and although three cases presented by Kasai and Zee (1978) were reported to have increased COR gain, normative data were not available. By contrast, a later study of five normal subjects and five patients with absent vestibular function concluded that the latter had normal neck-eye reflexes and that the COR did not seem to compensate for loss of labyrinthine function (Leopold et al, 1983).

The issues involved are clearly of clinical and theoretical importance which calls for further clarification. In the investigation to be described in this section the COR has been studied in 12 patients with absent labyrinthine function and in 13 normal subjects. The more general issues involved in this research relate to the interaction between the neck

proprioceptive input and the VOR. The first section will describe the type of eye movements elicited by cervical stimulation in normal subjects and in patients with absent vestibular function, and whether they may contribute to the compensatory and "anticompensatory" function of the VOR. Specific questions addressed are: (a) Does a tonic component of the COR make any contribution to the maintenance of eccentric gaze? (b) Is the COR enhanced in patients with absent vestibular function? (c) What is the COR influence in target acquisition and retention during head movements?. In the second section the interaction between cervical and visuo-motor reflexes in a group of patients with oscillopsia due to absent vestibular function will be investigated, in order to try to identify factors which might underly a better clinical compensation in some of the patients.

MATERIALS AND METHODS:

Eye movement recordings: In these and all other experiments in this thesis, eye movements were recorded with standard, direct current (DC) electro-oculography (EOG) after the subjects had been adapted to the dimly lit room for at least 15 min. The electrodes consisted of a disc of pure silver embedded in an epoxy resin (Araldite) cup. The electrode surface was chlorided in order to avoid polarization and contact with the skin was made by way of electrode jelly placed in the electrode cup. The skin was first cleaned with an electrode jelly containing a mildly abrasive substance in order to reduce skin resistance and electrodes were held in place with surgical sticky tape. Usually the two eyes were recorded together as a "cyclopean eye" with electrodes placed on the outer canthi. Exceptionally, in subjects with strabismus, monocular recordings were obtained, with electrodes placed on the outer and internal canthi. With this technique drift of the eye

position trace was minimal and resolution was approximately 1o. The bandwith of the system was at least up to 70 Hz and the eye position output was linear up to +/- 30°. Calibration signals were obtained by asking subjects to fixate on targets 10 to 30° apart in the horizontal plane.

Rotating chair: In these and all experiments in which angular motion of the trunk or of the whole body was required, the subjects sat on a "Barany chair" mounted on a silent, velocity servo-controlled, torque motor (80 ft/pound; Contraves-Goerz Inc.). The chair was fitted with restraining pads for the legs and hips as well as an occipital head rest and a bi-auricular head clamp. Chair velocity was transduced by a tachometer and, when angular chair position was required, electronic integration was available.

Patients: Twelve patients aged 22-73 years and 13 normal subjects aged 24-60 years were studied. The patients had either absent or grossly reduced nystagmic reactions to caloric tests with water at 30°C, and 44°C and occasionally 20° in the light and dark and to impulsive rotation of at least 60°/s in the dark. They had sought medical advice because of variable degrees and combinations of deafness, tinnitus, oscillopsia, imbalance and dizziness. In 8 cases ototoxicity by aminoglycoside antibiotics was the certain or possible cause, alone or in combination with meningitis (3 cases). One patient had Von Recklinghausen's disease with bilateral VIIIth nerve neuromas and another had lost VIIIth nerve function during a sub-acute illness with uveitis and skin lesion, thought to be Vogt-Kyanagi-Harada disease. In two patients with markedly reduced vestibular response no cause was found. The duration of loss of vestibular function ranged between 5 months and 30 years. All the experiments to be described were carried out in total darkness.

Studies with head fixed in space:

In order to examine the role of the neck reflexes in isolation it is

necessary to rotate the trunk while maintaining the head immobile. The subjects sat in the rotating chair which, for safety, was moved manually and were required to bite on a dental plate attached to a rigid frame mounted on the wall. A closed circuit TV display using an infrared camera directed at the subject's head testified to the absence of any inadvertant head movement. Some subjects who experienced difficulty because of dental prosthesis were assisted manually. Following preliminary trials during which the subjects were encouraged to relax their neck muscles few problems were encountered. In the following it is convenient to refer to these as trunk on head movement.

Ramp stimulation - trunk on head. In the case of ramp displacement stimuli the chair was moved randomly from left to right or vice versa over varying angular displacements between 10 and 50° at peak velocities ranging between 10 and 20°/s. A target light mounted in line with primary gaze was presented about 2-8 s following the termination of each discrete trunk movement. In this way it was possible to measure any residual deviation of the eyes from the primary position of gaze. All the subjects were required to fixate the target when it was switched on, but, in complementary experiments, some subjects were instructed to look straight ahead during the trunk movement, as if the target light was on all the time (imaginary target). This imagery task was always performed following the routine test and did not affect the subjects' ability to maintain their neck muscles relaxed.

Sinsuoidal stimulation - trunk on head. Sinusoidal trunk on head movements were applied manually over a range of frequencies from 0.07 to 0.4 Hz with amplitudes of approximately +/- 25° and peak velocities ranging between 10 and 50°/s. Additionally, a 0.3 Hz stimulus (in synchrony with a metronome) with an amplitude of about +/- 25° and peak velocity of approximately 45°/s was also applied. Repeated enquiry was made as to the subjects' ease and, if any discomfort developed, the highest frequencies were not used.

Studies with head free:

Ramp stimulation - head on trunk. By way of comparison the effect of neck torsion during active head movements (head on trunk) was also studied. For this purpose the subjects wore a light helmet connected to a low torque potentiometer which monitored horizontal head position. To its front was attached a 50 cm long rigid rod with a target light attached to its distal end which moved with the subject's head. Subjects were instructed to make discrete random head movements to the right and left over variable amplitudes. About 2-8 s following the termination of each movement the head-coupled target light was lit so that, following refixation, measurements could be made of any residual deviation of the eyes from the primary position of gaze. Additionally, in the case of the patients, in order to exclude any role played by volition, rapid ramp angular displacements of the head were passively and unpredictably deliverred by the experimenter in darkness. The head and the helmet were securely and firmly held by the experimenter in order to avoid any inadvertant slippage during the execution of this manoeuvre.

Adopting the same experimental set-up, target seeking strategies were also examined by requiring the subjects to look, using eye and head movements, at target lights presented randomly on a tangent screen 1.5 m to the front and covering visual angles between +/- 10 and +/- 50^{o}.

Sinusoidal stimulation - head on trunk. As a counterpart to the studies of sinusoidal trunk on head movements, sinusoidal head on trunk movements were studied by asking the subjects to move their head from side to side at a frequency of 0.3 Hz in time with a metronome over amplitudes of approximately +/- 25^{o}. Most subjects were guided manually by the experimenter in order to induce smooth movements. In the circumstances it cannot be claimed that these head movements were exclusively active or passive. Eight patients undertook this test, the two with some residual vestibular function being excluded.

Nine normal subjects served as controls.

In addition to the above studies the VOR in darkness was recorded in the same 9 normal subjects in response to whole body (i.e. trunk with head) sinusoidal oscillation at 0.3 Hz over $\pm$ 25° while they were performing mental arithmetic. In order to exclude any interference from the COR their heads were rigidly clamped to the chair. As an additional enquiry of the influence of neck torsion upon the VOR three normal subjects were rotated sinusoidally with their heads turned as far as comfortably possible (usually about 75°) to the left, care being taken to ensure that their eyes were in the primary position of gaze before the chair started to oscillate.

Chair, helmet and eye position, together with a target light signal, were displayed on an ink jet recorder (ELEMA Mingograph).

Data Analysis:

For the ramp tests (trunk on head and head on trunk) the amplitude of the residual eye deviation was plotted against the angle of neck torsion and a regression line fitted to the data, usually comprising some 15 measurements. The slope of the line will be referred to as amplitude gain.

Velocity gain is defined as the ratio between peak slow component velocity of nystagmus and either trunk or head movement peak velocity for both ramp and siusoidal tests. Gaze shift amplitude gain was taken as the ratio between peak eye displacement and peak trunk displacement, during sinusoidal COR. The recordings were analyzed by hand. In the case of sinusoidal stimuli, measurements were carried out over 20-30 s periods which included 2 and 8 cycles, respectively, of the lowest and highest frequencies.

RESULTS:

Studies with head fixed in space

Ramp stimulation - trunk on head. In normal subjects trunk movement initiated a somewhat irregular combination of fast and slow eye movements. In 9 of the

13 subjects the saccadic movements were predominantly in the direction of the head movement relative to the trunk while in 4 they were in the opposite direction. Slow phases were generally weak and ill-defined and irregular in direction. In no instances was a regular pattern of vestibular-type nystagmus detected. Presentation of the target light at the termination of trunk movement revealed a persistent or residual deviation of the eyes from primary gaze (Figure 1). In 5 subjects it was in the same direction of the relative head movement and in 8 subjects in the opposite.

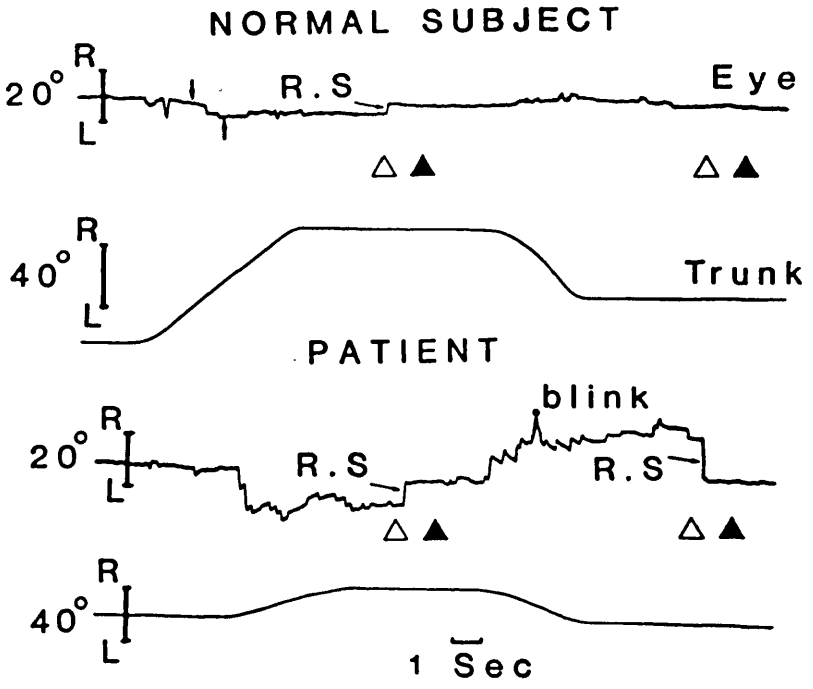


Figure 1. Eye movements elicited during ramp trunk displacement with the head fixed. Normal subject: during rotation to the right (R) (relative head movement to left), very weak slow eye movements were elicited, which changed direction (vertical arrows) during the course of the stimulus. A small residual eye deviation to the left (L) persisted for several seconds at the termination of movement as is evident from the recentering saccade (RS) required to bring the eyes on to the target light (open triangle). Closed triangles indicate target light off. Rotation in the opposite direction elicited equally irregular but weaker response. Patient: trunk rotation from centre to right and vice versa induced marked nystagmus and gaze shift in the direction of the relative head movement. The residual eye deviation persisted until its cancellation by presentation of the target light.

The VOR elicited in darkness has been shown to be markedly modified by

requiring subjects to fixate upon an imaginary earth-fixed target (Barr et al, 1976; Takahashi et al, 1980). Interestingly, a similar modification can be demonstrated with the COR. Thus, 3 subjects, two of whom had consistently deviated in the direction of the relative head movement, were instructed to imagine a visual target to their front. Under these circumstances saccadic activity was reduced and the eyes executed low velocity slow-phase movements mainly in a direction opposite to that of the neck torsion.

In the lower tracing of Figure 1 is shown a response to trunk on head ramp movement highly characteristic of the patients with absent vestibular function. The striking feature is the appearance of a saw-tooth nystagmus during trunk movement with the fast component beating in the direction of the relative head movement. The effect of imagining a fixed target in the case of a patient is shown in Figure 2. This procedure resulted in a marked suppression of fast phases and the eyes deviated in a direction opposite to the relative head movement. Visual fixation abolished all eye movements elicited by neck torsion in normal subjects and patients.

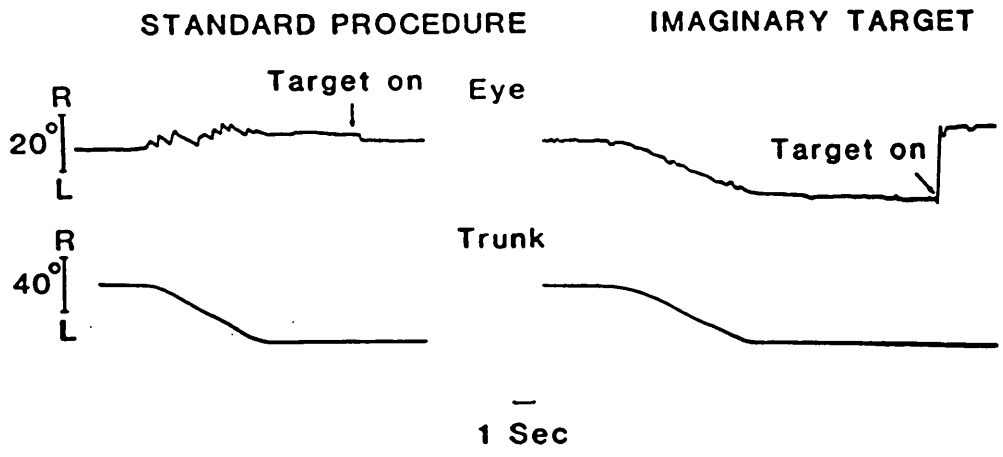


Figure 2. Effect of instruction to a patient upon eye movements elicited during trunk ramp displacement with head fixed. In the standard procedure the subject was required to look at the target when presented. With imaginary target the patient was instructed to look straight ahead "as if the target light was on all the time".

The results shown in Figure 3 illustrate the typical relationship between amplitude of trunk rotation and residual eye deviation in one normal subject and one patient in whom the deviation was in the same direction as the relative head movement. Findings in respect of patients and normal subjects are summarized in Table 1 where it will be seen that the amplitude gain (slope) of the former is almost 3 times that of the latter. In 8 out of 12 patients the residual eye deviation was in the direction of the relative head movement due to a prevalence of quick over slow eye movement components.

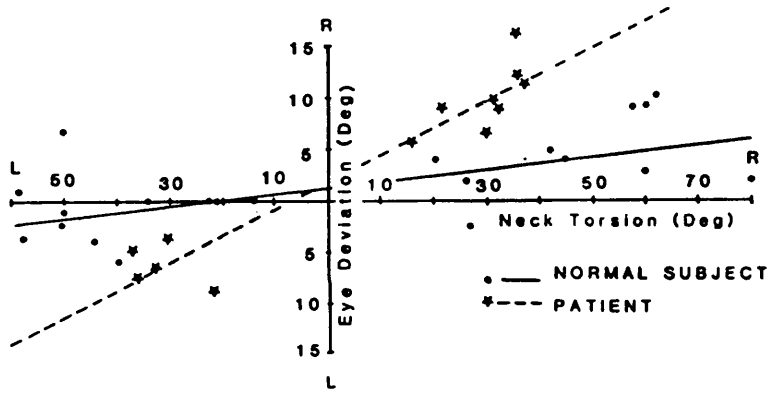


Figure 3. Relationship between amplitude of residual eye deviation and neck torsion angle following ramp trunk displacement with the head fixed. Slopes (amplitude gain) of the regression lines; normal subject, 0.05; patient 0.26.

TABLE 1

Results of ramp trunk on head stimulation

	Amplitude gain (slope)	Symmetry of response (y intercept)	Cases showing anti-compensatory responses[a]	Velocity gain
Normal controls	0.06(SD 0.03)	0.98(SD 0.98)	38%	0.05(SD 0.07)
Patients	0.16(SD 0.11)	3.84(SD 2.64)	66%	0.51(SD 0.26)

a: Residual eye deviation in the direction of the relative head motion.

In order to establish whether the residual eye deviation was a function of a tonic or dynamic neck input some subjects, following the initial target fixation, were kept in total darkness with neck torsion sustained before the target was re-presented. Under these circumstances in neither the patients nor the normal subjects did the residual deviation reappear once it had been cancelled by the previous target presentation. It follows, contrary to the expectation which motivated the design of the experiment, that the residual eye deviation is a balance of activity dynamically induced during trunk movement and not a manifestation of neck tonus. This is further supported by the fact that trunk movements from centre to lateral positions or from excentric to centre positions were equally effective in inducing eye deviation; an example of the latter is shown in the recording of the patient in Figure 1.

Sinusoidal stimulation - trunk on head. As with the ramp stimuli, marked differences were apparent in the responses of normal subjects and patients to sinusoidal trunk movement as exemplified in Figure 4. Whereas in the former

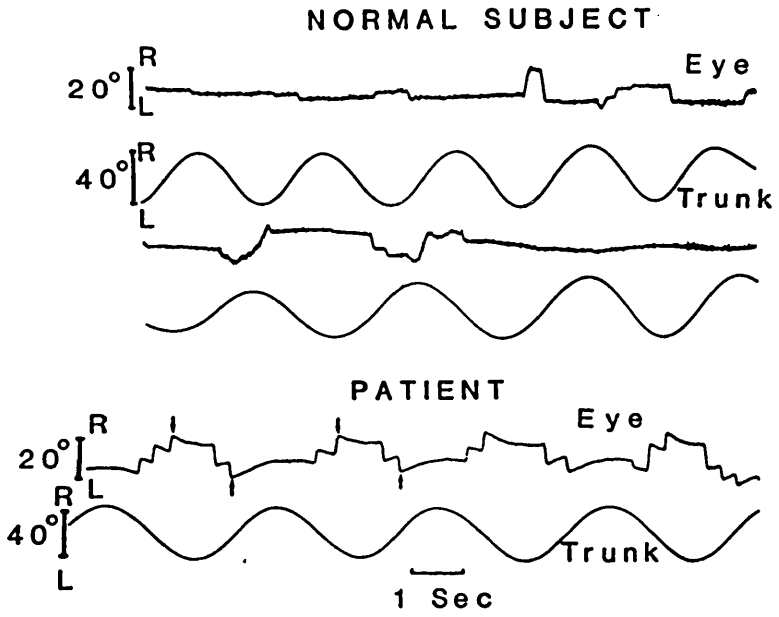


Figure 4. Sinusoidal trunk displacement with the head fixed. A consistent nystagmus pattern is apparent only in the patient. Slow components are opposite in direction to and approximately in phase with relative head movement. Peak gaze displacements, brought about by saccadic components and indicated by arrows, are in the direction of relative head motion, 90° phase-advanced.

eye movements were feeble, variable in direction and frequently difficult to correlate with the stimulus, in the patients the slow phase eye movements were always clearly identifiable as compensatory insofar as they were consistently in a direction opposite to that of the relative head movement.

In Figure 5 is shown the velocity gain of the COR in 9 patients successfully studied over a range of frequencies and of 5 normal controls from whom reliable responses were elicited. The remaining patients were incompletely studied but they also manifested a hyperactive COR at the frequencies tested. The velocity gain of the reflex consistently decayed with increase in stimulus frequency.

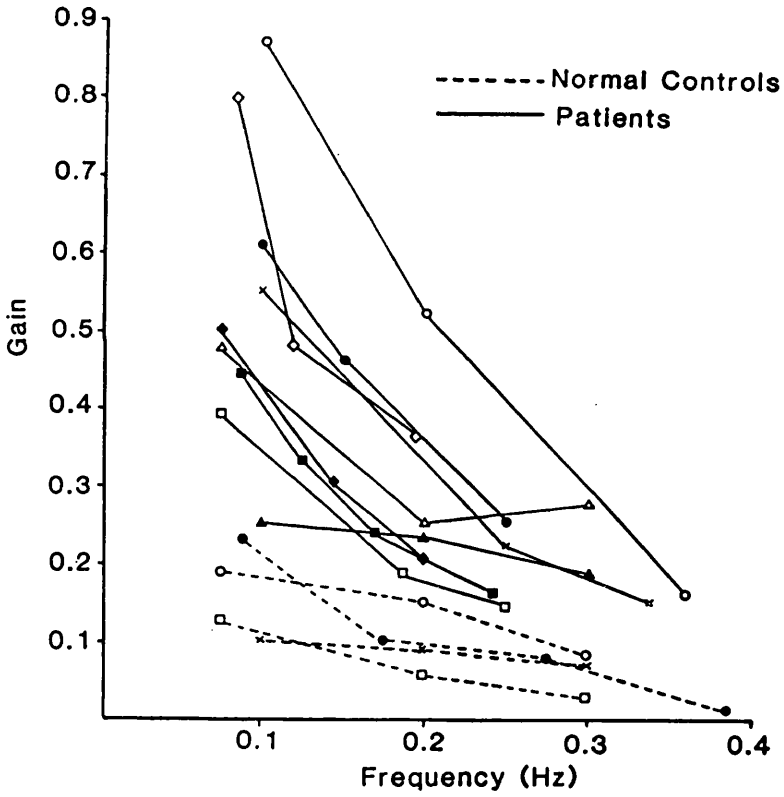


Figure 5. COR velocity gain (peak slow-phase eye velocity/peak trunk velocity) during sinusoidal stimulation. Individual data on 9 patients and 5 normal subjects.

Gaze shift amplitude gain was slightly increased in the patients (Mann-Whitney test; Z = 1.97, P = 0.05) but was not consistently related to frequency of stimulation, and considerable variation was present in both groups (Table 2).

TABLE 2

Gaze shift amplitude gain during sinusoidal COR (median and range)

	0.1 Hz	0.2 Hz	0.3 Hz
Normal controls	0.14 (0.09-0.63)	0.18 (0.10-0.60)	0.17 (0.03-0.60)
Patients	0.32 (0.15-0.54	0.23 (0.13-0.50)	0.26 (0.10-0.42)

This gaze shift, which occurred in the direction of the relative head movement in both groups, was brought about by saccadic components. In the case of the normal subjects, however, gaze shifts had variable phase relationships and lagged the stimulus by $32^{o} \pm 48$ (SD). By contrast, in the case of the patients it occurred characteristically 90^{o} in advance of trunk displacement, i.e. at zero trunk displacement and maximum stimulus velocity presumably triggered by acceleration (Figure 4).

Studies with head free:

Ramp stimulation - head on trunk. The pattern of eye movements evoked by active head turning in the dark was remarkably similar in both normal subjects and patients (Figure 6). It consisted of one or more saccades in the direction of head movement followed by a slow return of the eyes in the opposite direction i.e. towards the centre of the orbits. Saccadic activity tended to prevail in the accelerative and slow eye movements in the decelerative phase.

On cessation of head motion a residual eye deviation persisted in the

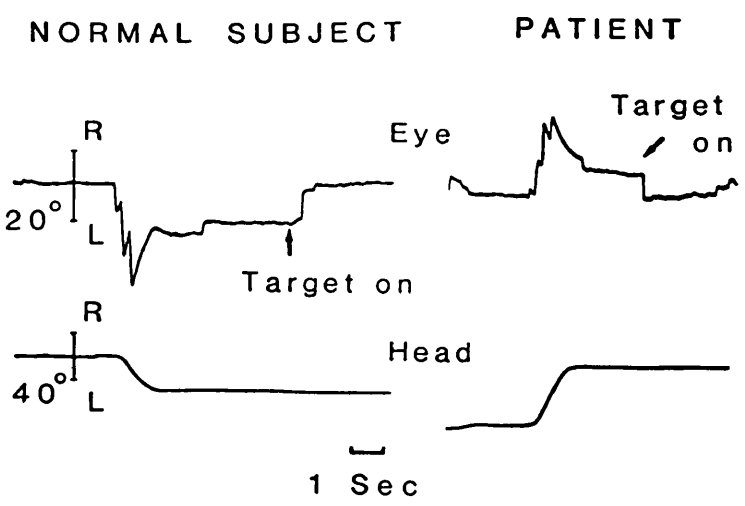


Figure 6. Active ramp head on trunk displacement. Note similarity of eye movements in normal subject and patient (same subjects as in Figure 1) and sustained eye deviation in the direction of head movement, revealed by presentation of target light.

same direction. Its magnitude, assessed in terms of the recentering saccade required to bring the eyes on to the target light, was a function of head deviation and comparable in both groups (amplitude gain or slope: normals, 0.22 ± 0.13 (SD), patients 0.18 ± 0.15 (SD)).

Eye movement responses to rapid ramp angular displacement of the head passively and unpredictably delivered, together with eye and head movement responses during active target seeking in a patient are shown in Figure 7.

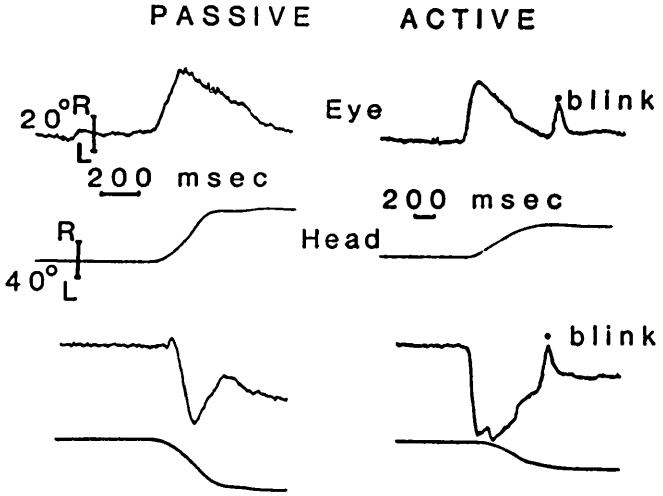


Figure 7. Left: eye movements elicited in a patient by sudden, passive rapid ramp head on trunk displacement in the dark. The pattern of eye movements is essentially similar to that elicited when the patient actively directed his eyes and head towards a visual target, randomly presented to the right or left of primary gaze (right).

Both are characterized by an initial saccade followed by a slow movement of the eyes in the opposite direction to head movement and similar to the eye movements shown in Figure 6 resulting from active head movements in the dark.

The latency of the eye movements elicited by passive head turns had a mean value of 50 ms ± 33 (SD) in 8 patients tested. This short latency is clearly indicative of the reflex nature of the response.

Sinusoidal stimulation - head on trunk. Sinusoidal head on trunk movements in the dark gave rise in all subjects to a consistent nystagmic reaction in the direction of head movement (Figure 8).

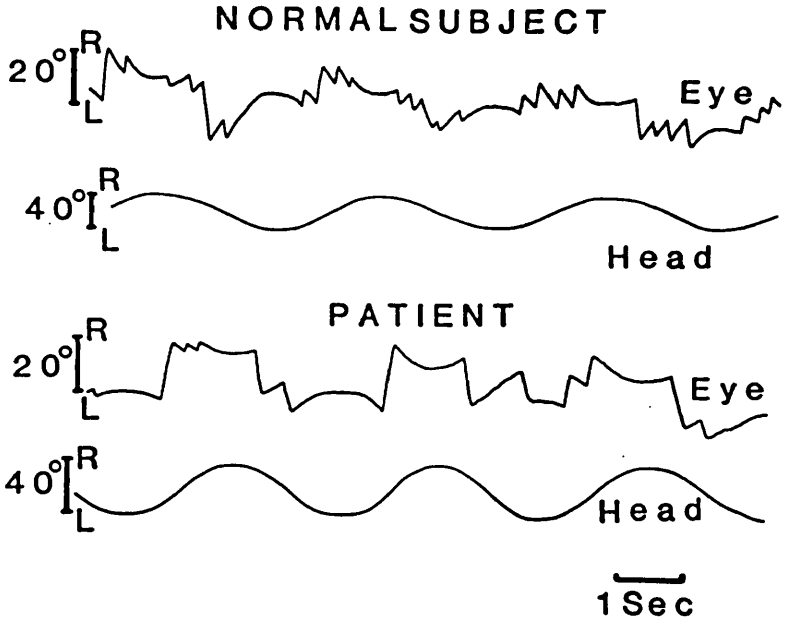


Figure 8. Sinusoidal head on trunk rotation in the dark. The nystagmic pattern is similar in the normal subject and the patient but slow phase velocities are slower in the former.

In the patient group, as a result of absence of the VOR, slow component velocity was much reduced as is reflected in the velocity gain measurements shown in Table 3 in which are included, for comparison, the gains for COR and

VOR. However, it is of particular note that the gain for head on trunk, 0.37, was significantly higher than that for trunk on head, 0.24 (paired t-test; $t = 2.52$, $P < 0.05$). Similarly, sinusoidal head on trunk movements in normal subjects induced velocity gains (0.82) significantly higher than those found with head-trunk en bloc rotation (0.60) (paired t-test; $t = 4.53$, $P < 0.01$).

TABLE 3

Velocity gain at 0.3 Hz sinusoidal stimuli in darkness

	VOR	Head on trunk	COR
Normal controls	0.60 (SD 0.21)	0.82 (SD 0.13)	0.02 (SD 0.03)
Patients	-	0.37 (SD 0.16)	0.24 (SD 0.09)

Sustained neck deviation to one side (left) did not consistently induce any asymmetry in the VOR as shown in Table 4 .

TABLE 4

VOR in darkness with head centered or turned left (normal subjects)

	Velocity gain				Phase error*			
	Head center		Head left		Head center		Head left	
	R VOR	L VOR	R VOR	L VOR	R VOR	L VOR	R VOR	L VOR
Subject 1	0.58 (SD 0.10)	0.67 (SD 0.09)	0.53 (SD 0.12)	0.57 (SD 0.21)	3.10 (SD 1.80)	2.30 (SD 0.98)	3.40 (SD 1.20)	4.70 (SD 1.40)
Subject 2	0.99 (SD 0.15)	1.02 (SD 0.05)	0.73 (SD 0.09)	0.71 (SD 0.05)	1.10 (SD 0.30)	0.60 (SD 0.40)	2.30 (SD 0.70)	0.50 (SD 0.20)
Subject 3	0.83 (SD 0.06)	0.95 (SD 0.20)	0.80 (SD 0.12)	0.95 (SD 0.14)	5.40 (SD 2.00)	-3.10 (SD 4.00)	6.80 (SD 4.80)	4.00 (SD 3.00)

* Values represent the difference (degrees) between slow component eye position and head position (- indicates phase lag).
R VOR, L VOR indicate VOR gain during hemicycles of right or left rotation.

DISCUSSION:

The main topics of interest that have emerged from these studies concern the tonic properties of the COR and the role of the COR in target acquisition and gaze stability. For convenience of discussion these will be addressed separately.

Tonic COR.

The studies using discrete ramp trunk movements with head restrained have shown that in normal subjects and patients with absent vestibular function a residual eye deviation was induced (markedly so in the case of the patients), the amplitude of which appeared to be linearly related to the angle of neck torsion. The evidence as it stands, however, indicates that it was dynamically induced and not the result of tonic activity associated with sustained neck torsion.

It seems, therefore, that tonic neck postural reflexes differ from the tonic neck-eye reflexes. In the case of the former, according to the classical descriptions of Magnus (1924), the reaction is tonic in the sense that it is produced not by the movement of the head, but by the new position imposed upon it, and that it persists as long as this is maintained. Although more recent work has added qualification to this view (Wilson, 1984), it contrasts strikingly with the nature of the COR as revealed by the present studies.

The COR in target acquisition and retention

'Anticompensatory' role of the COR.

There is evidence, derived from studies involving both ramp and sinusoidal head movements, that in man and animals compensatory and anticompensatory eye movements are subserved, respectively, by the slow and fast components of the VOR. Ramp step head movements in total darkness

initiate, in normal subjects, saccadic components in the direction of head turn followed by a slow return of the eyes in the opposite (Barnes, 1975; 1979. Since this pattern of eye movements is identical to that found during active target seeking it implies that in certain circumstances the initial saccade may be vestibularly induced (Barnes, 1979; Roucoux et al, 1981). To this can now be added these new observations that in the chronic absence of vestibular function passive and unpredictable head movements, as well as active head turning in the dark, all essentially reproduce the pattern of eye movements found during active target seeking. Similarly, during whole body sinusoidal rotation in the dark normal subjects present, in addition to the slow compensatory eye movements, a shift in eye position into the quick phase direction (anticompensatory gaze shift) 90^{o} phase-advanced (Mishkin and Melvill Jones, 1966). This too has its counterpart in the observations upon the COR in the patients and, in the circumstances, it would seem that in the absence of vestibular function the COR is able to take over the so-called anticompensatory properties of the VOR, inducing gaze shifts of the appropriate direction, velocity, phase relationship and amplitude such as to project the eyes in advance of an ongoing head movement. Presumably this is subserved by the neck muscle spindles responsive to the accelerative components of stretch (Richmond and Abrahams, 1979).

Compensatory role of the COR.

The trunk on head experiments in normal subjects confirm the findings of others that neck-induced slow eye movements make little if any contribution to retinal stability during head movement (Barlow and Freedman, 1980; Barnes and Forbat, 1979; Dichgans et al, 1973; Fuller, 1980; Jurgens et al, 1982; Takemori and Suzuki, 1971). This is evident from the very low gain and extreme variability in direction of the slow components of the COR. It follows that

the increased gain during sinusoidal head on trunk movement, compared to that of the VOR alone, cannot have resulted from a simple addition of COR and VOR. Instead, it seems more likely that an element of pre-programming is involved. This certainly accords with the finding of reduced intra and interindividual variance encountered in head on trunk VOR gain.

The striking enhancement of cervically induced slow eye movements in patients has its parallel in similar findings in monkeys and cats following bilateral labyrinthectomy (Dichgans et al, 1973; Peterson and Goldberg, 1982). As to its functional significance it is presumed that it serves to stabilize gaze during head movements, although it has to be admitted that there is as yet no direct evidence for this. Such evidence as there is derives from the obvious similarities between the COR in patients and what we know of the VOR. Thus under all experimental conditions including the unusual trunk on head movement the cervically induced slow eye movements were consistently compensatory, that is to say in a direction that would be expected to summate with the visuomotor reflexes (optokinetic and pursuit), thereby aiding retinal stability during ordinary head movements. Counter to this view would be the marked decrease in slow-phase gain of the COR with frequency (Figure 5) which indicates that the COR is not particularly effective within the frequency range of normal head movements i.e. above 0.2 Hz (Wilson and Melvill Jones, 1979). It is, however, worth recalling that head on trunk gain was significantly higher than that of trunk on head. This implies the existence of a pre-programmed mechanism of the kind already referred to and for which there is experimental evidence (Dichgans et al, 1973; Kasai and Zee, 1978), co-operating with the COR to stabilize retinal images in the patients during head movements.

Finally some comment is called for on the finding that instruction to imagine a stationary target exerts such a marked effect both in normal

subjects and patients upon the COR. Comparable effects are now well documented in respect of the VOR (Barr et al, 1976; Takahashi et al, 1980) and it is of some interest that the COR can be shown to be susceptible to similar central control.

Although experience indicates that this calls for a considerable conscious effort on the part of the subject and in its absence the COR reverts to its unmodified form, it does direct attention to possible influences operating upon the COR other than those from peripheral mechanisms. The cerebellum in particular is a case in point and seems to exert an inhibitory effect upon the COR similar to that which it is known to have upon the VOR (Bronstein and Hood, 1985). How significant these various central influences are remains to be determined in future studies of the COR.

COMPENSATION OF OSCILLOPSIA OF PERIPHERAL VESTIBULAR ORIGIN: THE ROLE OF THE CERVICAL INPUT

Derangements of the vestibulo-ocular reflex (VOR) may take the form of hypo or hyper activity; in either event head movements can give rise to a disturbing illusion of movement of the visual surroundings, termed oscillopsia, caused by images of the environment traversing the retina (Bender, 1965). Of these, hypo-activity caused by loss of vestibular function is by far the most disturbing and subjects typically complain of objects "bobbing", "jumping", "moving to and fro" or of "blurred vision" whenever they walk or move. Some, however, are appreciably less disabled than others and this may be due to the development of certain compensatory mechanisms involving in particular the cervico-ocular reflex (COR).

In the previous section it was shown that the COR, which is only minimally active in normal animals and man, becomes hyperactive after bilateral vestibular damage (Dichgans et al, 1973; Bles et al, 1984). Its phase and direction, variable and unstable in normal circumstances, becomes systematically compensatory such that slow eye movements are generated in a direction opposite to that of neck torsion suggesting that the COR may assume the role of the VOR in the absence of vestibular function. Those experiments, however, were conducted in the dark and could not have provided much information on how the cervical input might interact with visually guided eye movements, which may bear a more direct relationship to the clinical problem of oscillopsia.

The experiments to be described in this section have been undertaken to determine if any correlation exists between the degree of clinical disability produced by oscillopsia due to the absence of vestibular function on the one hand, and the development of compensatory gaze stabilising mechanisms, on the

other.

MATERIALS AND METHODS:

Eight out the 12 original patients with absent vestibular function described in the previous section were available for these studies. Two patients (3 and 6, table 1) had a few isolated nystagmic beats during the first 2-3 s after velocity steps of 80°/s in the dark; the remainder had no response. From the history they were classified according to the clinical severity of oscillopsia from grade 0 to III as follows:

Grade 0 - Oscillopsia denied by the patient.
Grade I - Oscillopsia not described spontaneously. On questioning the patient admitted it was present in certain circumstances such as running, but was not troubled at all by the symptom.
Grade II - Oscillopsia was a presenting symptom but was well tolerated and did not appear to impart any disability affecting the patient's mobility.
Grade III - Oscillopsia of disabling severity with gross interference in the patient's daily activities.

The relevant clinical data are included in table 1. Age at onset and progression of symptoms could not be established with certainty in patients 1 (grade 0) and 2 (grade I). Patient 1 had received a long course of treatment with streptomycin 30 years ago for a gangrenous wound due to Buerger disease. Neuro-otological symptoms and absent labyrinthine responses were documented for the first time 14 years before our current investigations. Patient 2 had von Recklinghausen's disease with bilateral slow growing tumours of the VIII nerve; the estimated age at onset refers to the first presentation of VIII nerve symptoms.

TABLE 1

Clinical findings

Oscillopsia grade	Patient no.	Sex	Age at onset (years)	Duration (years)	Aetiology	Deafness	Ocular counter-rolling	CNS signs
0	1	M	34	30	Aminoglycoside ATB	-	Weak asymmetric	-
I	2	M	17	7	Bilateral VIIInerve tumours	Severe	Weak	Cerebellar
II	3	M	29	3	Meningitis Aminoglycoside ATB	Severe	Absent	-
II	4	F	35	20	Meningitis Aminoglycoside ATB	Severe	Normal	-
II	5	M	20	35	Meningitis	Severe	Weak	-
III	6	F	71	1	Aminoglycoside ATB	-	Absent	Alternating nystagmus in the dark
III	7	F	73	0.5	Aminoglycoside ATB	-	Normal	-
III	8	F	50	0.5	Aminoglycoside ATB	Moderate	Absent	-

A full clinical neuro-otological examination was carried out including tests for spontaneous, gaze evoked and positional nystagmus. Doll's head manouevre was executed in the horizontal, vertical and coronal planes; head movements in the latter plane normally produce torsional compensatory eye movements and nystagmus (ocular counter-rolling) so providing some indication of the functional state of the vertical canals and the otoliths (Miller, 1970; Diamond and Markham, 1983). Vertical and horizontal saccades and smooth pursuit movements were also studied.

Experimental strategy:

I) The data collected from experiments described in detail in the previous section, were re-examined with a view to relate them to the degree of oscillopsia:

A. Head motion during target acquisition, as the subjects were required to look at target lights positioned at 10° intervals on a bar 1 metre to their front and subtending ± 50°.

B. Sinusoidal trunk movements in the dark (COR), with the subject seated on the rotating chair and the head fixed in space by means of a bite plate, at frequencies between 0.07 to 0.3 Hz. with amplitudes of approximately +/- 25°.

C. Sinusoidal head on trunk movements in the dark, at frequencies of 0.3 and 1 Hz. with amplitudes of approximately ± 25°.

II). Sinsuoidal head movements in the presence of fixation:

In order to study the contribution of neck input to gaze stability in the light, compensatory eye movements were measured and compared in two different conditions: head clamped and free. In the first, the subject seated in the rotating chair to which his head was firmly secured, was rotated sinusoidally at 1 Hz while fixating upon an earth-fixed target to his front at a distance of 5 metres. Peak velocity was varied between 80 and 140°/s. In the second condition the head was freed and the helmet (attached to a potentiometer) fitted. The subject was then instructed to relax his neck as much as possible and allow the examiner to move the head freely while fixating the target, care being taken to avoid any slippage of head and helmet. Frequency was kept constant at 1 Hz in synchrony with a metronome and the amplitudes of the oscillations were adjusted so that they matched those obtained during the head clamped experiment as monitored on the recording. In the interests of comparability eye movement measurements under the two conditions were carried out on those recordings which did not differ from each other by more than 5% in respect of frequency, amplitude and velocity of the stimulus. Patient 5 was not available for the head clamped experiment. For both procedures in addition to the routine eye calibration with targets 10°

apart, simultaneous head-eye calibrations were obtained by turning the head or chair slowly in the presence of optic fixation. These normalized values served as a baseline (gain=1, see below) for the analysis of the results.

Eye, chair and helmet position were recorded upon the ink-jet polygraph and the recordings analysed by hand. Gain was defined as peak slow phase eye velocity / head (or trunk) peak velocity; measurements were made on each individual half cycle and a minimum of 8 were included.

RESULTS:

The relevant clinical findings are presented in Table 1. It will be seen that Grade III is characterised by three older patients with a relatively short history of oscillopsia.

Ocular counter-rolling was (clinically) normal in patients 4 and 7. The remainder of the subjects had considerable weakness, asymmetry, or absence of the reflex. These derangements, however, did not relate to the patient's clinical status nor did the presence of a minimal residual nystagmic response during high velocity rotational steps in patients 3 and 6 (see material and methods).

No additional CNS involvement could be called in to account for the severity of the oscillopsia. Patient 6 (group III) was found to present bouts of alternating nystagmus in the dark, thought to be of central origin, which was accentuated by high velocity impulsive rotation in the dark. Patient 2, however, who had clear CNS damage as evidenced by mild cerebellar signs, exhibited only minimal oscillopsia.

Head motion during target acquisition:

Head velocity was measured during eye-head co-ordinated movements aimed at fixating randomly presented targets. It is well established that peak

velocity of the head increases linearly with the amplitude of target displacement (Barnes, 1979). Accordingly, a linear regression curve was fitted to the amplitude/velocity data of each subject, (typically comprising 15 data points) and the velocity value at 50° target amplitude established for each subject (see table II). From this and the curves displayed in Figure 1 it will be seen that patients in group III showed a tendency to move their heads more slowly than normal controls or patients less severely affected, presumably in order to avoid oscillopsia. This difference in head speed

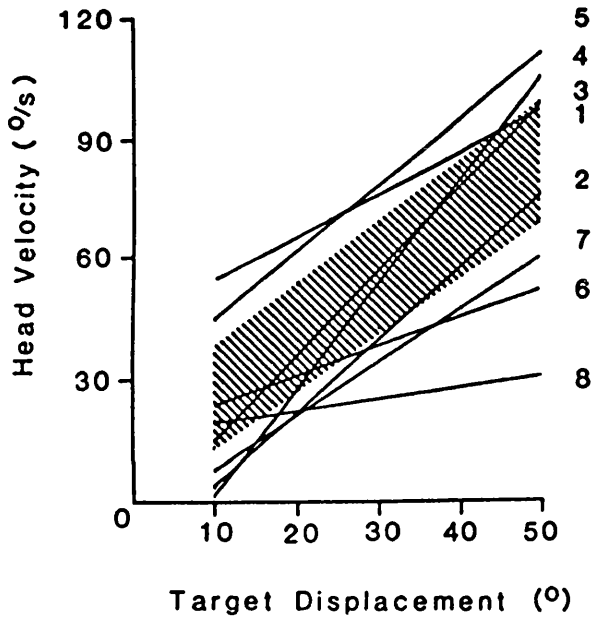


Figure 1. Relationship between amplitude of target displacement and peak head velocity during head-eye co-ordinated movements. The regression lines shown are from each individual patient; patients 6, 7 and 8 belonged to group III. The shaded area represents mean ± SD of 16 normal controls.

cannot be explained in terms of age since patient 8, who had the slowest head velocity, was younger than two patients in grade II and the patient in grade 0. Similarly, in the 16 normal subjects studied, aged between 22 to 70 years, no relationship between age and head velocity was found.

Sinusoidal trunk movements in the dark (COR):

Figure 2, derived from figure 5 of the preceding section, illustrates that there appeares to be no relationship between COR gain and clinical status.

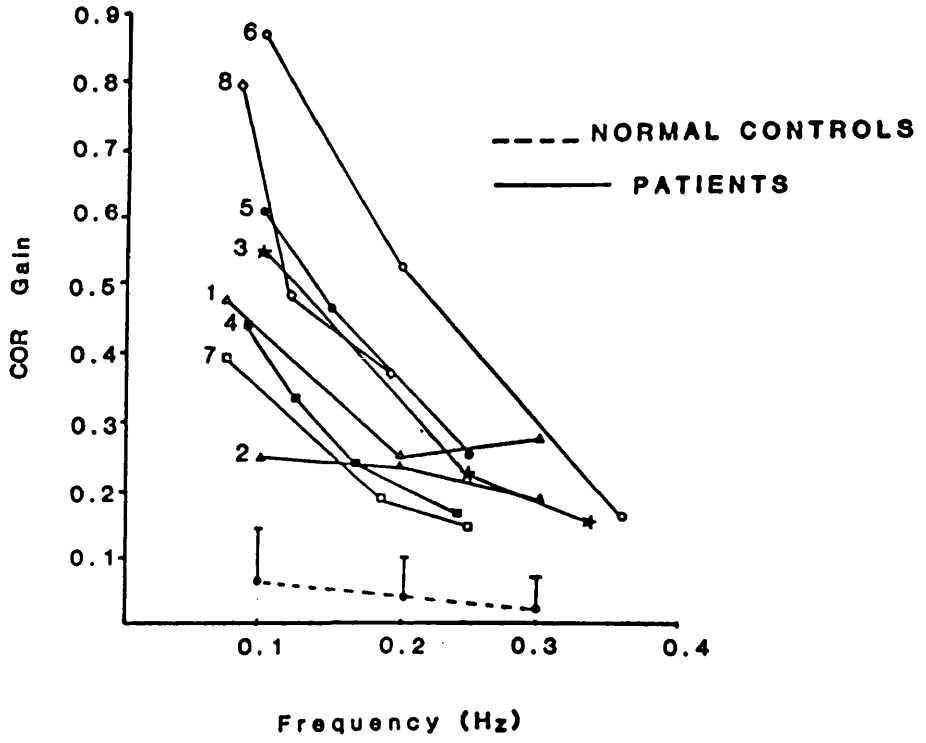


Figure 2. COR gain in the dark with sinusoidal trunk rotation about the head. Amplitude of oscillation was approximately ± 25°. Individual values of each patient (1-8) are presented, together with the mean + 1 SD of 13 normal controls. Although the COR is considerably enhanced in the patients, this did not correlate with the degree of oscillopsia.

Sinusoidal head movements in the dark (table 2):

During head upon body movements in the dark at 0.3 Hz the mean velocity gain of the slow compensatory eye movement was 0.38 SD 0.16 and 0.37 SD 0.19 at 1 Hz. indicating no consistent change with frequency. No obvious relation was apparent with the degree of oscillopsia.

TABLE 2

Test results

Patient no.	1	2	3	4	5	6	7	8
Target acquisition								
Head velocity at 50° (°/sec)	98	79	100	106	112	52	61	30
Sinusoidal rotation (gain)								
Darkness								
0.3 Hz	0.44	0.17	0.21	0.45	0.72	0.35	0.36	0.35
1 Hz	0.55	0.11	0.51	0.13	0.59	0.51	0.36	0.21
Fixating (1 Hz)								
Head clamped	0.59	0.62	0.71	0.51	-	0.71	0.74	0.76
Head free	0.73	0.87	0.98	0.81	0.74	0.69	0.67	0.73
[a]Clamped/free (%)	-20	-29	-28	-38	-	+11	+10	+4

[a] Refers to percentage reduction or increase in gain with head clamped relative to that with head free.

Sinusoidal head movements in the presence of optic fixation:

It is apparent from table II and the data presented in fig 3 that gain values, either with head free or clamped, were not related to the degree of oscillopsia. However, it is clear that in the patients with little or no oscillopsia gain values with the head clamped were between 20 to 38% lower than those with the head free; by contrast, patients with severe oscillopsia had gains with head clamped either marginally increased or within the range of those with the head free. An analysis of variance and covariance with repeated measures (BMDP2V, Univ. of California) showed that the interaction between the gains with head clamped and free and the mild (0-II) and severe (III) oscillopsic groups was highly significant ($f = 42.20$ $p = 0.001$). This

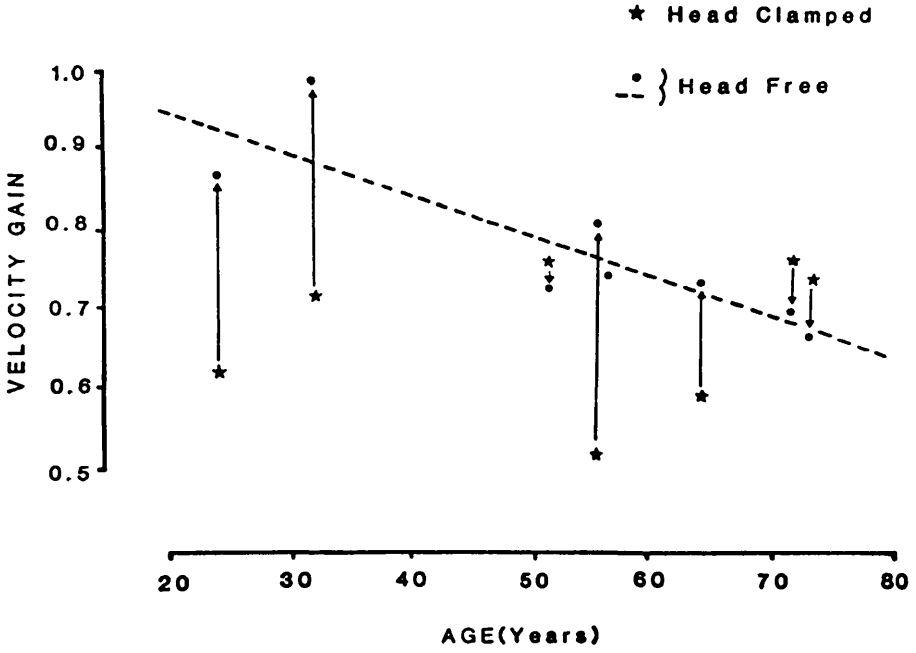


Figure 3. Relationship between age of patients and gain during sinusoidal rotation in the presence of optic fixation with head clamped and free. The regression line refers to gain with the head free. The 3 patients showing inversion of the two gains (downward pointing arrows) had grade III oscillopsia, relative to the 4 patients with less oscillopsia (upward pointing arrows).

did not hold for the two groups and the respective gains treated in turn ($f = 0.04$ $p = 0.847$) implying no direct effect of gain values with either head free or head clamped.

In view of the possibitity that age of the patients and gain values may be associated, the Kendall's rank correlation coefficient was calculated. A significant negative correlation was present between age and gains with the head free (tau coefficient = -0.62, $p = 0.03$) but not with the head clamped (tau coefficient = 0.42, $p = 0.12$). Although this showed that head free velocity gain decays with the age of the patients, the precise form of the relation between the two variables cannot be inferred from this particular analysis. This in fact is more appropriately exemplified by the linear regression shown in fig 3 ($r = -0.87$; $p<0.01$), which implies a linear relationship.

DISCUSSION:

The potentiation of the COR in the patients with absent vestibular function is thought to contribute to the restoration of gaze stability during head movements. Since during the development of this potentiation (which in the monkey takes several months (Dichgans et al, 1973)) more general symptoms usually diminish, it might be presumed that the two are related. It might, therefore, appear surprising that no obvious correlation is evident between the degree of oscillopsia and COR gain as assessed by rotation of the trunk around the head fixed in space.

This, however, involves an unnatural test situation designed to elicit the COR in isolation from the VOR and it is noteworthy that although the gains observed are appreciable they are most apparent at low frequencies where optokinetic reflexes could by themselves provide adequate gaze stability during head movements (Gresty et al, 1977). In this context, however, it needs to be recalled that during head on trunk movements in the dark these gains were further increased and extended well into the frequency range of normal head movements (Table 2). As discussed in the previous section, since both trunk on head and head on trunk rotation produce identical peripheral cervical stimulation it is presumed that, in the absence of vestibular function, the additional ocular-motor activity found during head on trunk rotation is pre-programmed in origin.

Of perhaps greater relevance in this respect are the findings embodied in Figure 3 concerning the gains obtained during head free (head on trunk) oscillation in the presence of optic fixation. These showed a remarkably good negative correlation with age and it will be noted that gain values approach a gain of unity amongst the younger well compensated members of the group. This seems clear enough evidence that when evoked by head on trunk rotation the

COR, in conjunction with its associated preprogrammed activity and optokinetic reflexes, is capable of taking on the role of the VOR in stabilizing gaze during head movements. Latencies of eye movements mediated by the COR, reported in the previous section, are considerably shorter than those of the optokinetic and smooth pursuit system and would be well suited to initiate this compensatory response (see section on otolith-visual interaction for a similar interactive effect between otolith and optokinetic elicited compensatory eye movements).

In contrast, during whole body oscillation with head clamped the stimulus, in the absence of both VOR and neck torsion, is solely optokinetic and the response showed no correlation with age. Since there is good evidence that optokinetic gain deteriorates with age (Sharpe and Sylvester, 1978; Spooner et al, 1980; Magnusson and Pykko, 1986; Simons and Buttner, 1985), the question arises: why was such a correlation so conspicuously absent in these data; instead, the gains in the patients relatively free from oscillopsia were markedly depressed, whereas in the case of the three patients in grade III the gains were marginally greater than those with head free and the highest in the group despite their advanced age.

The most likely explanation for these somewhat paradoxical findings rests in the fact that since the illusory movement of the environment in oscillopsia is consequent upon retinal slip it is possible that certain perceptual rearrangements might be engendered whereby image movement, unpleasantly interpreted as movement of the visual world, is in some way neglected or ignored as presumably occurs in some forms of nystagmus (Buchelle et al, 1983) and oculo-motor palsies (Wist et al, 1983). Viewed in this light, it is to be concluded that depression of the optokinetic responses may be an inevitable consequence of the development of those compensatory mechanisms which bring about a reduction of the perceived oscillopsia and

material to this is Zee et al's observation (1976) of just such a depression in three patients with long standing absent vestibular function; unfortunately data are not available from direct observations of standard OKN responses of the patients reported here. Whatever the mechanism underlying this possible reduction of sensitivity to visual motion, the results suggested that the effect can be immediately reversed in the presence of concurrent neck stimulation. The findings complement those in appendix C (Suppression of visually evoked postural responses), where it is shown that the unstabilising effects of movement of the visual surroundings (by way of a movable room), can only be suppressed in the presence of concurrent, reliable proprioceptive information. Both findings provide evidence that proprioceptive input, from the lower limbs and from the neck, interact centrally in such a way as to attenuate the effects (unsteadiness and oscillopsia respectively) of an unusual or disorienting visual input.

Provocation of vertigo is an essential element in rehabilitation procedures applied to patients with acute vestibular failure (Zee, 1985) so that by analogy the avoidance strategy adopted by patients with severe oscillopsia of moving their heads more slowly during head-eye coordinated movements may not be in their best interests at least in respect of the development of compensatory mechanisms.

SUMMARY

- In the introductory section the general background to cervico-vestibular interaction was reviewed. The dorsal roots of the first cervical roots generate inputs which interact with vestibular receptors during postural and ocular stabilisation. Muscle spindles and Golgi tendon organs located in small intervertebral muscles are the likely neck receptors. Convergence of vestibular and cervical signals occurs at various levels in the neuraxis, particularly the vestibular nuclei, the cerebellum and the cerebral cortex. In the vestibular nuclei the strength of the cervical input is considerably less in vestibulo-ocular than in vestibulo-spinal neurons. The interaction of vestibular and nuchal signals participates in the conscious perception of head and trunk motion and gives rise to postural reflexes acting on the head and limbs.

- In the second section of this chapter, the role of the COR was studied in 12 patients with absent vestibular function and 13 normal subjects. Ramp and sinusoidal displacement stimuli were applied with trunk on head and head on trunk movements. In all patients, trunk on head movements evoked a marked slow-phase compensatory COR while in normal subjects it was weak and variable in direction. Fast components of the COR induced gaze shifts in the direction of the relative head movement ("anticompensatory" direction) which could be suppressed by imagining an earth fixed target. No tonic component could be identified instead, in the case of ramp stimuli, a residual eye deviation was noted which was significantly enhanced in the patients and resulted from activity dynamically generated during the course of the trunk movement and not from its final angular displacement. Head on trunk ramp displacements in the dark evoked initial anticompensatory saccades followed by slow compensatory components, a pattern of eye movements remarkably similar to that seen during

active head-eye target seeking. Thus, in the absence of labyrinthine function, the COR appears to take on the role of the VOR in head eye co-ordination in (a) the initiation of the anticompensatory saccade which takes the eyes in the direction of the target, and (b) the generation of the subsequent slow compensatory eye movements. Central pre-programming, as revealed by comparing the effect of different instructions and active versus passive neck-induced eye movements, has a profound influence on COR functioning.

- In the third section, eight patients with absent vestibular function were categorised into four grades according to the disability they suffered from oscillopsia. They were studied with a view to correlating the severity of the oscillopsia with the development of gaze stabilizing compensatory mechanisms. Eye movements were recorded during head on trunk and whole body (head and trunk) oscillation at 1 Hz. in the presence of optic fixation of an earth-fixed target. Velocity gains (peak slow phase eye velocity/peak head velocity) during whole body rotation were significantly lower than head on trunk gains in the light in the better compensated patients. Since in the absence of vestibular function whole body rotation involves only the optokinetic system (OKN), this finding implies a depression of the OKN in these patients which can be corrected during head on trunk movements by virtue of a dynamic input from the neck. The results suggest that the processes of recovery from oscillopsia are dependant, in the main, upon the development of central mechanisms by means of which undesirable image movement across the retina is perceptually suppressed. Depression of OKN may be secondary to this perceptual rearrangement.

CHAPTER II

VESTIBULO-CERVICAL INTERACTION

REVIEW AND INTRODUCTION:

In the preceding chapter attention was given to the influence of proprioceptive input from the neck upon vestibulo-ocular motor reflexes. As a corollary, this chapter is concerned with the possible influence of activity arising in the vestibular system upon cervical musculature and head position.

The study of the mechanisms controlling head posture has been largely neglected in man. Impulses controlling the normal upright position of the head arise in the visual, vestibular and proprioceptive systems. There is general agreement that the relative importance of the vestibular system declines along the phylogenetical scale (Wilson and Melvill Jones, 1979).

In animals, stimulation of the labyrinths by angular or linear acceleration evokes a vestibulo-collic reflex (VCR) the function of which is to stabilise the head in space. Electrical stimulation of individual canal ampullary nerves has shown that vestibular evoked head movements are highly specified in direction (Suzuki and Cohen, 1964). The function of the cervico-collic reflex (CCR), elicited by stretch of the neck receptors, is to stabilise head position with respect to the trunk (Peterson et al, 1981). These two reflexes, in turn, interact in the behaving animal with head movements elicited by external (environmental) or internal ("volitional") stimuli. During passive head motion the VCR and the CCR are synergistic and together would, for example, counteract the effects of a mechanical push or of the gravitational pull on the head. During trunk motion, however, these two reflexes may be antagonistic since the CCR will tend to re-align the head with the trunk whereas the VCR will tend to maintain it steady in space.

Furthermore, during a voluntary or externally triggered reflexive head movement both VCR and CCR will have to be cancelled.

In man the existence of a VCR is less evident. However, during caloric tests a persistent deviation of the head in the direction of the slow phase of nystagmus can sometimes occur in neurological patients and thus it would be possible that in normal subjects VCR responses are not apparent because they may be inhibited by the CNS. In fact, it has been known for a long time that tonic neck reflexes, which cannot be easily elicited in intact man, appear in decerebrate states (Magnus, 1924). As will be discussed below, evidence pertaining to the presence of VCR activity in man has not only theoretical but also clinical interest, in particular as to the mechanisms involved in the generation of abnormal head posture in spasmodic torticollis.

Outerbridge and Jones (1971) noted that during angular rotation in the dark movements of the head occurred which were synchronised with the ocular nystagmus; these authors considered it likely that such head movements would help to achieve gaze stability. In contrast, Barnes and Rance (1974) questioned the existence of a VCR, at least with high accelerations, and attributed the resulting head movements to the inertial properties of the head/trunk system. The studies of Diener et al (1982) on postural stability of normal subjects standing on a movable floor also suggested the existence of specialized mechanisms of head stability which they attributed to VCR activity.

Abnormal head posture of vestibular origin

Lesions of the vestibular system can cause abnormal head posture although this is exceptional in peripheral lesions (Brain, 1926; Halmagyi et al, 1978). In a paper "On the rotated or cerebellar posture of the head"

Brain (1926) presented cases with peripheral otological lesions in which the head (occiput) tilted and rotated towards the affected side. This attitude can be reproduced experimentally in animals by labyrinthectomy or VIII nerve section (Magnus, 1924; Uemura and Cohen, 1973) and has also been occasionally described in patients with acoustic tumours (quoted in Brain, 1926). Finally, in young children a form of paroxysmal torticollis sometimes accompanied by pallor, vomiting, ataxia and "rocking movement of the eyes" has been considered equivalent to benign paroxysmal vertigo in childhood, although its vestibular origin has not been unequivocally established (Snyder, 1969; Gourley, 1971).

Damage to the brain stem can also give rise to abnormal head postures and Uemura and Cohen (1973) produced severe head tilt in monkeys with lesions in the vestibular nuclei. In man, extensive brain stem lesions induce head (occiput) deviation to the opposite side (Brain, 1926). Head tilt accompanied by skew deviation of the eyes in the same direction i.e. lowermost eye to side of tilt (Keane, 1975), suggests an imbalance in the vestibular system and is probably due to the unopposed action of the contralateral impulses. The lowermost side of the head indicates the side of the lesion in most cases. However, care should be exercised in the interpretation of asymmetric head posture in the presence of a brain stem lesion since this could result not only from interruption of vestibular pathways but also from damage to supranuclear or nuclear pathways controlling voluntary neck movements or from the adoption by the patient of a head attitude to compensate for oculo-motor defects.

In hemispheric lesions transient head rotation towards the same side accompanies the gaze palsy seen during the acute phase of stroke or is sometimes compensatory to a hemianopia. Vestibular pathways are not thought to play a part in this head deviation although it is known that hemispheric

lesions can produce asymmetry in the vestibulo-ocular system (Fitzgerald and Hallpike, 1942; Sharpe and Lo, 1981).

Finally, basal ganglia disease can severely interfere with mechanisms normally responsible for head posture. Purdon Martin (1967) described cases of post-encephalitic parkinsonism and Wilson's disease in which the head slowly abandoned the normal upright position and fell flexed forward either spontaneously or on blindfolding the patients. On voluntary command or on restoring visual information the normal posture was regained. This he took as evidence favouring the existence of a cortical mechanism regulating head position in man.

Although abnormalities of head posture are common in several conditions involving the basal ganglia, the more significant is that seen in spasmodic torticollis, a form of focal dystonia affecting cervical musculature. In contrast to the defective postures described above, the head attitude seen in spasmodic torticollis (ST), is due to a massive involuntary discharge of the postural muscles of the neck (Herz and Hoefer, 1949). The resulting asymmetric head posture and movements, whether rotational about the vertical axis or tilted with respect to gravity, have always directed attention towards a possible link with vestibular reflexes. Several cases have been reported in the literature in which ST developed in close association with unilateral lesions of the vestibular system or was modified by surgical procedures on the labyrinth (Barre, 1929; Barre and Guillaume, 1930; Hyndman, 1939; Svien et al, 1969). Vestibular mechanisms have also been invoked in relation to animal models of dystonia and idiopathic ST (Denny-Brown, 1966; 1988; Burke and Fahn, 1983; Shima, 1984). In Denny Brown's view (1966; 1968) hemiplegic dystonia, which can affect the neck and produce lateral torticollis, represents a disinhibited state of postural reactions of tonic otolithic origin. On the other hand, he considered that torsion dystonia and related ST with rotatory

displacement of the neck, was due to distortion of phasic (canal) vestibular reflexes. The former can be modified by tilt with respect to gravity whereas rotation about the longitudinal axis of the body influences the latter. Impressive and coherent as they may be, these observations have not been submitted to quantitative analysis with adequate techniques of vestibular research and require further validation.

In this chapter we will investigate two inter-related problems concerning the relationship between the vestibular system and the neck musculature: the existence of VCR in man and the possibility that ST be related to disordered vestibular function.

VESTIBULAR CONTRIBUTION TO HEAD STABILITY

As mentioned above, the question "Is normal human head stability in space dependant upon vestibular information?" has only rarely been addressed (Barnes and Rance, 1974; Outerbridge and Jones, 1971; Guitton et al, 1986). This apparent lack of interest may have been based on the fact that there seems to be obvious differences between man and animals as to the effects of peripheral vestibular lesions on head posture. In animals, unilateral labyrinthine lesions are known to provoke asymmetric head posture (Magnus, 1924), a feature much less striking and only occasionally encountered in human clinical practice (Brain, 1926; Halmagyi et al, 1978). Patients with bilateral labyrinthine lesions do not have any obvious abnormality of head posture, either with eyes opened or closed, although such clinical observations have only been made in static conditions. Therefore, in the experiment to be described, head stability will be assessed in dynamic conditions in normal subjects and in patients with absent vestibular function in order to determine whether VCR mechanisms contribute to head stability.

MATERIAL AND METHODS:

Six patients (age range 32-73 years) with absent vestibular function due to aminoglicoside toxicity were tested; in three of them these drugs had been administered for meningitis and thus a combined peripheral/VIII nerve aetiology is possible. The duration of the vestibular loss ranged between 1 and 35 years. Absent vestibular function was confirmed with bithermal caloric tests in the light and dark together with rotational tests in the dark with impulsive rotation of 60o/s or greater. Apart from the VIII nerve damage they were neurologically normal. Six normal subjects aged 18 to 62 years served as

a control group.

The experimental strategy consisted of assessing the stability of the head in space during whole body oscillation. This strategy is analogous to that used in determining gaze stability in space by measuring eye movements in response to head oscillation (Vestibulo-Ocular Reflex).

The subjects sat on the rotating chair with the head free to move in a well lit room. They wore a light helmet connected to a low torque potentiometer which monitored horizontal head position with respect to chair (trunk) position. Leg and hip clamps were fitted. The stimuli were delivered by hand by the author in all cases but one, when he acted as a control subject. They consisted of unpredictable horizontal sinusoidally shaped oscillations in which frequency, amplitude, velocity and direction of movement were constantly changed (see fig. 1). Maximum amplitudes were of approximately 70o. Peak frequency of the stimulus was 0.8 Hz (see below and fig. 2). The inertia of the chair with the subject on it determined a jolt-free, smooth stimuli. Chair (trunk) and helmet (head) position signals were recorded with an ink-jet recorder (Mingograph).

The subjects were required to look at a real tridimensional object 5 metres to their front; 4 patients and 2 control subjects had simultaneous DC EOG recording to monitor their visual fixation. However, pilot studies had shown that normal subjects and patients frequently restrained their head movements voluntarily during stimulation so that head and trunk rotated en bloc and only the eyes moved in opposite direction to that of the stimuli. Subjects therefore were encouraged to direct their eyes and head to the visual target and sample stimuli were delivered to familiarise them with the requirements of the experiment. This dependence on a relevant instruction in some subjects in order to obtain a head movement renders measurements of the amplitude of the response of doubtful value. Accordingly measurements were

made by hand of the time difference between the points of peak amplitude at which the chair and head reversed direction (maxima and minima). The first 10 seconds were not measured. Automatic techniques of spectrum analysis were available to compute data on-line from 3 of the original 6 controls, at the same time that the paper recordings were obtained, and from two additional subjects (a 31 years old normal subject and a 26 years old patient without vestibular function). The power spectrum of the stimulus and the coherence function between head and chair movements were measured with a signal processor (Solartron 1200). The coherence function measures the degree of association between two signals; its formula is:

$$\text{Coherence between } x,y = \frac{(\text{Cross Spectra of signals } x,y)^2}{\text{Power Spectra } x \cdot \text{Power Spectra } y}$$

Coherence varies, at each frequency of stimulation, between 0 (the two signals are totally unrelated) and 1 (the system output, i.e. the head movement is due entirely to the input). The stimuli were delivered over a period of about 100 s until 50 averages were obtained on the signal processor, set with a baseband between DC-200 Hz. and a frequency resolution of 0.4 Hz.

RESULTS:

Typically, head movements were compensatory to that of the chair motion, i.e. in a direction opposite to that of the stimuli and fairly sinusoidal in shape (Figure 1). Comparison of the points where the direction of the movement reversed (maxima and minima) revealed consistent differences between the two groups of subjects studied. Normal subjects reached turning points with head in advance of the chair whereas in the patients the opposite occurred (Figure 1, normal subject and patient 1). Table 1 summarizes the

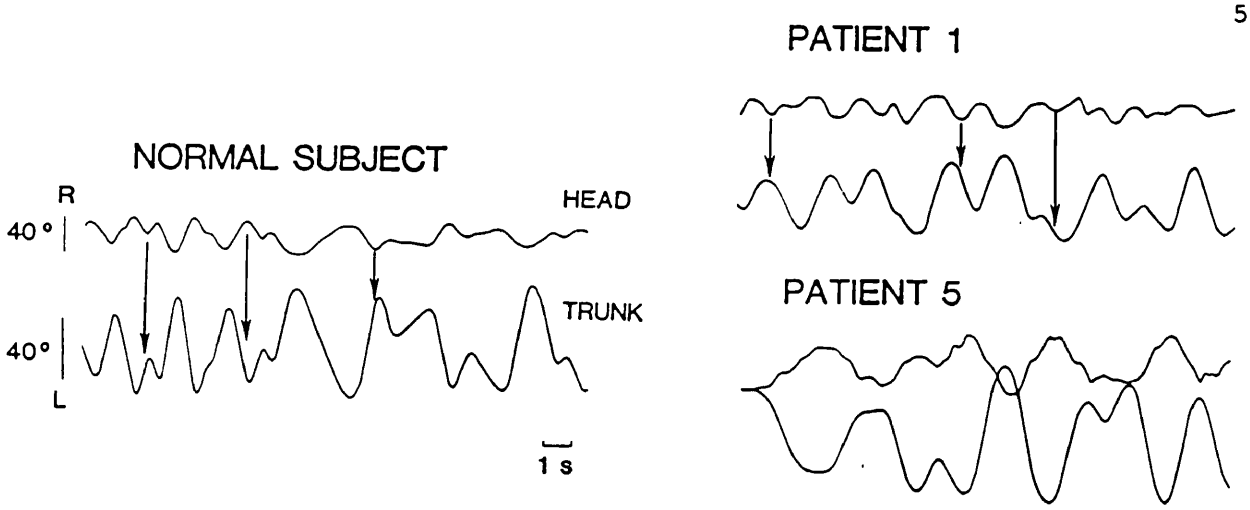


Figure 1. Compensatory head movements in response to trunk oscillation in a normal subject and in 2 patients lacking vestibular function. Arrows indicate that in the normal subject the head reverses direction in advance of the trunk (lead) whereas in patient 1 the head reverses direction after the trunk (lag).

TABLE 1

Time delay between maxima and minima (turning points) for the head/trunk movements[a]

	Mean (ms)	Range (ms)
Patient 1	156	80/240
Patient 2	Not measurable	
Patient 3	202	80/280
Repeat test	236	100/360
Patient 4	188	40/440
Patient 5	Not measurable	
Patient 6	130	40/280
Mean (n = 4)	169	
Control 1	-130	0/-250
Control 2	-153	50/-250
Control 3	-157	-100/-220
Control 4	54	0/100
Control 5	-58	0/-200
Control 6	-49	100/-160
Mean (n = 6)	-82	

[a] A negative value indicates a lead of head over trunk

time delay measurements between turning points of head and chair movements. In normal subjects there was a mean lead of head over chair of 82 ms whereas in the patients there was a mean lag of 169 ms. Considerable intra and inter-subject variability was present as shown in the ranges in the table. In two patients the head moved inconsistently, with irregularities in the trace which precluded time delay measurement due to the difficulty in determining maxima and minima (Figure 1, patient 5).

In the 5 cases subjected to Fourier analysis, the frequency of the stimulus was less than 1.2 Hz with a peak spectrum in the 0.8 Hz band (Figure 2, below). The results of the coherence function indicated that in normal subjects at least 50% of the power present in the head movement was linearly

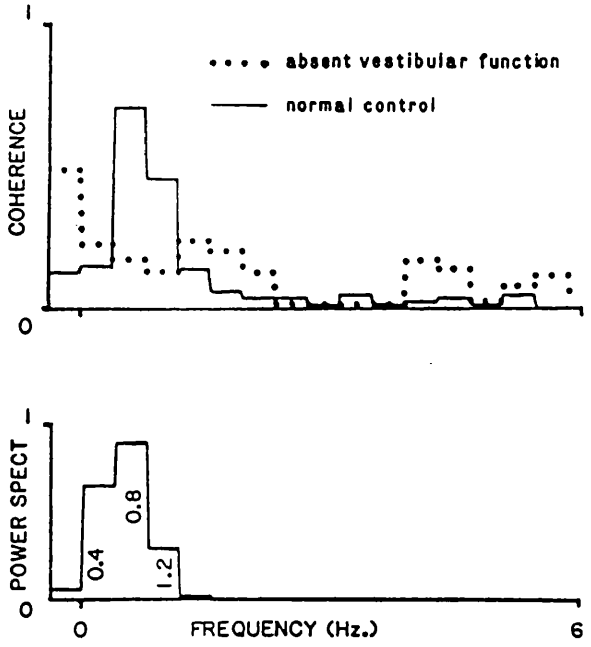


Figure 2. Above: Coherence between head and trunk movements in a patient lacking vestibular function and in a normal subject. Below: Power density of the stimulus (arbitrary units) showing the typical frequencies present (0.4, 0.8, 1.2 Hz).

related to the chair movement (coherence values between 0.50 and 0.82) whereas in the patient studied the values were considerably smaller (Figure 2, Table

2). Gain (in decibels), also shown in Table 2, show great variability and for the reasons given earlier are of questionable interest. However, a point to note on the amplitude of the response, as assessed from the raw records (Figure 1) is that the compensatory head movements were always of smaller

TABLE 2

Coherence and gain [a] of head movements elicited by trunk oscillation [b]

	Coherence	Gain (dB)
Control 4	0.68	-4.7
Control 5	0.82	-10.6
Control 6	0.68	-8.5
Control 7	0.50 (0.4 Hz)	-10
Repeat test	0.50	-4.8
Patient 7	0.22 (0.4 Hz)	-11.7
Repeat test	0.34	-7.7

[a] Amplitude head movement/amplitude trunk movement

[b] Maximum values of coherence are given, usually at 0.8 Hz, unless otherwise stated. Gain values are at 0.8 Hz.

amplitude (usually by about 40-50%) than that of the chair oscillation. This in turn implies that the head was always subjected to net displacement in the direction of the chair rotation.

DISCUSSION:

These studies have shown that during angular horizontal whole body movements labyrinthineless patients differ from normal subjects in their ability to stabilize their head in space as evidenced by the presence of a time delay between peak head-chair displacements and a low coherence between head and chair motion.

Normal subjects, on the other hand, presented negative time delays, that is, anticipated the reversal of chair direction. With ordinary sinusoidal stimuli such a time relationship between stimulus and response could be attributed to a "high order" predictive response but, under the present experimental conditions, this would not be likely because the stimuli were randomly delivered and unpredictable. More likely, the compensatory head movement followed a derivative of head in space displacement (i.e. acceleration) sensed by the vestibular system, thus giving the head/trunk position recordings an anticipatory or predictive appearance. It is thought that the vestibular system detects early head acceleration signals and provides the ocular-motor system with an estimate of final head position (Barnes, 1979); such an estimate could also be used to generate compensatory responses in the neck.

In partial agreement with these data is the recent work of Guitton et al (1986), assessing head stability during random body oscillation in subjects who had to make coincide a spot of light, which originated in a projector fixed to the head, with another earth-fixed target light. They reported that normal subjects achieved significant head stability in these conditions, or when blindfolded while attempting to stabilize an imaginary head-mounted light, whereas labyrinthineless patients performed significantly worse. Since their estimated delay values in normal subjects (mean 137 ms) were considerably larger than those reported here or the latencies found in neck muscles (50 ms, unpublished results) or lower limbs (Jones and Watt, 1971; Greenwood and Hopkins, 1976; Bronstein et al, 1985) during free fall, these long latency responses were interpreted as "long loop" vestibulo-spinal mechanisms under voluntary control. However, the prolonged delay may represent the additional time required by their subjects to process the visual feed-back of head position provided in the experiment.

In the absence of vestibular function the head can be stabilized in space by following the relative displacement of visual scenes in the opposite direction to that of the body. Thus, it is probable that our patients strategy during the experimental session may have been analogous to following with the eyes and head a slowly moving visual target while sitting stationary. It is noteworthy in this respect that similar time delays between target and head were seen in normal subjects required to pursue targets in an unpredictable manner within a comparable frequency range (Bronstein and Kennard, 1985).

The amplitude of the response was not systematically measured because of the fact that it was under strong voluntary control. The latter is not surprising since animals require two opposing strategies in different circumstances; on the one hand to stabilize the head with respect to the environment (VCR) and, on the other, to stabilize the head with respect to the trunk (CCR) (Peterson et al, 1981; Dutia and Hunter, 1985). Accordingly, a central gating mechanism appears to be needed in the behaving animal in order to re-weigh one or the other during different movement strategies. The existence of such a mechanism could account for the dependence on a relevant instruction needed to obtain compensatory head movements in some of our subjects. It would also help explain the variability which Outerbridge and Jones (1971) demonstrated in the head movement responses of normal subjects to angular velocity steps in the dark; some subjects did not respond at all whereas others displayed nystagmoid head movements synchronous with eye nystagmus. These gating mechanisms also seem to be present in lower mammals since in the absence of normal viewing conditions dynamic VCR responses elicited by trunk rotation are absent (Gresty, 1975; Fuller, 1981).

Limitations of VCR responses seem also to be imposed by the frequency of the stimulus. Thus, with trunk oscillation at much higher frequencies and

accelerations than those used here, no active VCR was identified in the work of Barnes and Rance (1974) and the resulting head stabilization was attributed to the inertial-mechanical properties of the neck-head system alone.

The experiments described here, however, show impaired dynamic stability of the head in space in labyrinthine deffective subjects, which suggests that VCR responses, gated by central mechanisms, operate in normal man.

VESTIBULAR INVOLVEMENT IN SPASMODIC TORTICOLLIS

Spasmodic torticollis (ST) is a motor disorder comprising involuntary activation of the neck muscles resulting in intermittent or persistent deviation of the head. Although the underlying patho-physiology is unknown, the disorder is usually considered to be one of the extra-pyramidal system particularly involving the basal ganglia. On the other hand, in animals vestibular lesions cause striking postural derangement of the head position and in man there are sporadic reports of vestibular abnormalities in patients with spasmodic torticollis (Barre, 1929; Barre and Guillaume, 1930; Hyndman, 1939; Snyder, 1969; Svien and Cody, 1969). Indeed operations on the vestibular system have been used as a treatment for ST in man (Hyndman, 1939; Snyder, 1969; Svien and Cody, 1969; Duane, 1988). More recently, measurements of ocular counter-rolling evoked at low frequency rotation have suggested abnormalities of otolith function in patients with spasmodic torticollis (Diamond et al, 1988). It is not clear,however, whether the vestibular abnormalities found in patients with ST are 1) primarily causative 2) the result of the abnormal head posture or 3) the result of abnormal central interaction with other sensory-motor modalities. The findings described in the previous section, indicating the existence of centrally gated vestibulo-cervical reflexes in normal man, suggest that the old hypotheses that ST might be secondary to perverted or disinhibited vestibular function should be re-investigated.

In considering the problem of the relationship between ST and the vestibular system the following questions have been addressed:

1. Are there vestibular abnormalities in idiopathic cases of ST?
2. Can a primary vestibular lesion give rise to ST?

As an initial attempt to clarify the first point, a review of neuro-otological findings in a group of patients with idiopathic ST will be presented here. The second question will be given attention in the next section where experiments carried out on three patients who developed ST in association with an VIII nerve disturbance will be described.

MATERIAL AND METHODS:

A detailed description of the clinical material and examinations carried out can be found in appendix E . There were 35 patients (18 female and 17 male) with idiopathic ST. Cases with otological diseases or additional neurological signs were not included. The mean age at the time of the neuro-otological examination was 46 years (24 to 70 years) with a mean duration of ST of 4 years (10 weeks to 19 years). In five cases the torticollis was markedly influenced by the position with respect to the gravitational vertical, being more prominent in the upright position in two and while lying supine in three. The direction of the torticollis was specified by the chin position relative to the mid line i.e. chin to the right is right torticollis.

A full clinical neuro-otological examination was carried out. Caloric tests were performed in the presence of visual fixation with the head held in the primary position in 31 patients. Methods and criteria used to establish abnormalities of the various caloric patterns were as in Fitzgerald and Hallpike (1942); 9 patients had, in addition, caloric testing in the dark while their eye movements were observed either with an infra-red viewer or with Frenzel's glasses. Four patients did not undergo caloric testing.

The EOG paper recordings of 24 patients were available and re-evaluated. All the recordings included traces on primary gaze and on 30o deviation to the right and the left both in the presence of visual fixation and in darkness.

OKN was investigated either with a small drum or full field stimulation in 18 patients. Smooth pursuit was assessed in 13 cases. OKN and smooth pursuit were inspected visually for asymmetry of the response from the paper recordings and, when in doubt, slow phase velocity was measured by hand. VOR responses to an impulsive rotation to a velocity of 40°/s were assessed in 13 patients and the duration of the nystagmic response to the start and the stop impulse was measured. Five patients underwent additional sinusoidal rotation in the dark at 0.3 Hz, peak velocity 50°/s, with the head firmly immobilized by means of rigid clamping.

RESULTS:

a) Rotational and caloric testing.

Labyrinthine function assessed by the caloric test (Table 1) or rotation (Table 2) were frequently abnormal. Only 8 of 31 patients (26%) in whom a

TABLE 1

Abnormalities in clinical vestibular testing

	Spontaneous nystagmus n=35	Positional nystagmus n=35	OKN DP n=35	SP n=15	Caloric test* (Fixation) n=31		Caloric test* (Darkness) n=9	
					DP	CP	DP	CP
Ips.	3%	0%	6%	0%	3%	13%	0%	11%
Contr.	11%	6%	21%	0%	39%	19%	78%	0%
Bil.	0%	0%	0%	0%	0%	0%	0%	0%
Normal	86%	94%	68%	100%	26%	26%	11%	11%

n = number of patients examined

Ips.-Contr. = abnormality in the same-opposite direction of torticollis in this and subsequent tables

OKN = optokinetic nystagmus

DP = directional preponderance of nystagmus

CP = canal paresis

SP = smooth pursuit

* Some patients had combined patterns of canal paresis and DP on caloric testing, which resulted in total percentages of cases greater than 100%.

caloric test was performed in the presence of fixation and 1 of the 9 patients (11%) who were also assessed in the dark had normal responses to irrigation. There was a caloric directional preponderance (DP) in the direction opposite to the torticollis in 33% of the patients in the light and 78% of patients in the dark. None of the 13 patients in whom rotational tests were done had a normal symmetrical response. In 76% of the patients a DP in the direction opposite the torticollis was found.

TABLE 2

EOG abnormalities

	Spontaneous nystagmus n = 24		OKN DP n = 18	SP n = 13	Rotation n = 13
	Light	Dark			
Ipsilateral	0%	12%	5%	0%	23%
Contralateral	0%	46%	39%	15%	76%
Bilateral	4%	17%	0%	0%	0%
Normal	96%	25%	55%	85%	0%

The degree of asymmetry found in the vestibular tests seemed to be inversely related to the duration of the disorder. Since the duration of caloric and rotational nystagmus was available in all cases a DP index was calculated using the following formula:

$$\frac{\text{Duration of nystagmus in the direction of torticollis (ds)}}{\text{Duration of nystagmus in the direction opposite to the torticollis (do)}}$$

From this it can be seen that if, ds/do < 1 the DP was opposite to torticollis while if ds/do > 1 the DP is in the same direction of torticollis; ds/do = 1

indicates symmetric responses.

The DP indices of 29 out of 31 cases who had caloric testing in the light were calculated; two cases had to be discarded because in one of them the caloric test had been repeated with contradictory results and, in the other, only one of the 4 irrigations induced nystagmus. The DP indices of caloric test in the light of ST patients with less than a years' duration were 0.77 SD 0.17 (n = 10), between 1 to 5 years = 0.92 SD 0.13 (n = 11) and more than 5 years = 0.97 SD 0.11 (n = 8) (Figure 1). There was a positive logarithmic correlation between the duration of the illness and DP index ($r = 0.55$; $p < 0.01$). This indicates that ST patients show a tendency to have more

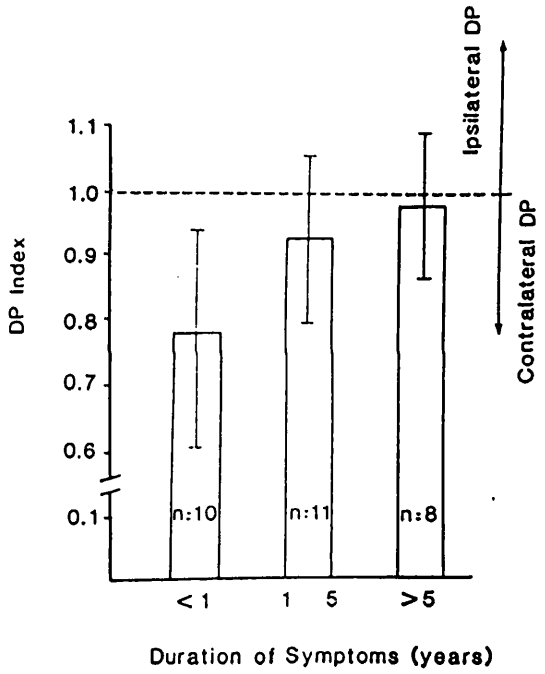


Figure 1. Relationship between duration of torticollis and directional preponderance (DP) indices of caloric test in the light. Means and SD are shown.

active nystagmus (DP) in a direction opposite to the torticollis and that this asymmetry, in the presence of optic fixation, tends to decrease with time. In

appendix E further analysis of these data is presented, indicating that although DP in the presence of fixation shows a progressive reduction with time, the DP in the dark (caloric or rotational) remains unchanged.

In the 5 patients (plus one with dystonia involving the arm not included in the preceding series) subjected to sinusoidal rotation with the head immobilized in the central position the gain of the VOR (slow phase eye velocity/chair velocity) was measured separately to right and left. From Figure 2, a case with left torticollis, it can be seen that nystagmus to the

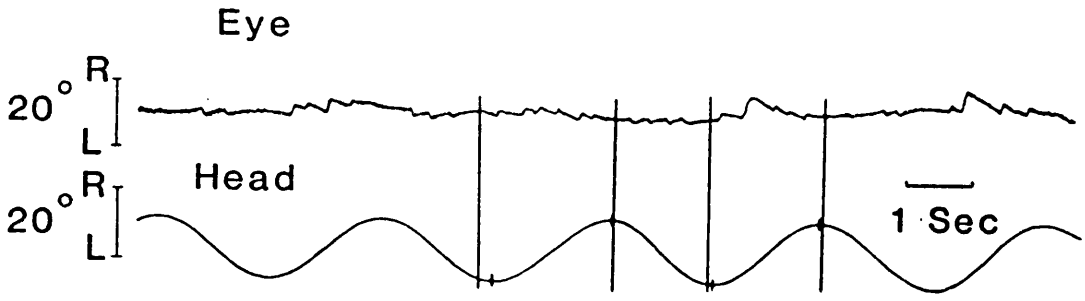


Figure 2. Eye movements in the dark during sinusoidal rotation with the head clamped (vestibulo-ocular reflex, VOR) in a patient with left torticollis. The short and long vertical lines indicate respectively the points at which the head and the slow component of the eye movement reverse direction. During rotation to the left the eyes are advanced relative to the head (phase lead indicated by the larger gap between short and long vertical lines). Thus, hemicycles of right beating nystagmus are of greater magnitude and duration than those to the left.

right was more active and of longer duration than in the opposite direction. All the other cases behaved similarly, VOR gain being higher during the half cycle in which the chair moved in a direction opposite to that of the torticollis [VOR gain during rotation ipsilateral to chin displacement, 0.70 (range 0.28 to 0.94) and contralateral, 0.82 (range 0.33 to 1.08)].

b) Pursuit and OKN testing.

OKN was essentially normal although in 23% (clinically, Table 1) and 39% (on EOG, Table 2) of the patients examined a slight DP in the direction opposite the torticollis was found. Smooth pursuit was normal in the 15 patients examined clinically and slightly abnormal (saccadic) in the direction opposite to the torticollis on EOG in 2 out of 13 patients (15%).

DISCUSSION:

These results show that neuro-otological abnormalities occur in patients with spasmodic torticollis (ST). The most consistent finding is the directional preponderance (DP) of vestibular induced nystagmus opposite to the direction of the torticollis. Since the DP is specified by the fast phase of the nystagmus the vestibular induced slow phase is greater in the opposite direction to the DP and thus in the same direction as the torticollis. The same trend was noted, although not emphasized, by Matthews et al (1978). Such a finding could be interpreted as due to a tonic imbalance of muscle activity both in the neck and the extra-ocular system which tends to deviate the head and the eyes in the same direction. That this directional bias of the eye movements is not a trivial consequence of the head posture or movement is supported by three observations.

First, in normal subjects, forced rotation of the head does not result in a DP of the rotational response, as shown early in Chapter I. Secondly, if the head is fixed during vestibular stimulation in a patient with torticollis the DP persists. Thirdly, if the DP were a consequence of the position of the head it might be expected to remain constant or even increase with time. In fact the reverse occurs in spite of the torticollis persisting. For these reasons it seems likely that the DP of induced nystagmus is more fundamentally related to the torticollis. From the available evidence the type of neuro-otological abnormalities found indicate that the vestibular system

itself, rather than other ocular-motor sub-systems, is affected. This is suggested by the much higher incidence of DP or spontaneous nystagmus in the dark than in the light, indicative of a preserved capacity to compensate for vestibular asymmetry by fixation, and by the relative integrity of the more purely visuo-motor tasks such as smooth pursuit and OKN.

At first sight since occasional patients have been reported to develop ST following an 8th nerve insult, it might be argued that the torticollis and DP stem from a vestibular end organ, 8th nerve or vestibular nuclear disturbance. Although this is a superficially attractive hypothesis, to be further explored in the next section, it is unlikely to be true since the vast majority of patients have no overt 8th nerve symptomatology. It is more likely that the neuro-otological abnormalities are due to a central disturbance of posture which also affects the tonus balance of the vestibulo-ocular system. The vestibular system has complex connections within the brain stem, thalamus and cortex where interaction with other sensory modalities can occur (Muskens, 1922; Montandon, 1964; Denny-Brown, 1968; Spiegel et al, 1965; Potegal et al, 1971). It is possible that the abnormality in ST is a break down of these central connections and particularly their interaction with other modalities signalling posture of the somatic musculature controlling head and eye position. Such a break down is consistent with a perverted or exaggerated response to sensory stimuli in patients with ST and would account for the observations that patients are able to control their head position by cutaneous stimulation (antagonistic gesture or "geste"), have increased sensitivity to proprioceptive input (Podivinsky, 1968) and for the effect of position with respect to gravity on the torticollis (Denny-Brown, 1968). Finally such a break down might account for those patients who do have an VIII nerve disturbance that apparently precedes the development of ST. It is possible that in such patients there is a

pre-existing abnormality of the type causing ST and that a critical alteration of vestibular function caused a break down of the patient's compensation sufficient to allow ST to become manifest.

SPASMODIC TORTICOLLIS FOLLOWING UNILATERAL VIII NERVE LESIONS. Neck EMG modulation in response to vestibular stimuli.

In the previous section data were presented from patients with spasmodic torticollis (ST) who did not have a previous history of vestibular disease. Since there have been several reports on the association between ST and vestibular lesions (Barre, 1929; Barre and Guillaume, 1930; Hyndman, 1939; Svien and Cody, 1969) three patients were selected in whom torticollis followed an insult to the vestibular system (VIII-ST) in an attempt to clarify a possible aetiological relationship between the two.

In addition to routine neuro-otological assessment neck EMG was recorded whilst various types of vestibular stimuli were delivered. It was expected that if there was a connection between the torticollis and the vestibular system some common clinical features would be present and the EMG activity from the dystonic muscles might be modulated by vestibular stimulation in a consistent way.

MATERIAL AND METHODS:

Case reports are described in detail in appendix F and a summary presented in table 1. In brief, case 1 was a 57 year old man with a left acoustic neuroma removed at the age of 52 years and torticollis to the right. Case 2 - A 62 year old man whith trigeminal neuralgia on the right, occasional blurred or double vision, dizziness and torticollis to the left. A CT scan showed the basilar artery looping into the right cerebello-pontine angle. Case 3 - A 52 year old man who at the age of 45 underwent a right vestibular neuronectomy for the treatment of vertigo. Six months after the operation he developed

torticollis towards the right. In the 3 patients the torticollis was clinically indistinguishabble from idiopathic ST.

Control groups:

Two groups of subjects were used as controls. The first consisted of 6 normal male subjects, aged between 21 and 55 years, and the second of six patients with idiopathic ST. The latter group comprised three males and three females aged between 32 and 59 years, with no previous history of otological disease; two had previously undergone a full neuro-otological investigation and had a directional preponderance of vestibular nystagmus in the direction opposite to the chin deviation.

Electro-myography:

Surface Beckman silver cup electrodes were used to record the EMG from the sterno-mastoid on both sides of the neck. Raw EMG was displayed on-line by means of an ink jet recorder and collected on magnetic tape for subsequent processing on a Fourier analyzer (Solartron 1200) which displayed the power spectra and calculated the energy dissipated by the signal (power in band between 10 and 500 Hz) in volts^2. The frequency limit of the system was either 313 or 625 Hz according to the tape speed used. The periods analyzed were approximately 30 s and usually included 30 averages. The first 10 s of EMG after each new vestibular stimulus was applied was not analyzed to allow for stabilization of the recording. Abnormally high peaks of activity at 50 Hz were deducted from the total power because this was always correlated with clearly identifiable noise on the paper recordings.

Vestibular stimulation:

Vestibular modulation of the neck EMG was studied in response to tilt with respect to gravity (otolith stimulation) and to horizontal rotation (semicircular canal stimulation). In order to obtain quantifiable body tilt a bi-axial gymbal was used; the patients sat on a chair which restrained their arms and pelvis. The trunk was strapped in with an "X" shaped seat belt; the legs and feet were also fitted with belts. The head rested backwards and was fixed, when required, with a binaural clamp. The position of the chair was monitored with a potentiometer. The subjects were tilted backwards in steps of 30° up to a maximum of 90° in the sagittal plane with the head resting backwards freely. Then the head was clamped and the patients tilted 45o backwards-forwards (sagittal plane) and right-left (coronal plane). These displacements were smooth and slow; the subjects stayed in the new position for at least a minute before being moved again. The effect of vision upon the EMG was assessed by obtaining records with eyes open and closed.

Rotational stimuli were delivered in the dark with the revolving chair rotating around the vertical axis at a constant acceleration of 2 to 3°/s-2 up to a maximal velocity of 100°/s. This velocity was then maintained for about 2 minutes during which the room lights were turned on and off for periods of about 45 s in order to assess the role of optokinetic stimulation. The procedure was carried out at least twice to the right and twice to the left resulting in a total constant acceleration duration in each direction of at least 132 s. During rotation the head was in contact with an occipital rest but was not clamped. The subjects were instructed to relax and keep their eyes open.

RESULTS:

A summary with the main clinical and neuro-otological findings of the VIII-ST patients is presented in table 1. There was no consistent

relationship between the side of the vestibular deficit and that of the torticollis. In cases 1 and 3 the neuro-otological findings, apart from the saccadic pursuit in the former, can be explained on the basis of the VIII nerve section. In contrast, in patient 2 the marked directional preponderance

TABLE 1

Clinical and neuro-otological summary in patients 1, 2 and 3 with ST following VIII nerve lesions

	VIII lesion	ST (chin)	Spont. nystagmus	OKN	SP	Caloric test	Rotational test
1	L	R	2°R	R DP	Saccadic (R > L)	L CP R DP	R DP
2	R	L	Nil	R DP	Saccadic	R DP	Not available
3	R	R	Nil	Normal	Normal	R CP L DP	Hypoactive bilaterally

OKN = Optokinetic nystagmus
SP = Smooth pursuit
DP = Directional preponderance of nystagmus
CP = Canal paresis

of caloric nystagmus in the direction opposite to that of the chin deviation is typical of idiopathic ST; although there was no unequivocal indication of peripheral involvement in the vestibular tests, the patient's symptoms and the radiological findings provide good evidence of unilateral vestibular impairment.

The results of EMG while the subjects were sitting up relaxed with the head unrestrained are presented in table 2. As expected these resting values, expressed as a proportion of maximal voluntary contraction, are increased in both patient groups by an order of magnitude. Due to this difference in the

resting EMG, it was necessary to normalize the data in order to compare the effects of vestibular stimulation. Thus, for each tilt and rotation experiment the mean of all the EMG activity values in the upright, resting

TABLE 2

Resting EMG*: Sternomastoid

NC =	n = 11	1.03 x	10^{-2} SD	1.86 X	10^{-2}
ST =					
Affected	n = 5	1.27 x	10^{-1} SD	9.82 X	10^{-2}
Unaffected	n = 4	3.48 x	10^{-1} SD	3.79 x	10^{-1}
VIII-ST =					
Affected	n = 3	1.06 x	10^{-1} SD	8.43 X	10^{-2}
Unaffected	n = 3	1.71 x	10^{-2} SD	2.04 X	10^{-2}

* Expressed as the ratio: resting EMG/EMG during forced voluntary head turn.

NC = normal controls
ST = Idiopathic spasmodic torticollis controls
n = number of muscles satisfactorily studied
Affected = more affected sternomastoid; contralateral to the chin deviation
Unaffected = least affected sternomastoid; ipsilateral to the chin deviation

position was calculated for each individual muscle and subject and this was taken as their individual basal value. Two main difficulties were encountered during data analysis, namely that the VIII-ST group was small and that there were important individual variations within both patient groups. As the latter produced considerable skewing of the data, the medians and interquartile ranges were plotted to give a clearer picture of the trends present in the patient group, as shown in figure 1 which summarises all the results for the tilting experiments. The detailed data is presented in tables 3 to 5 of the appendix F .

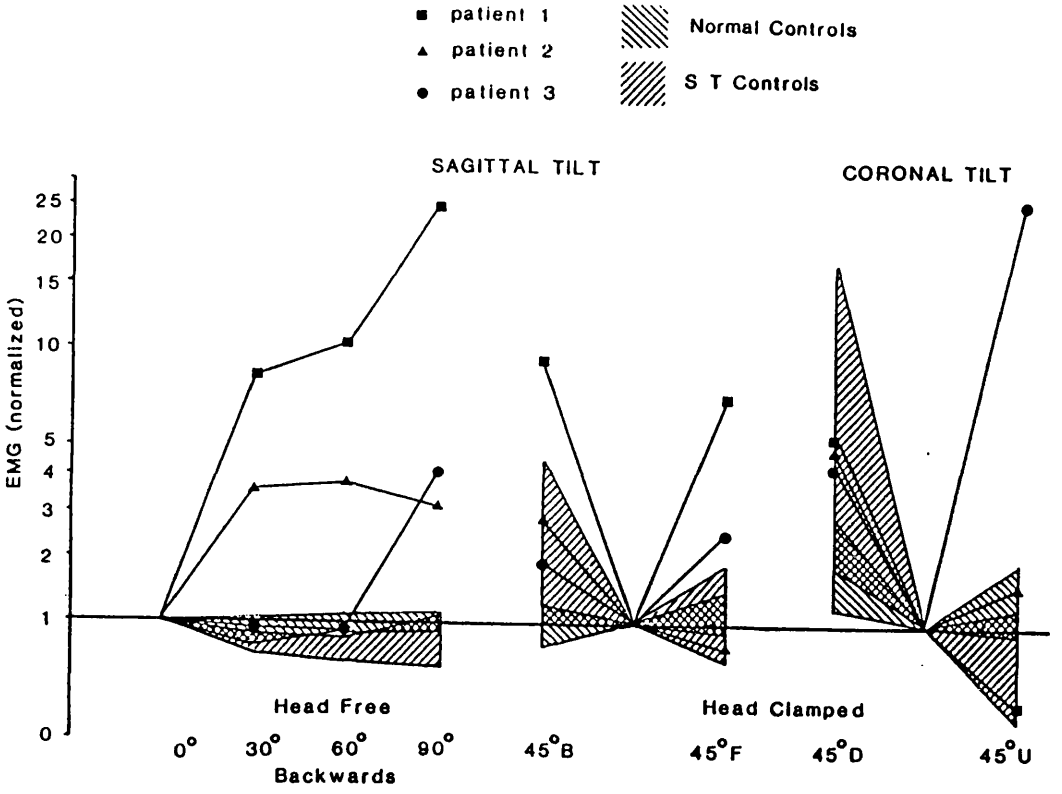


Figure 1. EMG of the more affected sternomastoid in response to tilt backwards (B) forwards (F) side down (D) or side up (U). Shaded areas represent the interquartile range in the normal and ST control groups. Median values are presented for the VIII-ST patients. EMG was normalised for each subject and test condition so that a value of 1 represents the upright position.

The greatest difference between the 3 groups tested was found during backwards tilt with the head free. In normal subjects the effects were negligible but in the VIII-ST patients a marked increase of EMG activity usually occurred. This was related to the degree of tilt and was maximal in the muscle most affected clinically (fig 2). Two of the three patients were tested on more than one occasion with similar results. In no case did a ST patient have a comparable enhancement of the EMG in the more affected muscle.

On the contrary, two ST patients had a significant reduction of muscle activity as they were tilted backwards (fig 3). Activity in the clinically less affected muscle activity was not altered by this manoeuvre in 5 of the 6 ST patients.

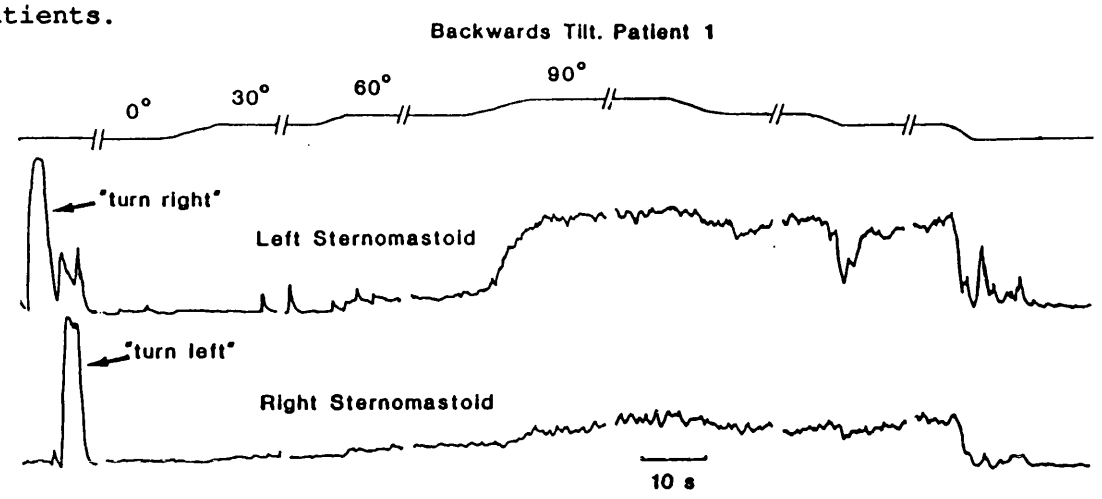


Figure 2. Rectified and integrated EMG in a patient with a left acoustic neuroma removed and ST with chin rotation to the right. The patient was tilted backwards with his head freely resting. "Turn right" and "turn left" are voluntary forced head turns used as calibration. Record interruptions, shown with parallel lines, were between 10 - 40 seconds.

During 45° tilt backwards or forwards with the head clamped, neck EMG usually increased in the VIII-ST patients. This effect was also commonly seen in the ST group but not in the normal control group. Since ST patients did not show EMG enhancement during sagittal tilt with the head free it is impossible to say how much of this effect was due to the tilt and how much due to the forced fixation of the head. Eye opening or closure did not affect the sagittal tilting responses.

Tilt in the coronal plane also had to be carried out with the head clamped. During this experiment all groups produced a similar pattern of EMG responses. Thus when the subjects were tilted to the right it was mainly the right sternomastoid which was activated as if opposing the tendency of the head to turn passively in that direction and vice versa on tilting to the

left. This response was more prominent in the patient group than in normal subjects and especially in the clinically more affected muscles. Although the subjects were encouraged to relax it is not clear whether this EMG modulation was the result of voluntary or involuntary activity.

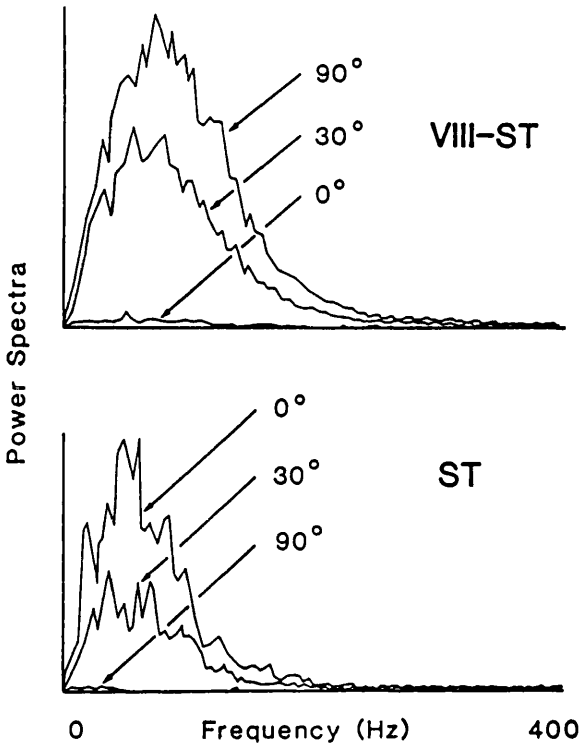


Figure 3. Power spectra of EMG from the more affected muscle in patient 1 and in a ST control patient at various angles of tilt backwards with the head free. Power was measured in V^2 and normalised to 0^o of tilt.

During rotational tests no consistent modulation of the EMG was found in the normal subjects or the VIII-ST patients. Some ST patients, however, did have a rotational modulation of their muscle activity. From what is known of the vestibulo-ocular and vestibulo-cervical reflexes, it is conceivable that during acceleration say to the right, the head would turn to the left. Thus, it was considered that EMG modulation consistent with stimulation of the horizontal semicircular canals occurred either when the sternomastoid

ipsilateral to the direction of the acceleration increased its discharge or the activity in the contralateral muscle diminished (table 2). If a change of at least 10% of EMG activity is used as a criteria, a consistent vestibular EMG modulation occurred 1 in 8 instances (12%) in the normal subjects, 1 in 6 (16%) in the VIII-ST cases and 6 in 11 (55%) in the ST patients. There was no systematic optokinetic modulation of the EMG in any group nor were there any

TABLE 2

EMG* during horizontal rotation

		Ipsilateral	Contralateral	Cases with corresponding modulation of EMG
NC	n = 8	1.08 SD 0.21	1.16 SD 0.28	1 - (12%)
ST				
Affected	n = 5	1.23 SD 0.71	1.02 SD 0.60	3 - (60%)
Unaffected	n = 6	1.13 SD 0.32	1.16 SD 0.42	3 - (50%)
Patient 1		1.20	0.33	Yes - (33%)
Unaffected		0.77	1.31	No
Patient 2				
Affected		0.46	0.73	No
Unaffected		0.93	1.56	No
Patient 3				
Affected		0.03	0.21	No
Unaffected		1.02	1.19	No

* Expressed as the ratio: EMG during acceleration/EMG during periods of no acceleration
Ipsilateral = right sternomastoid during rotation to the right or left sternomastoid during rotation to the left
Contralateral = right sternomastoid during rotation to the left or left sternomastoid during rotation to the right

consistent differences in the frequency content (power spectra) of the EMG in the various groups. Highest levels of activity were in the region between 50-90 Hz with minimal power beyond 200 Hz.

DISCUSSION:

The possible existence of a link between ST and the vestibular system has interested neurologists for a long time and, not infrequently, isolated cases of "otogenic" ST have been reported (Barre, 1929; Barre and Guillaume,

1930; Hyndman, 1939; Svien and Cody, 1969). However, some of these cases had irritative labyrinthine lesions with marked fluctuations of the symptoms in whom a precise topographic diagnosis was difficult to establish. In contrast to this, in the present series two of the three patients undoubtedly had unilateral destructive lesions (nerve division in cases 1 and 3). The torticollis in these two patients was towards the right in both cases in spite of the nerve section being on the right in one case and the left in the other, arguing strongly against the tempting view that unilateral vestibular lesions can produce ST by virtue of an asymmetric vestibulo-collic reflex. This does not necessarily mean, of course, that the vestibular system and ST do not influence each other.

The present investigations show that the three VIII-ST patients differ in their postural control from the cases of idiopathic ST and normal subjects. In particular the response of the cervical muscles to backwards tilt with the head free was consistently different in the three groups of subjects studied. In the normal controls this manoeuvre did not modify the resting EMG and in the ST group either it did not change the activity significantly or reduced it. In the three VIII-ST patients neck EMG was markedly enhanced especially that from the more affected sternomastoid. It is known from animal work that these effects are probably dependent upon otolith macular activity. Magnus (1924) described static vestibular reflexes in which maximal tonus in the decerebrate preparation occurred in the supine position and minimal tonus while prone. More recent studies have indicated that it is in these positions that macular units reach their maximal and minimal firing frequencies respectively (Loe et al, 1973; Fernandez and Goldberg, 1976). Since the utricular macula is approximately horizontal when the animal is standing this position is also the point of optimal sensitivity, i.e. maximal change of discharge frequency per angle of head deviation relative to gravity.

It is reasonable to expect that during backward tilt macular discharge will activate both sternomastoids in order to keep the head upright or at least, in the absence of a supporting surface, to keep it aligned with the trunk. Clearly, if one VIII nerve is sectioned, tilt backwards will produce a maximal imbalance of macular input to the CNS since one macula will greatly increase its activity while the other is silent. Such a patient who also has ST may be reasonably compensated in the upright position because the remaining utricle is in its optimal position for signalling changes of linear acceleration and is discharging at a moderate rate.

The situation is different in the supine position. In these circumstances the utricular macula will be at its maximal firing frequency and minimal sensitivity. Unilateral absence of vestibular function in otherwise neurologically normal subjects does not seem to produce a significant increase in the EMG; in 3 such patients tested, sternomastoid EMG increased by a factor of 1.22 in the muscle contralateral to the vestibular loss and 1.09 in the ipsilateral one (median values) when tilted from 0 to 90° (unpublished observations). However, in the presence of deranged central control of head position such as occurs in ST, this could well lead to a pathological enhancement in the neck EMG discharge. Thus, it is likely that the abnormal tilt/EMG reaction present in the VIII-ST group is due to the unique combination of two different factors: imbalance of peripheral macular signals (due to the VIII nerve lesion) and perverted central control of head posture (due to basal ganglia dysfunction).

In summary, the cases presented here do not indicate that a peripheral labyrinthine disorder can be held directly responsible for the clinical picture of ST. However, there is some evidence that an VIII nerve lesion can modify, aggravate and perhaps precipitate ST by inducing further disruption in the processing of sensory information about head position. As far as

management of patients with ST is concerned, these investigations suggest that operations on the vestibular system are unlikely to be therapeutically effective - indeed aggravation of the torticollis might be expected.

FURTHER INVESTIGATIONS ON THE INTERACTION BETWEEN HEAD POSTURE AND THE VESTIBULAR SYSTEM IN SPASMODIC TORTICOLLIS: The VOR before and after botulinum toxin injections.

The significance of vestibular abnormalities in ST is still uncertain. In particular, it is not definitely established whether they are a reflection of an underlying abnormality responsible for the torticollis, or whether they are secondary to the abnormal head posture.

The recent development of botulinum toxin (Tsui et al, 1986; Stell et al, 1988), which blocks neuro-muscular transmision, to treat such patients allows further investigation of this question by analyzing vestibular function before and after the correction of the abnormal head posture.

PATIENTS AND METHODS:

Eight patients with spasmodic torticollis causing predominant horizontal rotation of the head were studied (table 1). None of the patients had other abnormalities on routine neurological and clinical oto-neuro-ophthalmological

TABLE 1

Patient characteristics

Patient No	Sex	Age (years)	Disease duration (years)	Pre-treatment Torticollis*	3 weeks after Botulinum toxin	10 weeks after
1	M	35	6	15°L	5°L	0°
2	M	40	12	35°L	25°L	25°L
3	M	42	5	50°L	35°L	25°L
4	F	31	8	60°L	35°L	15°L
5	F	53	22	40°L	10°L	15°L
6	M	56	20	30°L	20°L	20°L
7	F	47	8	50°R	30°R	15°R
8	F	59	3	70°L	0°	20°L

* The degree of deviation of the chin (in degrees), either to the right (R) or left (L), in the horizontal plane is shown before, and 3 and 10 weeks after injection of botulinum toxin.

examination. There were 4 females and 4 males, with a mean age of 44 years (range 31 - 59). Mean disease duration was 9.5 years (range 3 - 22). Seven patients had rotation of the chin to the left and one to the right. Medications were continued as long as they had not been commenced within two months of the study. The angle of head rotation and/or tilt was measured with a protractor.

Eye movement recordings and horizontal rotation were obtained with the standard procedure already described. The vestibular stimulus consisted of sinusoidal rotation in the dark at a frequency of 0.3 Hz and peak velocity of 50°/s. Slow phase velocity of nystagmus during sinusoidal rotation was measured manually and at least 6 slow phases in each direction were averaged to calculate the gain of the vestibulo-ocular reflex (VOR), defined as the ratio of peak eye velocity to peak head velocity. A qualitative observation of the phase of the VOR was made according to whether the reversal of the direction of the slow component preceded or followed the reversal of chair direction; this was then expressed as either a phase lead or lag respectively. In addition, velocity steps of 40°/s to the right and left in the dark were delivered, and the peak velocity and the time constant of the slow component of nystagmus were measured. Time constant was defined as the time taken by the initial peak eye velocity to drop by 63%.

All patients were injected by Dr. R. Stell at the National Hospital, Queen Square, with botulinum toxin in a dosage of 500 mouse units to each of the two most active muscles selected either clinically or on EMG. The patients were studied just prior to injection, and again at 3 weeks and approximately 10 weeks post-injection. Twenty normal subjects (age range 20-61 years) underwent sinusoidal rotation and 13 of these also underwent step rotation, for comparison.

RESULTS:

Figure 1 shows raw EOG records of patient 8 during sinusoidal rotation pre and post-treatment. This patient's head rotation was 70° to the left pre-treatment, and 0° and 20° to the left at 3 and 10 weeks respectively. On rotation of the chair to the right the slow phase velocity of the induced nystagmus persistently exceeded the velocity of the nystagmus induced by rotation to the left. There was no alteration in this asymmetry in the nystagmic response following treatment.

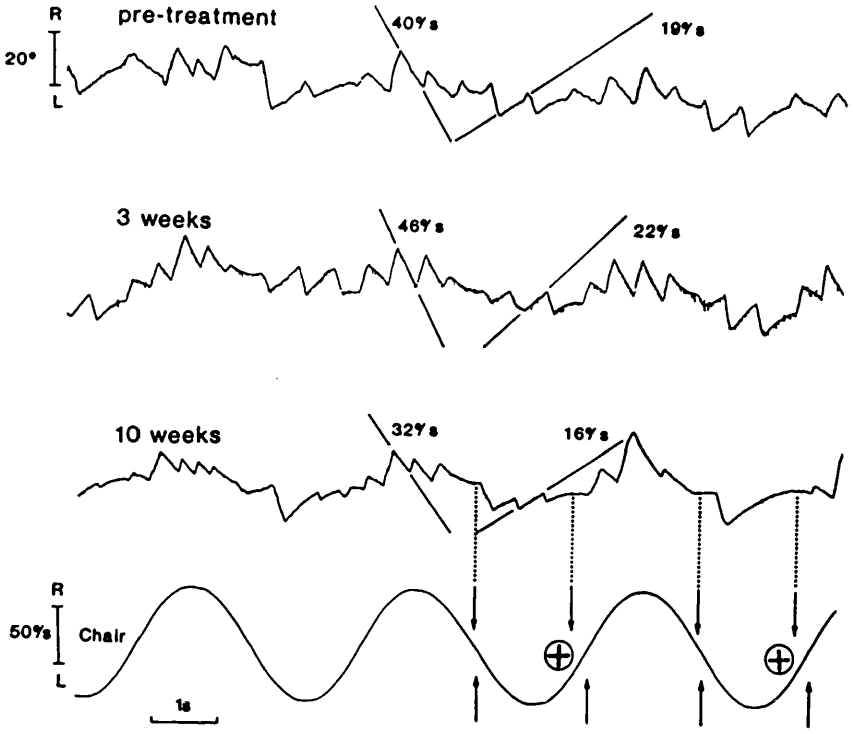


Figure 1. Eye movements elicited by sinusoidal rotation in the dark in patient with torticollis (chin to the left) before, and 3 and 10 weeks after correction of head posture with botulinum toxin. Slow phase velocities to the left (that is, during nystagmus to the right), are greater than in the opposite direction in all instances. Bottom right: the upward arrows indicate the zero velocity points on the chair velocity trace (at the time of peak chair displacement), and the downward arrows indicate the points where the slow phase eye movements reverse direction. The + sign indicates a phase lead of the change in direction of the slow phase of the induced vestibular nystagmus with respect to peak chair displacement during leftward rotation.

The results of sinusoidal rotation for all patients are summarised in table 2. For all patients with torticollis, the mean pre-treatment VOR gain (right and left combined) was 0.73 (SD 0.17), and the control value was 0.66 (SD 0.16); no patient lay outside 2 standard deviations from the mean of the normal subjects.

TABLE 2

VOR gain (to right - R, or left - L) during sinusoidal rotation before, and 3 and 10 weeks after treatment with botulinum toxin

Patient No	Torticollis	Pre-treatment		3 weeks		10 weeks	
		R	L	R	L	R	L
1	L	0.97	0.73	0.27	0.23	0.40	0.30
2	L	1.04	0.55	1.28	0.69	0.80	0.54
3	L	0.51	0.39	0.54	0.36	0.36	0.26
4	L	0.75	0.85	0.76	1.06	0.62	0.80
5	L	1.00	1.05	0.83	0.94	0.68	0.80
6	L	0.82	0.59	0.82	0.53	0.55	0.34
7	R	0.59	0.53	0.78	0.66	0.86	0.76
8	L	1.01	0.61	1.08	0.68	0.68	0.56

In order to assess the significance of the asymmetries found, the formula:

$$\frac{\text{(VOR gain to the right - VOR gain to the left)}}{\text{(VOR gain to the right + VOR gain to the left)}} \times 100$$

was applied. Confidence limits were set at two standard deviations from the mean of the normal population. The control group had a mean value of 3.94% (SD 3.34). Five patients (cases 1,2,3,6,8) had an asymmetry of VOR gain with the more active nystagmus contralateral to the direction of the torticollis (chin), but this was within the confidence limits in patient 1. Two patients (cases 4 and 7) had a more active response ipsilateral to the torticollis but in none of these was it significant. Patient 5 had no asymmetry despite a marked degree of torticollis. There was no clinical difference between these subgroups of patients. In all patients with a significant VOR gain asymmetry a phase lead for the slow phase of the vestibular nystagmus was found during chair rotation in the direction of the lower gain (see figure 1, bottom right), the net result being a prolongation of the duration of the nystagmus in the direction of the higher VOR gain.

Figure 2 summarises the change in head posture and figure 3 the asymmetry in VOR gain following botulinum toxin injection in all patients. For graphic purposes VOR symmetry is presented as the ratio between VOR gain ipsilateral divided by VOR gain contralateral to chin deviation, so that cases with VOR more active in the same-opposite direction of the torticollis are clearly identified. Arbitrarily, in the normal control group right VOR gain was divided by left VOR gain.

It can be seen that a considerable improvement of head posture was achieved in all patients but, despite this, the VOR asymmetry persisted essentially unchanged. A paired Student's "t" test confirmed that changes in head posture between pre and 3 weeks post treatment were statistically significant ($t=4.89$; $p<0.01$) whereas changes in VOR asymmetry were not ($t=1.43$; $p>0.05$). Patient 7 increased the degree of VOR asymmetry (more active ipsilateral to the torticollis) post-injection despite the improvement in head posture.

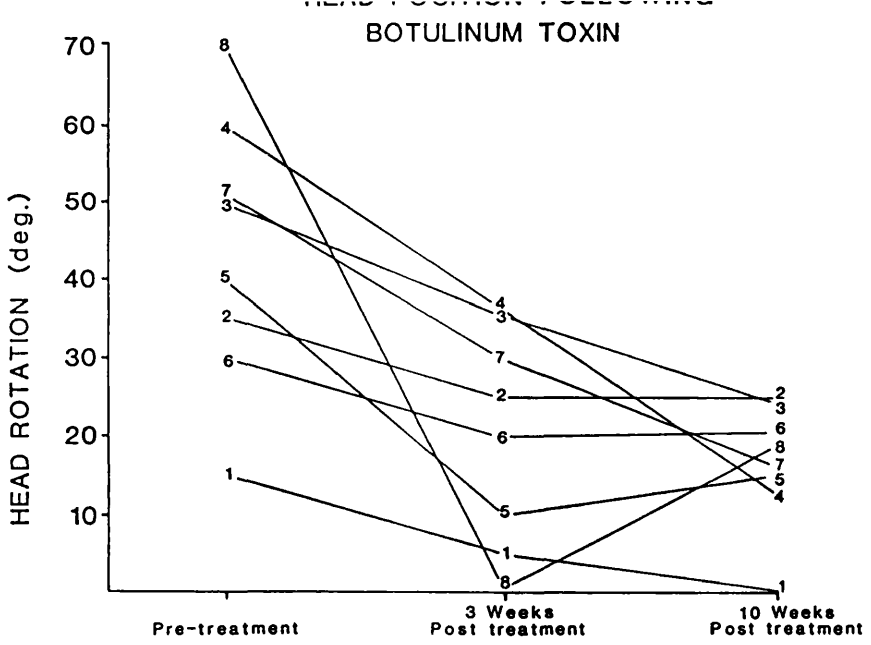


Figure 2. Head position due to torticollis (horizontal rotation in degrees) before, and 3 and 10 weeks after botulinum toxin treatment. The numbers identify the individual patients as in table 1.

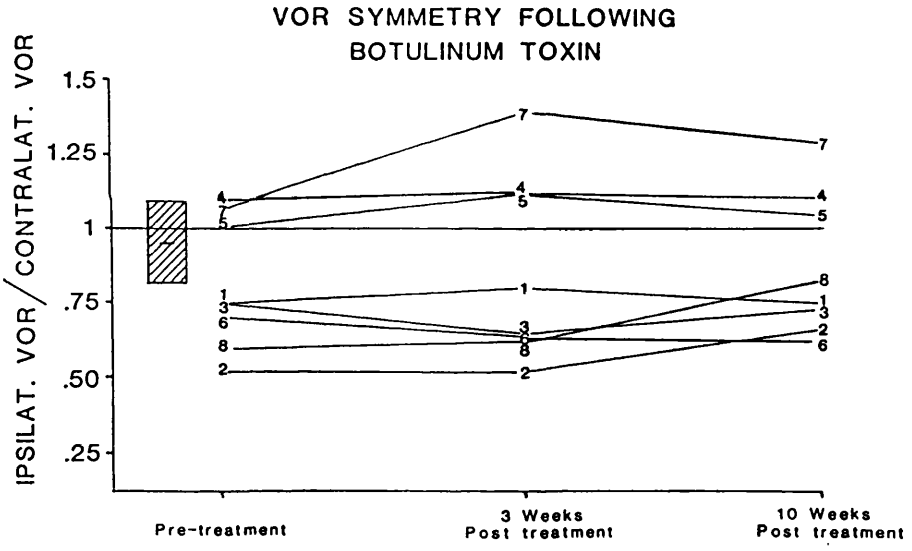


Figure 3. Symmetry of the VOR during sinusoidal rotation before and 3 and 10 weeks after botulinum toxin, assessed as the ratio between VOR gain ipsilateral to the torticollis and VOR gain contralateral to the torticollis. Cases with a value < 1 have a VOR more active during rotation in the direction opposite to the chin deviation due to the torticollis. The hatched area represents mean ± 2 SD of the normal controls after dividing VOR gain to the right by VOR gain to the left. The numbers identify the individual patients as in table 1.

The results of the velocity step rotational test are shown in table 3. These were in general agreement with those of the sinusoidal test. The mean slow phase velocity (right and left combined) for control subjects was 32.04 °/s (SD 8.01) and for the patients was 26.45 °/s (SD 5.86). There was no statistical difference between these values ($t=1.68$; $p>0.05$). The mean time constant (tc) for control subjects was 13.35 (SD 4.45) and for patients 14.98 (SD 2.34); this difference was not significant ($t=0.95$ $p>0.05$). The formula used above to assess the significance of VOR asymmetry was applied to peak slow phase velocity of nystagmus. The control group had a mean value of 2.00 % (range -7.32 to 15.22). Six patients (cases 1,2,3,4,6,8) had an asymmetry of the step rotational response with the more active nystagmus contralateral to the direction of the torticollis; in 3 of these (cases 3,4,8) the values lay outside the normal range. Two patients (cases 5,7) had slightly more active nystagmus ipsilateral to the torticollis but in both of these it lay within the normal range. In 3 patients (cases 2,3,8) there was a considerable asymmetry of the time constant and in these cases it was shorter with rotation in the direction of the lower VOR gain and peak slow phase velocity of

TABLE 3

Peak velocity (PV) (°/s) and time constant (TC) (s) of nystagmus during velocity step rotation, before and 3 and 10 weeks after treatment with botulinum toxin

	Pre-treatment				3 weeks				10 weeks			
	(PV)		(TC)		(PV)		(TC)		(PV)		(TC)	
Patient No-Side	R	L	R	L	R	L	R	L	R	L	R	L
1L	33.5	27.5	13.5	12.5	53.5	40.5	14.5	14.0	23.0	16.5	9.8	8.0
2L	37.5	30.0	20.0	10.5	49.5	39.0	18.0	10.5	45.0	40.0	16.0	10.0
3L	23.0	16.5	16.5	11.0	45.5	37.5	18.0	12.5	28.0	20.0	20.0	22.5
4L	29.5	21.5	13.5	10.0	38.0	55.0	17.0	20.0	27.0	38.5	09.5	14.5
5L	33.0	35.0	20.0	18.0	42.0	37.0	17.5	22.0	32.0	34.0	23.5	23.0
6L	31.0	25.0	17.5	15.0	35.5	30.5	16.5	12.0	17.0	12.5	19.0	12.5
7R	23.0	21.5	17.0	16.7	63.5	59.0	12.0	65.0	36.0	32.0	17.5	23.0
8L	28.0	18.0	20.5	7.5	25.0	22.0	15.0	11.5	20.5	7.5	30.0	27.0

nystagmus. There was no significant change in the symmetry of peak velocity ($t=0.47$; $p>0.05$) and time constant ($t=1.77$; $p>0.05$) of vestibular nystagmus before and after treatment.

DISCUSSION:

This study confirms the findings presented in a previous section as to abnormal vestibular function in some patients with spasmodic torticollis. Four out of the 8 patients with predominantly rotational torticollis had a significant asymmetry of the VOR, with the more active nystagmus occurring in the direction opposite to that of chin deviation. There was good agreement between the various parameters measured during testing; a higher VOR gain in one direction during sinusoidal rotation usually was accompanied by a phase lead in the opposite direction. In addition, during the velocity step, there was a greater peak slow component velocity with a longer time constant contralateral to the torticollis. These results provide further quantitative support to the clinical review presented earlier in this chapter, in which approximately 70% of ST patients showed a directional preponderance of vestibular nystagmus in the direction opposite to the torticollis (slow component of the VOR more active ipsilateral to the direction of the torticollis). As the slow component is generated by the vestibular system, this may indicate that in ST there may be a tonic bias of neural activity affecting cervical muscles and vestibulo-ocular balance in the same direction.

Following botulinum toxin injection, improvement in head posture was achieved in all patients. This benefit reached its maximum one week after injection and remained relatively stable until the patients were restudied 10 weeks later. Despite this sustained improvement in head posture, there was no change in the VOR asymmetry evident in either the sinusoidal or step rotational test, suggesting that the abnormal VOR is not secondary to the head

posture per se. This conclusion is also supported by the following evidence, 1) in normal subjects, voluntary forced head rotation has no consistent effect on the symmetry of the VOR as shown in chapter I; however, acute voluntary head rotation may not be strictly analogous to chronic involuntary torticollis 2) all patients were studied with their heads held in an almost neutral position, particularly after botulinum toxin treatment, which considerably facilitated adequate head positioning in the rotating chair, 3) preliminary recordings of the cervico-ocular reflex in ST patients suggests that an abnormal input from the neck proprioceptors onto the vestibular nuclei cannot be held responsible for the asymmetric VOR described (see Figure 1 in appendix H). It may be concluded that these asymmetric vestibular responses may be directly related to the underlying disorder producing the abnormal head posture in spasmodic torticollis.

There are at least two ways in which spasmodic torticollis and the vestibular system may relate to each other. First, it has been postulated that the torticollis may be due to hyperactive, disinhibited or perverted vestibulo-collic reflexes (VCR). Suggestive evidence for this conclusion was provided by Denny-Brown (1968), who described patients in whom the severity of their torticollis was significantly modulated when turning the head. However, a difficulty with this line of argument is that the influence of the VCR upon head posture diminishes as one ascends the phylogenetic scale. Although evidence has been presented (section 2, this chapter) that vestibular signals do contribute to human head stability, it seems that hyperreactivity of the VCR in patients with torticollis does not occur (section 4, this chapter). Whilst neck EMG activity during rotation at constant angular acceleration was shown to modulate in a proportion of patients, this was not of a magnitude sufficient to indicate a causal relationship between VCR and torticollis.

Similarly, an analysis of head movements evoked by random whole body oscillation has not provided evidence for a major effect of the VCR in these patients (Gresty, 1987). The fact that the mean VOR gain of our patients was essentially equivalent to that of the normal control group also argues against hyperexcitable vestibular responses. Accordingly, it could be suggested that modulation of the torticollis on turning the head, noted in some patients, may represent the response to a specific motor act rather than to the vestibular stimulus itself.

A second possibility is that the VOR abnormalities in spasmodic torticollis are a consequence of a more generalised disruption of the mechanisms controlling head posture and movement. Such a process would be expected to involve not only vestibular mechanisms, but also the processing of other sensori-motor signals relevant to head position, which might explain the commonly associated finding in spasmodic torticollis of exaggerated responses to somato-sensory cues (Denny-Brown 1968; Podivinsky, 1968). This probably underlies the mechanism of the "antagonistic gesture" used by many patients to improve their head posture. Further support for a more diffuse disorder is the finding of abnormal brain stem reflexes e.g. blink reflexes (Tolosa and Montserrat, 1985) in some patients with ST. These abnormalities may be explained by malfunction of reticular polysynaptic interneuronal pathways (Tolosa et al, 1988). The intimate relationship between the reticular formation and the vestibular system is well known (Fukushima et al, 1979; Wilson and Melville Jones, 1979); for example, most eye movement related neurons in the reticular formation are known to send descending branches which influence the cervical musculature coordinating head and eye motion (Buttner-Ennever and Holstege, 1986) and, reciprocally, descending vestibular signals significantly influence reticulo-spinal pathways (Fukushima et al, 1979). Of particular relevance are animal studies in which selected reticular nuclei

have been lesioned to produce experimental torticollis and tonic eye deviation (Tarlov, 1969; Foltz et al 1959; Fukushima et al 1985; 1987). The most notable of these reticular nuclei is the Interstitial Nucleus of Cajal, which has bi-directional connections both with the vestibular nuclei and the basal ganglia. Unfortunately, detailed vestibular tests of animals with lesion-induced torticollis have not been reported, so that at present the relevance to human disease is not clear. Diseases affecting the basal ganglia in man are known to produce dystonia (Rothwell and Obeso, 1987), and could do so via the projections to structures such as the Interstitial Nucleus of Cajal.

SUMMARY

- The presence of a vestibulo-cervical reflex in man has been open to debate since peripheral and central vestibular lesions lead to abnormal head posture in animals but only rarely in man. The clinical literature on the subject has been reviewed in the introductory section of this chapter.

- In order to assess a possible contribution of dynamic vestibular signals to head spatial stability, horizontal head movements in response to unpredictable horizontal oscillations of the trunk were studied in 6 patients with absent vestibular function and in 6 normal subjects. In order to obtain compensatory (i.e. stabilizing with respect to earth) head movements all subjects were required to look at an earth fixed target using their eyes and head. The turning points (maxima and minima) were determined from head and trunk position records. It was found that normal subjects reversed the direction of head movements in advance of trunk movements (mean lead = 82 ms) whereas the patients reversed head direction after the trunk (mean lag = 169 ms). The coherence function between head and trunk movements, measured with a spectral analyser in an additional labyrinthineless patient, was considerably lower than in normal controls. It is concluded that patients with absent vestibular function have impaired stabilization of the head in space which can be taken as indirect evidence of the existence of active dynamic vestibulo-collic reflex (VCR) mechanisms in normal man. The lead found in normal subjects, notwithstanding the unpredictability of the stimuli, may reflect the detection of early acceleration signals by the vestibular apparatus to organize compensatory head movements.

- The question of whether there is a relation between abnormal vestibular function and spasmodic torticollis was investigated. Vestibular findings in a group of 35 patients with spasmodic torticollis (ST) without

other otological or neurological symptoms were reviewed in section 3. The most consistent abnormality, present in more than 70% of cases, was a directional preponderance (DP) of vestibular nystagmus in the dark in a direction opposite to the head (chin) deviation. Rigidly clamping the head to a rotating chair did not abolish the DP. In the presence of optic fixation the DP was less frequent and its severity tended to diminish as a function of the duration of the disease. Smooth pursuit and optokinetic nystagmus were only occasionally affected. The results are indicative of primary involvement of the vestibular system in ST and are discussed in terms of a break-down of the central mechanisms conveying sensory information responsible for head and eye orientation.

- In section 4, three patients with spasmodic torticollis following VIII nerve lesions (VIII-ST) underwent quantitative assessment of their sternomastoid EMG during vestibular (otolith and semicircular canal) stimulation. The results were compared with a normal control group and with 6 patients with idiopathic spasmodic torticollis (ST). Backwards tilt of the VIII-ST patients resulted in a marked increase in the EMG, especially in the more affected sternomastoid, whereas this manoeuvre did not have a significant effect in normal subjects, or had a variable effect in the ST group. These results suggest that VIII-ST patients are a distinct group. Since there was no relationship between the side of the VIII nerve lesion and the direction of the torticollis a direct aetiological link between the two is, however, unlikely. The unusual EMG/tilt responses are explained on the basis of peripheral imbalance of utricular signals (maximal in the supine position) in the presence of central deranged processing of information concerning head posture.

- In the fifth section, in order to establish whether vestibular abnormalities often found in spasmodic torticollis are secondary to the

abnormal head posture, the vestibulo-ocular reflex (VOR) was studied in 8 patients before and after correction of head posture with botulinum toxin. Eye movements were recorded in the dark during sinusoidal and velocity step rotation. Four patients showed a significantly asymmetric response, with the slow phase of the VOR more active ipsilateral to the torticollis (chin). Despite significant improvement of the head posture in all patients for up to 10 weeks following treatment no correction of the vestibular asymmetry occurred. This suggests that the VOR abnormalities are not caused by the head posture itself. These findings are taken as further evidence of primary involvement of the vestibular system in torticollis and imply a widespread derangement of the sensory-motor mechanisms controlling head posture in this disease.

CHAPTER III

INTRA-VESTIBULAR (OTOLITH-CANAL) INTERACTION

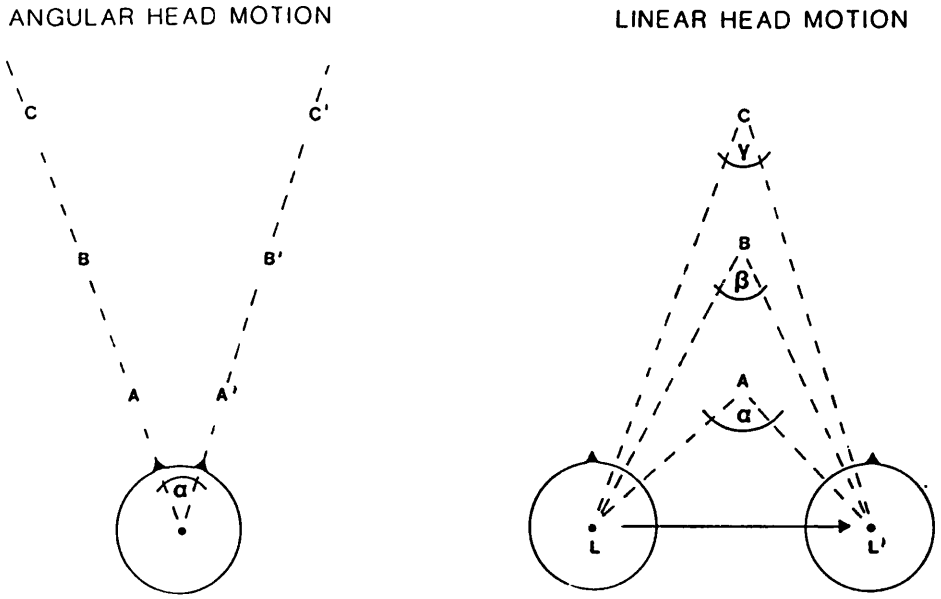
REVIEW AND INTRODUCTION:

In human subjects, natural head movements consist of both linear and angular displacements. During these movements, the eyes remain reasonably well stabilised on features of the earth-fixed visual surround so that visual acuity is preserved. It is well established that pursuit, optokinetic reflexes and vestibular-ocular reflexes from the semi-circular canals of the labyrinth, which transduce skull rotation, all contribute to provide eye movements which are compensatory for head motion. In contrast, it is not clear whether stimulation of the otoliths, which are responsive to linear acceleration, can also evoke adequate compensatory eye movements.

Theoretical considerations indicate that the otoliths should only give rise to compensatory eye movements under certain conditions. In the first place, since gravitational acceleration (g) stimulates the otoliths, there must be some indication of which aspects of the otolith signal come from head movement or from the effects of gravity, and compensatory movements should only be evoked in response to actual movement (discussed by Parker et al, 1985). For example, if the head is held tilted sideways g gives a strong lateral stimulus to the otolith but does not provoke a lateral compensatory eye movement which would be quite inappropriate since the head is stationary; in contrast a rapid lateral movement of the head, such as would occur during sparring, also involves a lateral stimulus to the otolith and might require a compensatory eye movement. The second consideration is that linear compensatory eye movements are only needed if the head is displaced with respect to a near target but not to a distant one. The reason for this comes

from the Euclidian axiom that parallel lines meet at infinity. If the eyes are fixated at a distance then a linear head displacement has little effect on the direction of the target. If, however, the eyes are fixated on a nearby object, say at arms length, then a small linear head displacement will cause a significant angular displacement of the direction of the target (diagram A).

Diagram A

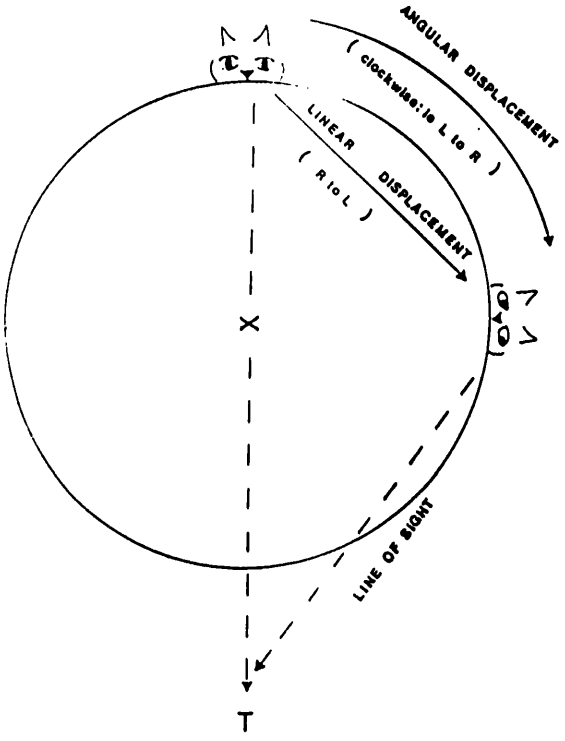


During pure angular motion the distance between the head and targets A, B, C (and A', B', C') does not influence the required compensatory eye movement (α) (Assuming head and eye axis of rotation are the same). In the case of linear head motion, from L to L', the distance from the head to targets A, B, C require different compensatory eye movement (α β γ). If target is at infinity no compensatory eye movement is needed.

A third consideration is that the head can be exposed to simultaneous linear and angular acceleration acting in opposite directions. In such circumstances, as in the example depicted in diagram B, the compensatory eye movement required should arise from canal and optokinetic signals acting together whereas otolith-evoked slow phase eye movements would have to be suppressed since they would be inappropriate in direction. These examples

illustrate that a rigidly wired, robust otolith-ocular reflex could be, in many circumstances, neither desirable nor needed.

Diagram B



*In the case shown rotation of the head upright to the right in the horizontal plane (yaw) is combined with linear displacement to the left. Hypothetical otolith induced compensatory eye movements would be to the right and, therefore, inappropriate. **X** is the axis of rotation and **T** is a visual target.*

Not surprisingly, therefore, previous experimental investigations of otolith effects on eye movements (collated by Barnes, 1980; Buizza et al, 1980) in which subjects were tested in darkness, without instructions, have shown only weak eye movement responses to otolith stimulation. The hypothesis can be put forward that significant otolith-ocular responses can only be generated if, in addition to head linear acceleration, concurrent sensory information and/or an appropriate mental set resolve the inherent ambiguities involved in interpreting head linear acceleration signals. In this chapter

the interaction between canal and otolith signals will be investigated by combining linear and angular head oscillation; in the following chapter the question of otolith-visual interaction will be studied.

Previous reports on simultaneous otolith-canal stimulation have involved sustained rotation at constant angular velocity in yaw (around the longitudinal "Z" axis of the body). It is well known that during such sustained rotation with the subject's "Z" axis positioned vertically, the horizontal nystagmic response decays exponentially until it dissapears completely after a period of about 40 seconds. However, Guedry (1965) and Benson and Bodin (1966) observed that if the axis of rotation is positioned horizontally ("barbeque spit rotation") a sinusoidally modulated nystagmus in the direction of rotation persists, which was attributed to the continuous reorientation of the otolith with respect to the gravitational vector. A similar mechanism operates in what is generally known as "off-vertical axis rotation", in which the "Z" axis is inclined with respect to earth vertical, thereby exposing the otolith to changes in linear acceleration below 1 g. Following arrest from rotation with the "Z" axis tilted or perpendicular to gravity, the duration of the nystagmic response and the post-rotational sensation are less than those found during ordinary upright rotation, a finding attributed to the conflicting information conveyed by the canals, wrongly signaling head rotation and the otolith, indicating no change in head position with respect to gravity. This "otolith-dumping" of the post-rotational canal responses, as well as horizontal or tilted "Z" axis rotation, involve long time constant interactions between the otolith and the canals. However, they provide little information on the type of eye movements elicited in response to transient combined head angular-linear acceleration.

The study of the interaction of canal and otolith signals bears a direct relationship to the clinical problem of understanding positional nystagmus of central type. Patients with this ocular-motor sign are frequently thought of as having disinhibited otolith-ocular reflexes, in that tilting of the head with respect to the gravitational vertical induces sustained nystagmus, usually (but not always, see "clinical applications") beating in the direction of g acceleration. However, in a study on central positional nystagmus it was found that in some patients the otolith, stimulated by head tilt, seemed to "switch in" an abnormal canal-ocular reflex, rather than being directly responsible for the appearance of the nystagmus (Gresty et al, 1986). This finding raises the possibility that the otoliths main functional access to the ocular-motor system might be indirect, eg modulating the gain of canal-ocular reflexes, rather than directly generating otolith-ocular responses to purely linear head acceleration.

As mentioned above and in the introductory chapter, major obstacles to the quantitative testing of otolith-ocular function have been the difficulty in providing controlled linear acceleration in the clinical setting and the weakness of the associated eye movement response. The development of such a test is one of the outstanding challenges posed to clinicians and scientists involved in the study of patients with balance disorders. Experiments based on prolonged constant velocity rotation in the dark, in the absence of any specific instruction to the subjects, however, might create neither an appropriate mental set nor a sensory frame of reference for otolith-ocular reflexes to become manifest. In addition, responses to transient head oscillation might be more appropriate in that they would probably reproduce more accurately the type of head movements encountered in every day life and also be better tolerated by patients.

In this chapter the compensatory eye movements elicited by combining transient linear and angular acceleration will be investigated. The first two sections will describe a simple technique which allows simultaneous stimulation of the otolith and the canals in normal subjects with different stimuli configuration and mental set. The last section will describe some preliminary uses of the technique as a clinical diagnostic procedure.

EYE MOVEMENT RESPONSES TO COMBINED LINEAR AND ANGULAR HEAD MOVEMENT

In this section the possibility that compensatory eye movements derived from the otolith can only be detected during certain combinations of linear and angular displacements of the head is investigated. The experiment compared the velocities of eye movement produced by purely rotatory head movement with the velocities produced with the head rotating eccentrically from the axis in order to induce a significant tangential linear acceleration.

MATERIAL AND METHODS:

Five normal subjects were studied 3 women and 2 men, age range 20 to 40 years, with no history of visual or neuro-otological disease. Three were tested in the eccentric before the centered attitude. Subjects were seated on the rotating chair either with their head centred on the axis of rotation to provide predominately angular motion stimuli or with the head displaced forwards 30 cm in order to provide an additional tangential linear acceleration acting laterally through the plane of the utriculus. The same upright orientation of the head was maintained in the centre and eccentric position with head clamps. A subject positioned on the rotating chair can be seen in figure 1 of the appendix J . Possible deviations from upright were indicated by gravity related offset signals from the linear accelerometer. In addition, the subjects' heads and necks were monitored for possible movements during the trials using an infra red sensitive video camera which was mounted in parallel alignment with the subjects' eyes and target.

Chair motion was transduced by a tachometer. Angular head movement was transduced using a precision angular servo-accelerometer and tangential linear

head motion was transduced using a precision piezo-resistive linear accelerometer, both strapped to the skull with tape.

At the beginning of the experiment an initial EOG calibration was obtained using markers placed at 1m from the subjects' eyes. Following each experimental condition (ie either head centred or head eccentric) a calibration was made by turning the chair through various angular displacements whilst the subject fixated the visual target at 70 cm from the eyes. The eyes were then recalibrated on the markers to determine changes in the corneo-retinal potential. The potential did not change significantly through the experimental proceedure and so the calibrations derived from chair motion were used as the basis of measurements. The target was a visual acuity test chart which was earth-fixed at eye level at a distance of 70 cm for both attitudes. Before each experimental run the subject fixated a central point on the chart, was then put into darkness and oscillation commenced. After 10-20 cycles the light was turned on and the subject fixated the target. During the dark periods the subject tried to maintain imaginary fixation on the target. Measurements were taken of mean and range of peak eye velocity for the first 10 cycles of response and of concurrent mean peak head accelerations and waveform distortion expressed as power.

The motion stimuli consisted of abrupt onset sinusoidal oscillation at 0.5 and 1.5 Hz. Actual head accelerations/velocities achieved varied between subjects and depended upon the relationship between body weight and the limited performance of the torque motor. Data were rejected if the distortion of the head acceleration waveforms (expressed as power) exceeded 5%. The range of variations are indicated in Table 1.

RESULTS:

Examples of raw data in Figure 1 show that a higher peak amplitude of eye movement in the dark is attained with head eccentric than with head centered for comparable levels of angular acceleration. As with all subjects,

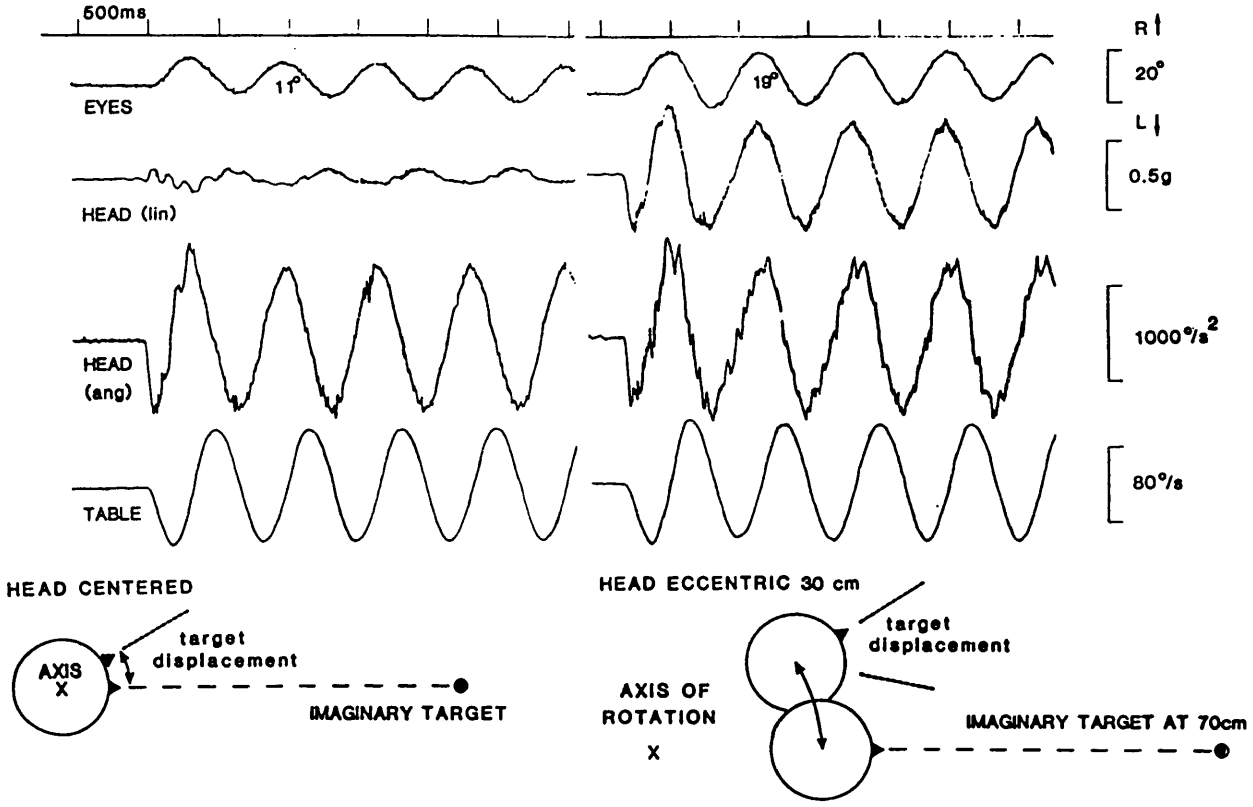


Figure 1. Raw data records of lateral eye displacement, linear and angular head accelerations and motor tachometer signal relating to rotation about a vertical axis, taken from a subject seated in the head-centred and head-eccentric positions as indicated in the diagrams below each set of data records. The diagrams indicate the geometrical relationships between target and subject for equal-angle rotation in the head-centered and head-eccentric attitudes. Note that the relative angular displacement of the target is greater in the head eccentric position. The oscillation was performed in the dark with the subject imagining an earth-fixed target at 70 cm distance.

The increase in amplitude was apparent on the first stimulus cycle and shows little amplitude variability (within $\pm$ 1°). All subjects showed elevated peak velocities of eye movement in the eccentric attitude (Figure 2 and Table 1).

TABLE 1

Mean peak velocities (ranges in brackets) of eye and head movements of 5 subjects during oscillation in Yaw at 0.5 and 1.5 Hz with head centred and head eccentric performed in the light and in the dark whilst imagining a target at 70 cm. distance

Oscillation frequency	**0.5 Hz**	**1.5 Hz**
Angular head velocity achieved (centred or eccentric)	60°/s (56-69)	72°/s (56-81)
Linear head velocity achieved when head was eccentric	31 cm/s (27-35)	42 cm/s (32-51)
Eye velocity/head centred		
in darkness	41°/s (27-60)	73°/s (69-75)
in light	60°/s (52-71)	76°/s (71-85)
Eye velocity/head eccentric		
in darkness	65°/s (60-70)	95°/s (85-104)
in light	92°/s (61-120)	108°/s (85-142)

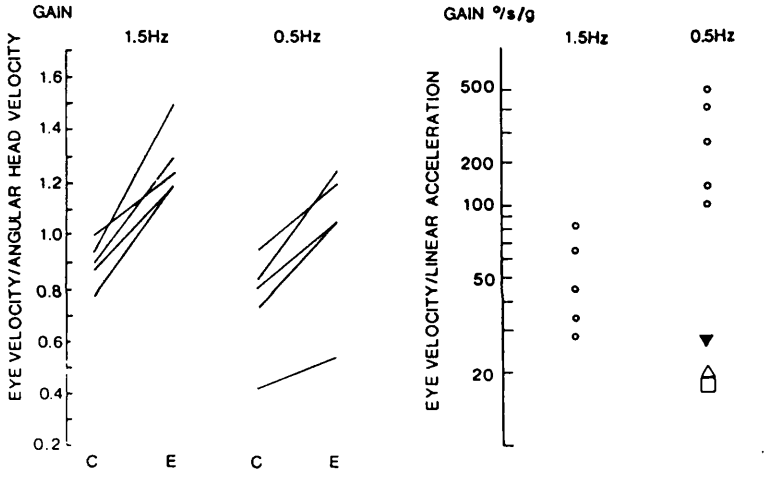


Figure 2. On the left: gains of peak eye velocity/peak angular head velocity of 5 subjects. Each subject is represented by a line connecting the gain calculated in the head-centred attitude (C) with the gain in the eccentric attitude (E) for imaginary fixation on a target at 70 cm during oscillation at 0.5 and 1.5 Hz. On the right: gains of eye velocity/peak head acceleration, for 5 subjects (open circles) during oscillation in the head eccentric attitude, in the dark. The eye velocities used in computing the gains were estimates of the additional eye velocities attained during eccentric, in comparison with centred oscillation, which resulted from the additional linear stimulus. Previous highest gains were reported by Steer (1967) (filled triangle), Correia and Guedry (1966) (open triangle) and Niven et al (1966) (square) obtained at frequencies about 0.5 - 0.8 Hz.

Estimates of the additional eye velocity attributable to the linear stimulation were made on the basis of the velocities achieved during head centered oscillation with allowance for the small linear component of motion in the head-centered attitude. The additional velocity averaged 22°/s peak at 1.5 Hz with a 0.4 g peak linear stimulus and 20o/s peak at 0.5 Hz with a 0.1 g stimulus. Certain individuals attained additional eye velocities with head eccentric of up to 40°/s in the dark. By comparison the highest eye velocities previously reported (Niven et al, 1966) were 9°/s (mean of 4 subjects) in response to a ± 0.58 g stimulus. Previously reported otolith-ocular reflex gains, which, by convention are computed as °/s per 'g' are shown in Figure 2. In the light, eye movement gains, calculated as eye displacement with respect to overall angular displacement of the head from the direction of the target, were within 5% of unity gain. However, the eye movements in the light could derive from smooth pursuit and from optokinetic as well as vestibular mechanisms.

DISCUSSION:

The findings demonstrate that eye movements can be evoked by combining linear with angular oscillation which are significantly higher in velocity than those evoked by angular stimuli alone. The more likely explanations of these eye movements are that they are otolithic in origin, or derive from 'voluntary, non-visual enhancement of the vestibular ocular reflex' (Barr et al, 1976). Since non-visual enhancement of canal reflexes by imagining the relative target movement would particularly apply to predictable stimuli as employed in the present experiment, further experiments using more unpredictable stimuli will be described in the following section. However, it should be noted from these results that the enhancement we observed occurred on the first cycle of unexpected movement in the dark and is, hence, unlikely to be attributable to imagery.

COMBINED LINEAR AND ANGULAR ACCELERATION: THE EFFECTS OF UNPREDICTABLE STIMULI AND TARGET IMAGERY.

The present study is an investigation of the dynamic characteristics of eye movements evoked by combined linear and angular head motion and their dependence upon the type of instruction issued to subjects, in response to stimuli which are more unpredictable than the ones used in the preceding section. Imaginary targets will be used as an attempt to fulfill the visual requirements for linear compensatory eye movements as discussed earlier.

METHODS:

The experimental apparatus and recordings were identical to those used in the preceding experiments.

Stimulus parameters: The stimulus parameters of head velocity and eccentricity and angular acceleration used were chosen from prior recordings of natural head movements (Gresty et al, 1986). The shape of the stimulus was chosen to be of short duration, so that subjects would not tire; to be sinusoidal for ease of measurement and similar to the shape of natural head movements; to be relatively unpredictable; to give little transient response so that within the accuracy of our recordings the responses would reflect a pure sinusoidal stimulus and, finally, to give a smooth ride to help in fixing the head and body to the chair. The time course and power spectrum of the stimulus designed to satisfy these requirements is shown in figure 1 and consists of 2 cycles of a sinusoid preceeded and followed by a half cycle raised cosine and shaped by a trapezoidal window. The stimuli were constructed of sinusoids of 0.02, 0.1, 0.5 and 1.2 Hz with a peak velocity of 60o/s. With the head eccentric the linear tangential accelerations were respectively 0.004, 0.02, 0.1, and 0.24g peak at these frequencies. The angular displacement of the visual direction of the target due to the head

being eccentric was approximately one half of the angular displacement displacement due to angular chair motion; thus at 0.5 Hz, the displacement of the target was 19o peak with head centred and 28o peak with head eccentric.

Experimental design: The experiment was designed to compare the eye movements evoked when the head was centred on the axis of rotation with those evoked when the head was in an eccentric attitude, and the effects of (imaginary) fixation on near and distant targets. In trials requiring subjects to imagine visual targets they were assisted by being shown real, tridimensional objects immediately before each stimulus presentation. The objects consisted of an 8 cm high toy monkey at 60 cm distance from the nasum for the near target and a 30 cm high toy teddy bear at 5m distance from the nasum for the far target. The distance of the near target was chosen on the basis of the length of the human arm. Subjects were tested in darkness to exclude visually guided eye movements. So that the effect of target distance could be studied, subjects were given instructions to imagine targets in order to induce an appropriate mental set. The following experimental designs were employed:

i) No instructions were given to imagine visual targets. Six naive subjects were tested of whom three were tested in eccentric before centred attitude. In each attitude the 1.2, 0.5 and 0.1 Hz stimuli were each presented twice in overall random order. This was followed by one presentation of the 0.02 Hz stimulus which was reserved because our previous experience indicated that this stimulus was soporific and adapting and could interfere with subsequent results. The direction of onset of each stimulus (rightwards or leftwards) alternated for each stimulus frequency.

ii) Instructions were given to imagine where the near target was in the darkness and to try to keep the eyes pointed in that direction during the stimulus. They were told that if they felt that the stimulus displacement was too great (0.1 and 0.02 Hz) they should imagine picking up new targets at the same distance. A further six naive subjects were used of whom three were tested in the head centred before the head eccentric attitude. The stimuli were presented as in design (i).

iii) Stimuli were given only with the head in the eccentric attitude and instructions were given to imagine the near target at 60 cm and a far target at 5m and to keep the eyes pointed in the target direction during the motion. Six subjects were used of whom three were tested firstly while imagining near targets. Only two randomly ordered presentations of each of the 1.2 and 0.5 Hz stimuli were employed since the results of experiments i and ii suggested that the low frequency stimuli were not suitable for testing linear compensatory eye movements.

The subjects comprised normal healthy adults with an age range of 20 to 55 years and of equal sex ratio. The subjects in experiments i and ii had not experienced this type of experiment previously. Two of the subjects in experiment iii had experienced experiment ii, otherwise the subjects were not exposed to the stimuli before the experimental runs.

Pursuit: In the presence of vision it is possible that smooth pursuit adds to angular compensatory eye movements to provide overall compensation for combined linear and angular head movement (Eckmiller, 1982). In order to obtain some impression of whether pursuit could provide compensation for the linear motion component of our stimuli, pursuit was assessed in three subjects

(from experiment iii). The subjects were seated with head fixed and presented with a red laser target projected onto a tangent screen at a distance of 3 meters. The target moved laterally with the stimulus waveform used to drive the turntable. The stimuli parameters were 0.05 Hz, 10o peak displacement and 1.2 Hz, 4o peak displacement. These were selected to be the same as the target displacements attributable to the linear motion component when the subjects were tested in the head eccentric attitude.

Measurements: measurements were taken only during the central sinusoidal part of the stimulus pattern. For eye movements of each subject, angular velocity was measured by hand using a cursor to follow the tangent to the eye movement curve, and readings were taken of peak velocity for rightwards and leftwards movements for the two stimulus presentations. The resulting 4 values were averaged. The recordings of head acceleration were used to indicate whether there was undue head movement, and whether the head was properly positioned centrally or eccentrically.

RESULTS :

All subjects felt that the stimuli gave smooth rides, which would be of importance should they be used for clinical testing. The 1.2 Hz stimulus was considered quite unpredictable while the lower frequency stimuli felt predictable to some extent. The eye movement responses to the high frequency stimuli tended to be purely sinusoidal in shape with few saccadic intrusions.

Experiment (i): no instructions. The velocities of eye movement evoked with head eccentric were greater than those evoked with head centre at 0.5 and 1.2 Hz only ($p<0.05$, paired observations t-test). The individuals' data for this experiment, expressed as gain of peak eye velocity/peak angular head velocity,

are presented in figure 2. For both head centred and eccentric a gain characteristic rising with increasing frequency was observed.

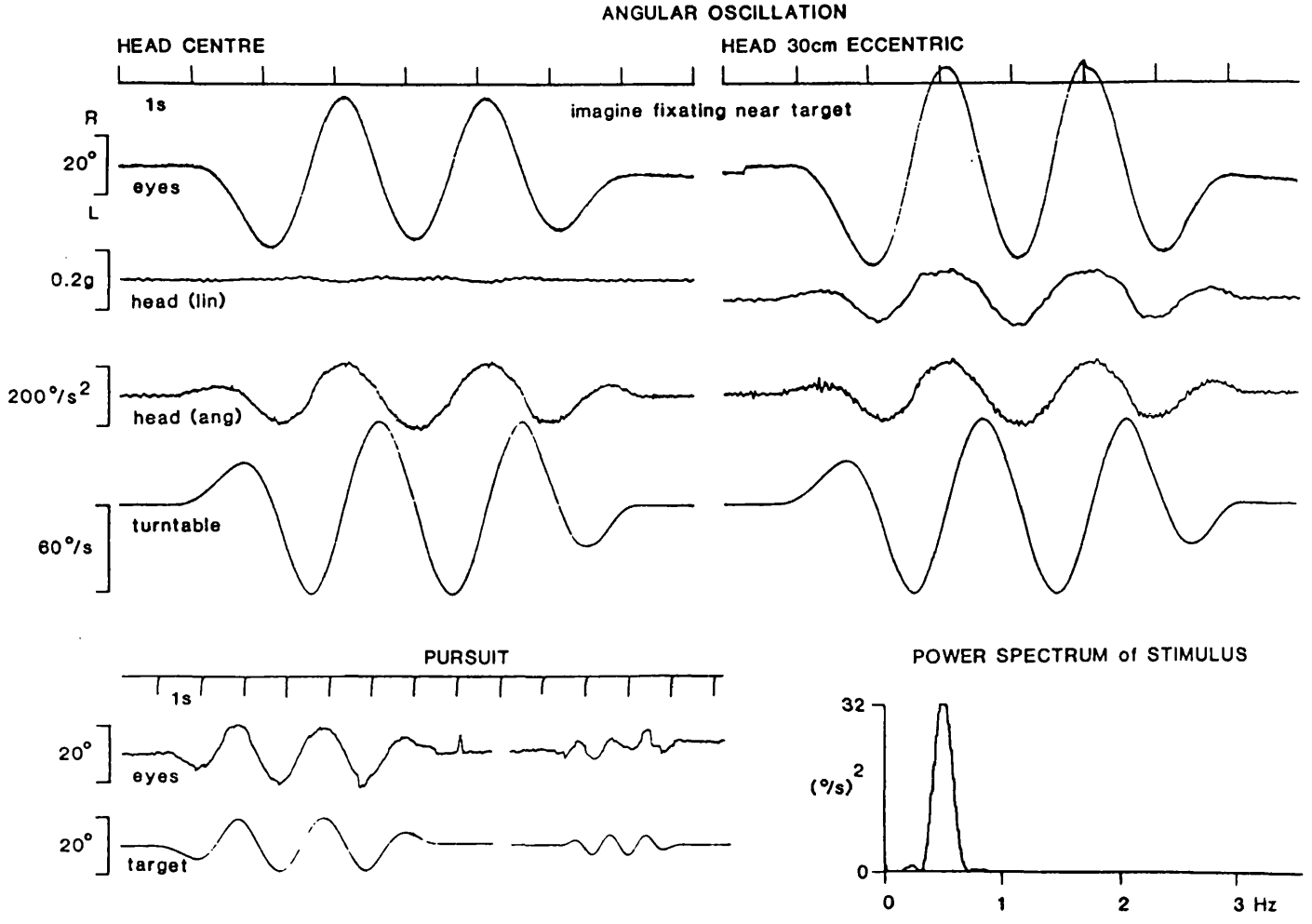


Figure 1. The upper records are of the raw data of a subject in experiment (ii) showing the eye movement responses to a 0.5 Hz stimulus in the head centred and eccentric positions whilst imagining a target at 60 cm distant from the nasum. The lower right hand graph shows the frequency power spectrum of the stimulus. The lower left hand records illustrate a subject's pursuit in response to a visual target moving with the same waveform as the vestibular stimulus at 0.5 and 1.2 Hz with amplitudes equivalent to the angular target displacement which the linear component of the eccentric oscillation would induce.

Experiment (ii): imagine a near target. The eye movement velocities achieved in the head eccentric position were much higher than those evoked with head centred for all subjects at stimulus frequencies of 1.2 ($p<0.001$) and 0.5 Hz ($p<0.01$). There was a trend towards higher gains in the eccentric attitude at

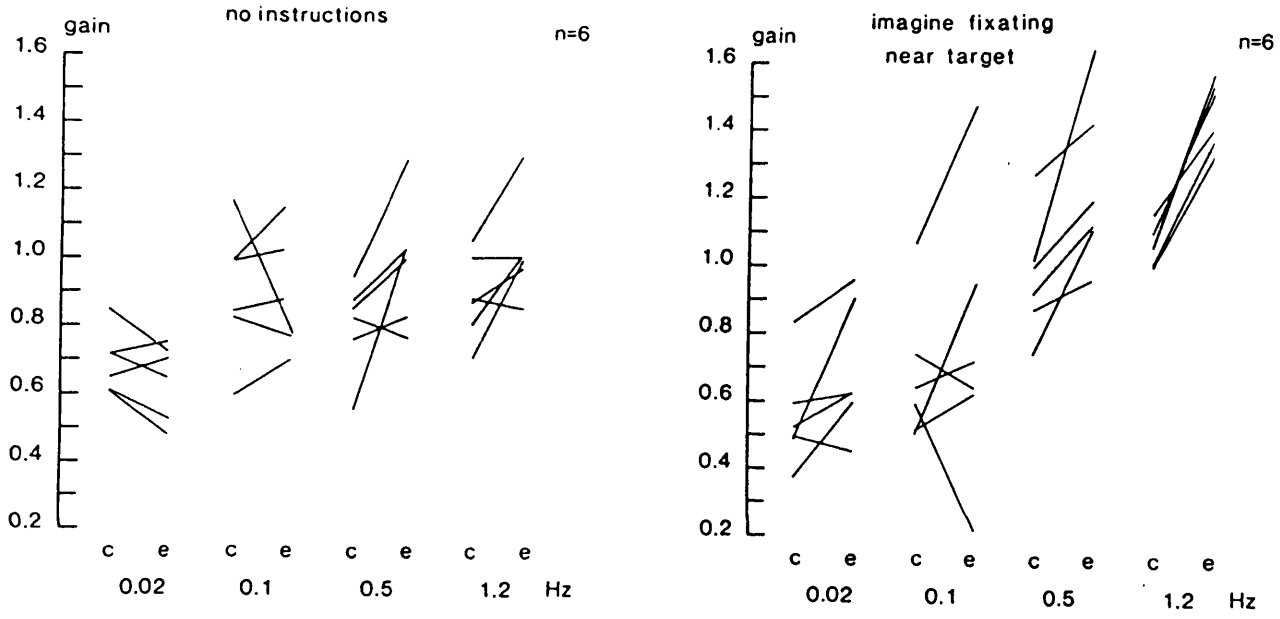


Figure 2. Plots of each individual's averaged responses in experiments (i) and (ii) indicating the instructions issued. Each bar represents a subject and connects the gain obtained with centred "c" oscillation with the gain obtained with eccentric "e" oscillation. The gains are calculated as (peak eye velocity/peak angular turntable velocity).

the lower frequency stimuli but this did not reach significance at the 5% level. There also appears to be increased gain of eye movement with head

centre at 0 .5 and 1.2 Hz compared with the gains found with no instruction, although these are not easily comparable because the two experiments employed different subjects and individual variation in vestibular responses is high. Examples of raw data records obtained in this experiment are presented in figure 1 and individuals' data expressed as gain of peak angular eye velocity/head velocity are presented in figure 2. For both head centred and eccentric, gain rose with increasing frequency. The gain of the eye movement response to the linear component of motion was calculated by doubling the values found by subtracting the gain achieved with head centred from the gain found with the head eccentric (figure 3) *. The gain of the portion of the eye movements due to the linear motion, calculated as eye-velocity/tangential acceleration and using the means for all subjects, was inversely related to frequency (figure 4) with a slope of approximately -1. The actual additional eye velocities achieved with head eccentric ranged from of 21o/s at 1.2 Hz to 9o/s at 0.02 Hz (mean values).

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* FOOTNOTE. In the centred position the required gain for target stabilisation is 1. The eccentric position requires 50% more eye movement because of the linear head movement which is a gain of 1.5 if expressed as (eye velocity/angular head velocity). The extra 0.5 angular gain represents unity linear gain. END OF FOOTNOTE.

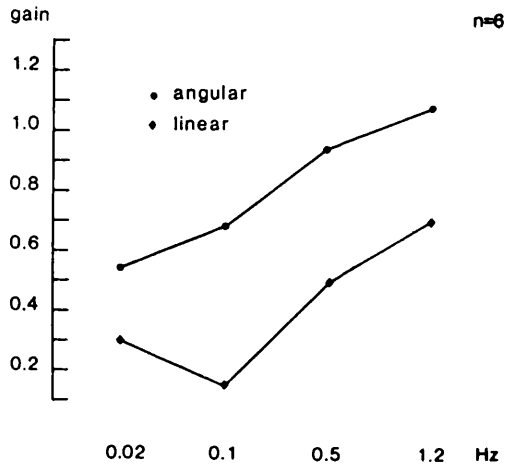

Figure 3. Gains of the angular and linear component contributions to eye movement responses obtained in experiment ii (imagining near target, head eccentric). The gains are calculated as (eye movement velocity/velocity required for unity gain compensation on a real visual target) and are averaged over all subjects. The linear component was obtained by subtracting gains in the head centred position from those obtained with the head eccentric.

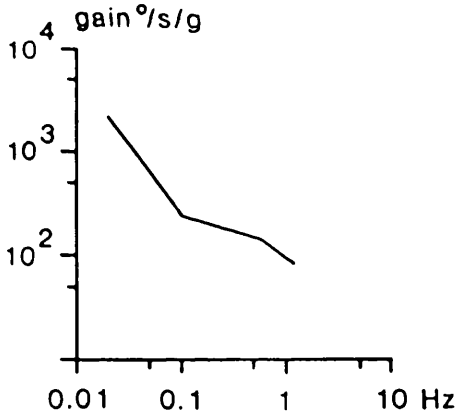

Figure 4. Gains of the linear component of eye movement responses (obtained by subtraction) obtained in experiment ii (imagining near target head eccentric) calculated as (eye velocity/acceleration in g units) and averaged over all subjects. The slope of the characteristic approximates -1.

Experiment (iii): imagining near/far targets. The eye velocities evoked by imagining a near target were significantly higher than those produced whilst imagining a far target ($p<0.01$, both frequencies). Individuals' data, expressed as gain of peak angular eye velocity/head velocity are presented in figure 5. The gains attained with the far target were comparable with those found for head centre in experiment ii. The gains found with the near target were comparable with the gains in the eccentric position in experiment (ii).

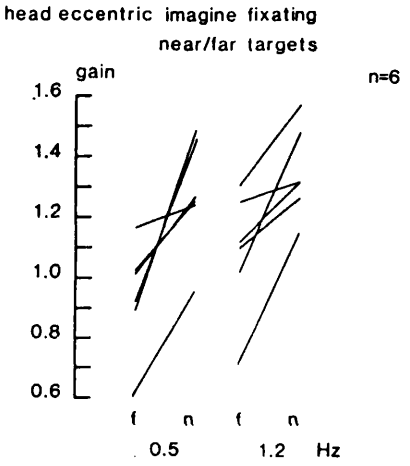

Figure 5. Plots of each individual's averaged responses in experiment iii (head eccentric oscillation, imagining near -n- and far -f- targets). The gains are calculated as peak eye velocity/peak angular turntable velocity.

Phase. For all experimental conditions a phase advance of eye velocity with respect to head velocity which ranged between 9 and 30o was found for the 0.02 Hz stimulus with no differences between head centre and eccentric. At other frequencies no systematic net phase shift was observed.

Pursuit. Examples of responses to the pursuit stimuli are presented in figure 1. They show that smooth eye movements can be generated by pursuit which,

when added to angular compensatory eye movements, can be of sufficient amplitude to provide compensation for the linear component of head motion for the stimulus parameters used in these experiments.

DISCUSSION:

The experimental results show that high frequency angular oscillation of the head combined with a linear acceleration acting laterally can evoke lateral eye movements of significantly higher velocity than those produced by angular oscillation alone. Although this effect is present without instructions it occurs more strongly with the mental set of imagining nearby targets. The importance of the mental set could be expected on the theoretical grounds that a linear compensatory eye movement should only occur for proximal targets.

There are several mechanisms to be considered which could give rise to the higher velocities of eye movement observed in the eccentric position; viz:

I) The interrelated factors of "Voluntary, non-visual enhancement of the VOR" (Barr et al, 1976), prediction of movement and arousal. It is well established that prediction of movement, the general state of arousal (affected by the mere presence or absence of instruction) and the use of instructions to imagine targets can elevate or depress canal reflex gains. However, these experiments, as well as data from the literature (Barr et al, 1976), show that enhancement of the canal-VOR with head centre can only raise gains to levels of around unity or just above at high frequencies.

There is also the possibility that if a subject could predict the changing geometrical relationships in the head eccentric attitude then he may be able to enhance his canal-VOR by some central predictive mechanism. The

element of predictability in these experiments was removed by using fresh naive subjects for each experiment and subjecting them to a novel stimulus which was unpredictable at high frequencies (the subjective experience of the 1.2 Hz stimulus is that one has little concious awareness of what is happening or directive control of the eyes because the stimulus is so brief). The experimental design ensured that 50% of the naive subjects were exposed to the high frequency eccentric stimulus as their first experience and they showed the same enhancement as more experienced subjects. It is also of note that the more predictable low frequency stimuli did not give rise to greatly increased eye movement velocities in the head eccentric position. These observations suggest that the eye velocity enhancement at high frequencies is not mediated by prediction of the stimulus.

II) Body attitude, particularly of the neck. There is no evidence that static posture of the spine-neck-head alters the gain of the canal-VOR in normal human subjects. In particular, experiments described in chapter I showed that the canal-VOR gain is not systematically affected by extreme static torsion of the neck. Hence it is doubtful that the enhanced gains observed with head eccentric are attributable to the particular pattern of proprioceptive input from the neck.

III) Stimulation of the semi-circular canals. Despite elegant physiological demonstrations that the canals can be sensitive to linear acceleration (reviewed in Benson, 1974), it is difficult to accept that this mode of stimulation can provoke significant eye movements because the strong linear stimulus produced by head tilt does not normally induce lateral eye movements.

IV) Otolith signals. At the high frequencies the responses are compensatory for the combined angular and linear motion. Therefore the drive signal for the linear compensatory eye movement must be linearly related to the head motion and work automatically at gain levels which are appropriate to real or imagined target distance. This drive signal most probably arises in the otolith organs of the labyrinth and has fairly immediate access to slow phase oculomotor mechanisms.

The signals which are recorded from the primary afferent fibres of otolith organs (in animals) show a response characteristic of gain (spikes/s/g) rising with frequency for irregular units and a more or less constant gain for regular units. Similarly, previous investigations (compiled by Barnes, 1980) of eye movement responses to linear stimuli have tended to show a gain characteristic (^{o}/s/g) which is flat or rises with frequency (peak acceleration held constant). In contrast, (accepting the low frequency values which show a trend) our experiments show a gain (^{o}/s/g) which decreases with frequency (figure 4). This latter dynamic characteristic is what one would expect for compensatory eye movements because linear velocity decreases with frequency if a constant level of peak acceleration is maintained. (The higher actual velocities of eye movements seen with higher stimulus frequencies arise as a consequence of the much higher levels of linear acceleration attained). The slope of -1 represents an integration of the regular signal seen in the primary afferent and indicates that the eye velocity signal is a constant proportion of the linear head velocity signal. This characteristic is also in accord with the frequency response of abducens motorneurone activity during lateral, sinusoidal linear acceleration as determined by Eckmiller (1982) in the monkey. The value of the proportionality is presumably a function of the target distance and would be small for more distant targets and increase in

value for nearer targets.

The eye movement responses to linear motion must be subject to a complex control process which involves consideration of target distance and changes in the direction of the g vector. This complexity suggests various ways in which the "otolith-oculomotor" signals may be processed. There is the possibility of a direct otolith-oculomotor pathway which is gated, amplified or attenuated by other oculomotor mechanisms so that it becomes fully effective when there is a requirement for visual stabilisation on nearby objects. Alternatively, the otolith signals may be fed to other mechanisms and used indirectly, for example, they may be used to bring about gain changes in canal reflexes or used as input to the mechanisms of smooth pursuit. It would seem unlikely that the otolithic influences are mediated by the pursuit mechanism for two reasons. Firstly, the gain characteristic rising with frequency for the linear compensatory eye movements is comparable with that of canal reflexes and unlike that of smooth pursuit in the light. Secondly, the low frequency stimuli, which would be easier to pursue because they were more predictable and well within the dynamic range of smooth pursuit, gave low eye velocities. This is not what would be expected if pursuit was enhancing the VOR gain. As a consequence, if the otoliths influence eye movements indirectly, it is likely to be via their effect on the gain of canal reflexes.

In every day life situations it is difficult to assess whether compensation for linear head movement is preferentially derived from otolith signals or is due to smooth pursuit. The observations of Lisberger et al (1981), together with our own data have demonstrated smooth pursuit eye movements of significant velocity in the frequency range of the stimuli used in these experiments and, under most everyday circumstances, may provide the predominant compensation required for visual stabilisation during linear head movement (Eckmiller, 1982). However, smooth pursuit responds poorly to

unpredictable target motion at frequencies above circa 1.5 Hz, partly because of the delay during visual processing. If otolith signals access the oculomotor system at a brainstem level the processing delay is much shorter, which suggests that otolithic influences may be of significance for high frequency, unpredictable head movements.

In the present experiment employing combined linear and angular head motion, the velocities of eye movements attributable to the linear component are much higher than those previously reported for linear stimuli alone. It is not known if linear motion alone is also able to produce high velocities of eye movements if subjects are given the appropriate instructions; this will be investigated in the following chapter. Pure linear acceleratory stimuli can be equivocal in giving rise to sensations of movement and/or tilt with respect to gravity (Graybiel, 1974, Guedry, 1974). In addition, head movement is more accurately interpreted when there is combined angular and linear motion which is the case during everyday locomotion (Guedry, 1974).

The theory that otolith-ocular reflexes work in the presence of canal reflexes, provides an explanation for positional nystagmus and positional effects on eye movements found in neuro-otological disease (Gresty et al, 1986). In normal subjects, otolithic influences on eye movements are released in the presence of asymmetrical canal signals produced naturally by rotation. The possibility arises that some patients may have an asymmetry of canal signals due to a pathological imbalance. As with normals, this could release otolithic influences which become manifest as positional nystagmus when the otoliths are stimulated by head tilting.

ROTATION WITH THE HEAD ECCENTRIC. PRELIMINARY CLINICAL APPLICATIONS.

In contrast with the relative abundance of conventional vestibular tests concerned with semicircular canal function, there is no reliable way of quantifying otolith function in the clinic. This is not only due to the financial and technichal difficulties encountered to provide controlled linear acceleration but also to the fact that the ocular-motor response found has been weak and variable, so making it inappropriate for clinical purposes.

Symptoms of abnormal of otolith function are misjudgement of true earth vertical, false sensations of lateropulsion or tilt and linear vertigo (Brandt and Daroff, 1980; Brandt and Dieterich, 1987). Clinical signs suggestive of otolithic abnormalities are tilted body posture (particularly of the head) (Brain, 1926; Halmagyi et al, 1978) positional nystagmus of the central type * (Nylen, 1950; Cawthorne and Hinchcliffe, 1961) and comitant torsion and skew deviation of the eyes (Halmagyi et al, 1978; Keane, 1975, 1985).

The fact that the otoliths are sensitive to tilt of the head with respect to the gravity vector has been exploited as a way of exploring their function. This constitutes the so called static function of the otolith and involves subjective and objective elements of the response. The subjective perception of tilt is strongly influenced by contact and proprioceptive cues; attempts to minimise this influence for instance by assessing subjects during immersion are inapplicable to clinical work (Graybiel et al, 1968).

In lower mammals with laterally placed eyes, tilt of the head around a fronto-occipital axis gives rise to compensatory skew deviation of the eyes in which the eye on the side of the lowermost ear elevates and viceversa. In man this response is not present in normal circumstances but certain central lesions result in two related conditions which seem to have relevance to this vestigial compensatory ocular response: "skew deviation of the eyes" in which

one eye is depressed and the other elevated (Keane, 1975; Brandt and Dieterich, 1987), and "see-saw nystagmus" in which there is a continuous alternation between one eye elevating and the other depressing (Daroff, 1965).

Another tilt related phenomenon is ocular counter-rolling. During head rotation around the fronto-occipital axis there is torsional nystagmus with the slow, compensatory component in the direction opposite to head motion; this dynamic phase of ocular counter-rolling which has a gain of approximately 0.6 it is thought to include an important contribution from the vertical canal VOR (Collewijn et al, 1985) and, with limitations, can be assessed clinically by direct inspection (see section on oscillopsia, chapter I). During slow head rotation or tilt there is a tonic counter-rolling of the eyes which is only vestigial in that it gives a maximal compensation of about 10% of the head tilt (Diamond and Markham, 1983). This purely otolithic response cannot be assessed easily in the clinic because of the difficulties encountered in delivering quantifiable tilt and recording torsional eye movements. Thus, to date, the most informative manouevre that the clinician wishing to investigate static otolith function can perform is to tilt his patients and look for positional nystagmus. In the following experiments the technique described in the preceding chapters, combining angular with linear acceleration, will be applied in the clinical setting as a clinical tool for investigating otolith function. The "prima facie" advantage of this test procedure is that it is tolerable to most patients and that it only requires standard rotatory chairs with a simple adaptation to place the head forward eccentrically.

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* Note on "positional nystagmus": Definitions and mechanisms.
Positional nystagmus is a nystagmus which is provoked or modulated in slow phase velocity by static tilt of the head with respect to the gravity vector

and occurs with disease of the central nervous system, the vestibular end organ or nerve. "Ageotropic positional nystagmus" - the nystagmus fast phase or "beats" are in the opposite direction to the earth; the slow phase is towards the earth. "Geotropic positional nystagmus" - the nystagmus fast phase or "beats" are in the direction of the earth; the slow phase is away from the earth. If the head is tilted sideways to horizontal with one ear down, gravity effects a stimulus to the otoliths which is the same as an acceleration upwards in the direction of the upper ear. If the head were actually moving then one might expect a compensatory slow phase eye movement to be made in the downwards direction; eg head accelerating upwards to the left ear, eyes compensate by moving rightwards producing ageotropic nystagmus. Normal subjects do not have a reflex eye movement when tilted for the brain correctly interprets that the head is tilted and not accelerating. Ageotropic nystagmus in patients may be evidence of the "release" of some form of compensatory eye movement. Geotropic nystagmus is in the wrong direction to be compensatory.

METHODS:

The experimental technique described in the previous section, using relatively unpredictable "enveloped sinewaves" with constant peak angular velocity of 60o/s and centred on frequencies of 0.02, 0.1, 0.5 and 1.2 Hz, was applied. Each stimulus was delivered twice, one commencing with rightwards rotation, the other with leftwards rotation. Overall stimulus presentation is randomised except for the lowest frequency stimulus which is presented last because it is soporific. Testing is performed in darkness and subjects were given no instructions other than encouragement to be alert because difficulties of comprehension in some neurological patients may be encountered. Slow phase velocity measurements were seperately averaged for rightwards and leftwards movements and expressed as velocity ratios (ie mean peak eye velocity rightwards/peak turntable velocity leftwards). Phase of response was measured as the relationship between the turning point of the slow phase eye movement with respect to zero turntable velocity. Phase measurements for 1.2 Hz condition may be up to 5^{o} in error. Phase estimates are more reliable for lower stimulus frequencies.

RESULTS:

The data from the patients was compared to those from normal subjects presented in the preceding section. Certain patients have been selected to illustrate test results because they exhibit various combinations of enhanced/decreased responses with head eccentric and geotropic/ageotropic positional nystagmus. In addition, most had normal horizontal canal-vestibular-ocular reflexes on conventional, head centred rotation tests.

i) Absence of positional nystagmus. Failure to enhance the VOR with lateral acceleration.

Case example: B52832. Female aged 59 who had suffered three episodes of vertigo over the previous two years. When examined she was found to have bidirectional gaze paretic and rebound nystagmus in the lateral plane and almost absent smooth pursuit. Extensors were plantar. Magnetic Resonance Imaging showed pictures compatible with demyelination. Conventional rotational (with head centred) and caloric tests showed symmetrical hypoactive vestibular responses. There was a complete failure to evoke enhanced responses when tested with head eccentric.

ii) Positional nystagmus beating ageotropically with enhancement of the VOR by lateral acceleration (eye movement provoked by gravity in the same direction as eye movement provoked by acceleration).

Case example: B45846. Female aged 45 who was examined one year after the removal of a left sided acoustic neuroma. The significant vestibular findings were a total left sided canal paresis with spontaneous, right beating nystagmus in the dark which enhanced on positioning with the left ear down. On head centred oscillation the slow phase eye movements evoked by head leftwards stimuli were at the low limit of normal range at all frequencies. Responses to rightwards stimuli were all of consistently higher gain and within normal limits. With head eccentric the responses to rightwards stimuli were elevated beyond the normal range, at high frequencies. Responses to leftwards stimuli were not different from the responses to head centred leftwards stimuli (figure 1b). Response phase data for leftwards (L) and rightwards (R) slow phase eye movements were as follows:

	1.2 Hz	0.5 Hz	0.1 Hz	0.02 Hz
Head centre	0°R, 11°L	2°R, 10°L	3°R, 8°L	16°R, 27°L
Head eccentric	0°R, 13°L	0°R, 15°L	0°R, 16°L	15°R, 36°L

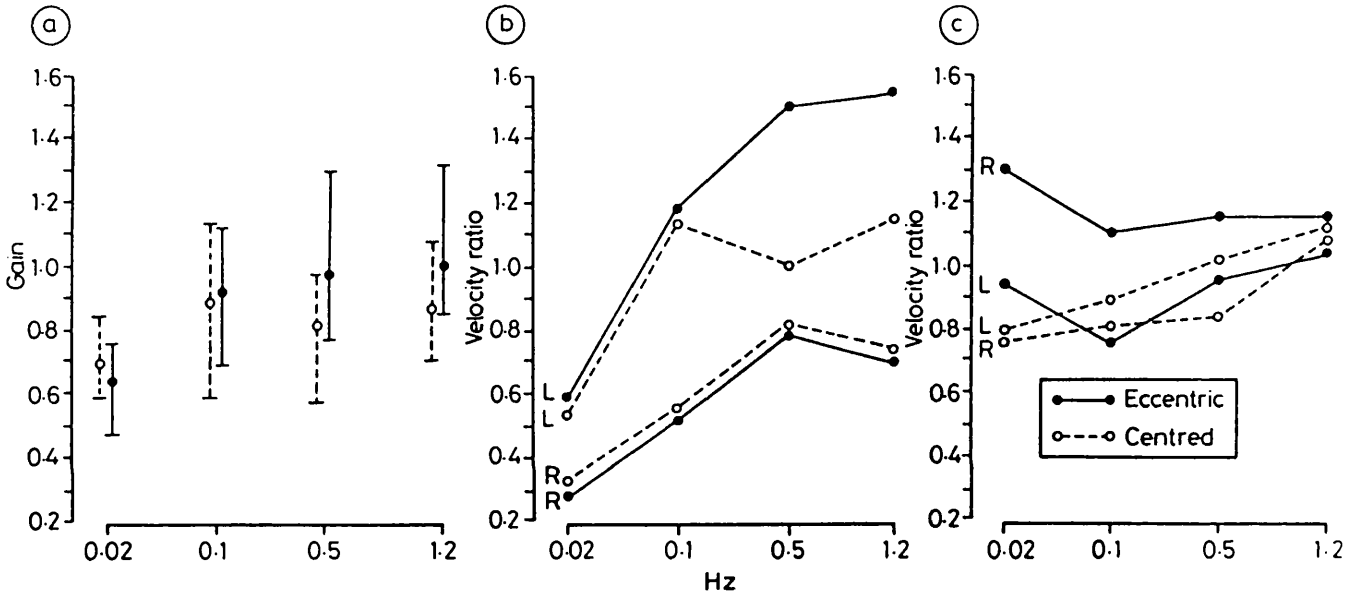

Figure 1(a). Normal data of gain against frequency showing means and ranges. Rightwards and leftwards responses grouped together. In the present discussion, patients responses are only identified as abnormal if they lie outside the normal range. (b) Patient B45846. Velocity ratios of peak eye velocity rightwards and leftwards/peak turntable velocity leftwards and rightwards respectively. (c) Patient B11526. Velocity ratios of peak eye velocity rightwards and leftwards/peak turntable velocity leftwards and rightwards respectively. R= rightwards slow phase eye movements in response to leftwards rotation. L = leftwards slow phase eye movements in response to rightwards rotation.

iii) Positional nystagmus beating ageotropically with reduction of VOR by lateral acceleration (the eye movement produced by gravity is in the opposite direction to the acceleration vector; the eye movement produced by lateral acceleration is in the same direction as the vector). A patient showing this pattern has not been found.

iv) Positional nystagmus beating geotropically with reduction of the VOR by lateral acceleration in the head eccentric attitude (the eye movements provoked by gravity and lateral acceleration are both in the same direction as the acceleration vector).

Case example: A38668; Female aged 64 who, in 1968, was shown to have a cystic lesion extending from the level of C1 to the floor of the 4th ventricle which was successfully treated with radiotherapy. In summer 1985 there was a reccurrence of symptoms. When examined in April 1986 she had diplopia due to a left convergent strabismus. Abduction was restricted bilaterally, but saccades in all directions were of near normal velocity. There was gaze paretic nystagmus in all directions, with bidirectional rebound nystagmus. Pursuit was absent and there was "slow build up" optokinetic nystagmus. Vestibular ocular reflexes were hypoactive. Ocular counterrolling was intact. There was positional nystagmus beating leftwards when lying horizontally with the left ear down and beating rightwards with the right ear down. Magnetic Resonance Imaging demonstrated a low density mass, probably an ependymoma, which lay to the left of the midline, extending from the upper cervical cord to the floor of the IVth ventricle and invading the low brainstem and posterior vermis of the cerebellum.

The gains of the slow phase eye movements evoked by head oscillation in the eccentric position were uniformly reduced by 18% at 0.1 and 1.2 Hz and by

30% at 0.5 H. The slow phase eye movements provoked by the gravity acceleration vector in this patient are in the same direction as the slow phase eye movements provoked by the tangential acceleration vector during head eccentric oscillation.

v) Positional nystagmus beating geotropically with enhancement of the VOR by lateral acceleration (the eye movement provoked by gravity is in the same direction as the acceleration vector while the eye movement provoked by lateral acceleration is in the opposite direction).

Case example: B11526. Male aged 50 years who, in 1980, developed headaches, neck pain, unsteadiness and rotatory vertigo with vomiting. A CT scan demonstrated a posterior fossa mass. Craniotomy revealed a tumor which was seen protruding between the two cerebellar hemispheres in the midline, which biopsy showed to be a low grade astrocytoma. The tumor and lining of the cystic cavity were removed macroscopically. In July 1968 the patient was reviewed. He complained only of "height vertigo" and dizziness on neck extension. On examination, pursuit was mildly hypometric, there was right beating positional nystagmus evoked with the right ear down, and a left beating positional nystagmus evoked with the left ear down (figure 2). There was some weakness of the shoulder girdle. A high resolution CT scan at this time (presented in figure 5 of appendix K) showed a large CSF density space between the cerebellar hemispheres with no evidence of recurrence of the tumor. Slow phase eye movement responses to oscillation with head centred were normal. With head eccentric the gain of the slow phase eye movements was significantly increased at low frequencies of stimuli for head leftwards stimulation (figures 3, 1c).

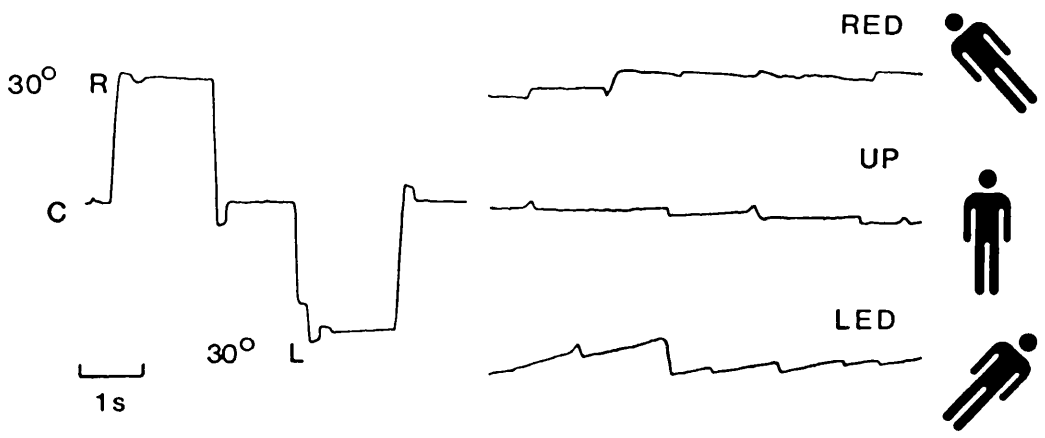

Figure 2. Patient B11526. Positional nystagmus with lateral tilts of 45° left and right in the dark.

The slow phase eye movements provoked by the gravity acceleration vector in this patient are in the opposite direction to the slow phase eye movements provoked by the tangential acceleration vector during head eccentric oscillation. Response phase data for leftwards (L) and rightwards (R) slow phase eye movements were as follows:

	1.2 Hz	0.5 Hz	0.1 Hz	0.02 Hz
Head centre	6°R, 0°L	4°R, 0°L	5°R, 6°L	9°R, 9°L
Head eccentric	-4°R, 9°L	5°R, 5°L	5°R, 2°L	17°R, 6°L

In addition to the above, normal responses have been found in a variety of patients whom one might have expected, from their symptoms or signs, to have otolithic disorders. For examples:

i) "Benign paroxysmal vertigo" attributed to degeneration of the otolith organ. Two patients with classical paroxysmal vertigo with torsional nystagmus provoked by positioning failed to show abnormal responses with head eccentric rotation.

ii) Cerebellar-pontine angle lesion from presumed ectatic basilar artery loop.

A normal pattern of responses was found in this patient who had deafness and complete canal paresis on the left side. Perhaps of significance, this patient did not have positional or spontaneous nystagmus which may indicate that he compensated well for the loss of vestibular function.

iii) Chronic vertigo of unknown aetiology. Normal responses were identified in a patient with a four year history of illusory sensations of linear motion of her self and the ground, "mal de debarquement". The linear nature of the illusory movement makes one suspect a disorder of otolith function.

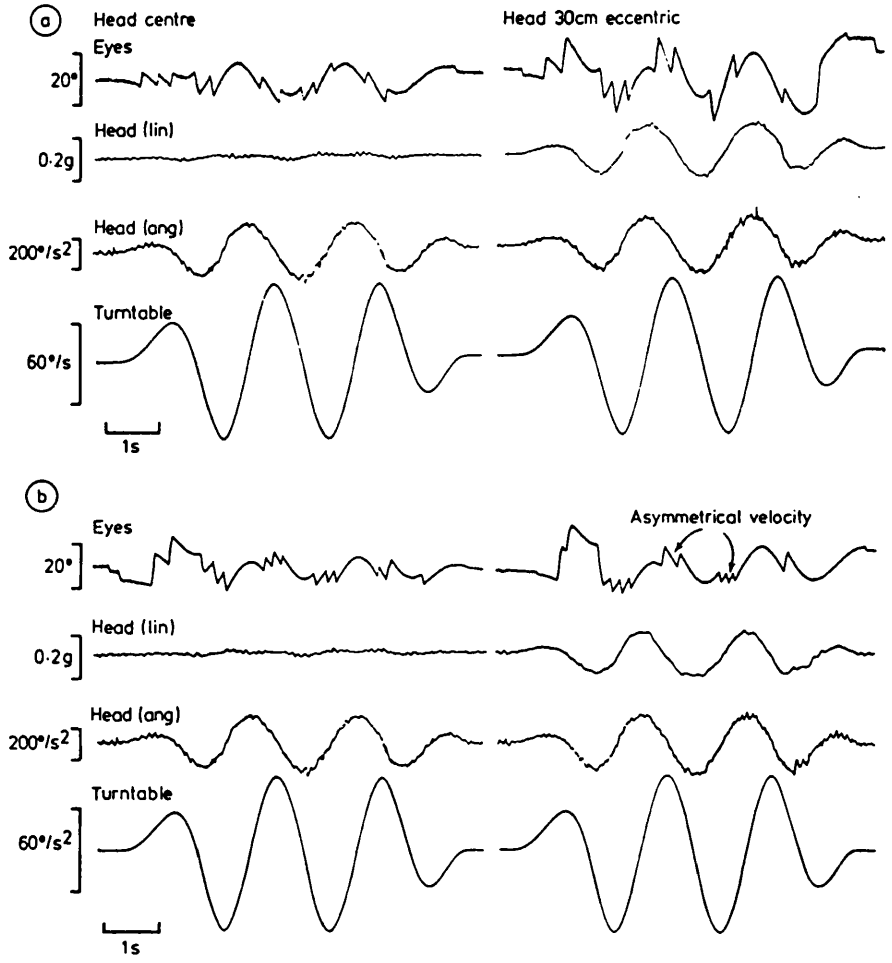

Figure 3(a). Raw data records of a normal subject's responses to centred and eccentric oscillation at 0.5 Hz. (b) Raw data records of the responses of patient B11526. Head (lin): tangential linear acceleration acting laterally on the head. Head (ang) angular acceleration of the head.

DISCUSSION:

The findings show that rotational vestibular testing performed with head eccentric oscillation can reveal abnormalities of eye movement responses in patients who are normal on conventional head centred rotational testing. Therefore, this method of investigating vestibular ocular reflexes has the potential of adding significantly to the understanding of a patient's neuro-otological status. However, to date, abnormalities have only been detected in the head eccentric position in patients in whom there was also positional nystagmus. This suggests that the technique may be more of a research tool than a decisive clinical investigation for it constitutes an over-elaborate procedure in comparison with the simple task of identifying positional nystagmus.

The significant findings in these patients which relate to current concepts of otolith function are the enhanced gains (velocity ratios) associated specifically with high frequency stimuli (ii, patient B45846) or low frequency stimuli (v, patient B11526).

I) High frequency abnormalities: In normals, high velocities of eye movement attributable to otolith stimulation occur particularly with high frequency stimuli. The patient who had had an acoustic neuroma removed showed higher gains for both centred and eccentric stimuli for movement in the direction of the intact side at the higher stimulus frequencies. Thus it is likely that her asymmetrical responses in the head eccentric position are attributable to otolithic effects which have become asymmetrical because of the nerve section, in a similar way to the canal reflexes. It is notable that in patients with acoustic neurectomies, the eye movements evoked by movement to the lesioned side are similar for both head attitudes. This observation would suggest that

whereas their remaining canal could generate eye movements in both directions, the intact otolith on one side could only generate eye movements towards the contralateral side.

II) Low frequency abnormalities: The type v example of abnormal response (B11526) shows a unidirectionally enhanced velocity ratio at low stimulus frequencies. Responses provoked by low frequency stimuli may not be related to the otolith contribution to compensatory reflexes which our data suggests are mainly high frequency sensitive. Instead, they may reflect abnormalities of otolith function related to adaptation and eye velocity storage mechanisms (Cohen et al, 1982), both of which involve long time constants which one would associate with low frequency performance.

In types iii and v the slow phase lateral eye movements evoked by the gravity acceleration vector are in the opposite direction to the enhancement of the slow phase eye movements produced by lateral acceleration during oscillation with head eccentric. In types ii and iv the eye movements evoked by gravity are in the same direction to those produced by lateral acceleration during oscillation with head eccentric. These observations underline two unresolved problems of otolith pathophysiology. Firstly, if we are to consider ageotropic nystagmus as a "released" compensatory phenomenon, what is the explanation of geotropic nystagmus which is in the opposite direction? Secondly, how can the response to phasic linear acceleration, even at low frequencies, be in the opposite direction to the static response as indicated by the direction of positional nystagmus?

One of the original intentions was to design a technique to investigate the otolith contribution to compensatory eye movements in patients with neuro-otological disease. In some, particularly those with feelings of "mal de debarquement", one suspects otolithic abnormalities because of the nature

of their symptoms. However, not all such patients show abnormal responses on head eccentric testing although, clearly, the technique reveals some otolith-oculomotor abnormalities. These observations indicate that this method can provide valuable insights into vestibular-oculomotor pathophysiology, and will be worth extending to motion about other axes such as head pitch. However, the negative findings also underline the fact that we have to rely too heavily on vestibular-ocular performance as an indicator of the integrity of balance.

SUMMARY

- Previous investigations have failed to find significant compensatory eye movements in response to linear motion of the head. In the introductory section of this chapter it was argued that this may have partly been a consequence of testing the otolith system in the absence of a sensory context or instructions to the subjects which would make a compensatory eye movement in response to linear head motion relevant. Since visual acuity seems essentially preserved during natural head movements, which combine both linear and angular components, it is likely that compensation for linear translation occurs.

- The hypothesis that eye movements of significant velocity in response to otolith stimulation can be elicited when linear and angular acceleration are combined was examined. Lateral eye movements were produced by angular sinusoidal oscillation, in the dark, in yaw at 0.5 and 1.5 Hz, 80^{o}/s peak, with the head both centered and positioned 30 cm eccentric forward from the axis of rotation in order to produce an additional linear acceleration acting tangentially. The combined stimuli produced high velocities of eye movement which were much greater than those produced by angular motion alone. The findings are interpreted as evidence of a linear-compensatory reflex, probably otolithic.

- The effects of mental imagery and stimulus unpredictability on the lateral eye movements evoked by linear head motion during similar eccentric oscillation were studied. The stimuli used were enveloped sinewaves at 0.02 to 1.2 Hz, 60o/s peak angular velocity, 0.004 to 0.24 g peak tangential acceleration, and subjects were either given no instructions or were told to imagine fixating on targets at 60 cm or 5 m distance. Eye movements of significantly higher velocity were evoked in the eccentric position,

particularly at the higher frequencies and when subjects imagined near targets. The increase in velocity of eye movement was attributed to the linear stimulus and probably derives from stimulation of the otolith organs. The frequency response of the gain (^{o}/s/g) of these movements gave an approximate slope of -1, indicating that the eye velocity bears a constant proportionality to linear head velocity. The findings are in accord with the theoretical prediction that eye movements compensating for linear head motion should only be required for viewing near targets. These otolithic influences on eye movements could either be mediated by a direct "otolith-ocular reflex" which is subservient to viewing conditions or, alternatively, the otolith signals may modify the activity of other oculomotor mechanisms.

- An attempt was made to develop the technique of combined linear-angular acceleration into a clinical test of otolith function. Eye movement responses with head centred and eccentric were compared in various patients with known/suspected neuro-otological abnormalities. Patients with vestibular neurinectomies showed greater VOR asymmetry with head eccentric at higher stimulus frequencies. Some patients with cerebellar lesions showed abnormally enhanced or depressed and asymmetrical responses with head eccentric in comparison with head centred responses which could be normal. The enhancing effects could be specific to low frequency stimuli. All patients who showed abnormal responses with head eccentric also had positional nystagmus provoked by the gravity acceleration vector when the head was tilted laterally. The direction of the positional nystagmus with respect to the gravity vector was not neccessarily the same as the direction of the effect on eye movements of lateral acceleration during eccentric oscillation. Patients with benign paroxysmal vertigo or chronic linear vertigo in whom otolithic abnormalities are suspected were not found to have abnormal responses with head eccentric.

CHAPTER IV

OTOLITH-VISUAL INTERACTION

REVIEW AND INTRODUCTION:

During normal viewing conditions, retinal image stability during head motion is achieved by a combination of visually guided and vestibularly elicited compensatory eye movements. The existance of powerful, vestibular compensatory eye movements is demonstrated by turning the head from side to side whilst reading from a book, chart, etc, and comparing this performance with that of reading with the head stationary whilst oscillating the book; visual acuity, in this example reading performance, is clearly superior during head movements than during target movement because of the canal VOR (Benson and Barnes, 1978). A similar though less clear cut effect is experienced if one tries to move the head linearly, which might indicate the presence of a purely linear otolith-ocular reflex (OOR). Unfortunately, quantitative psycho-physical experiments to confirm this impression are scarce, possibly because of the considerable technical difficulties in generating adequate levels of head linear acceleration and, in the few studies available, a clear distinction between angular and linear head displacement has not always been made (reviewed in Griffin and Lewis, 1978). Thus, assessment of otolith-ocular reflexes (OOR) in the past have had to rely on measurements of slow phase eye movement velocity in response to linear acceleration in the dark to exclude interference by visually guided eye movements. As discussed early, however, previous attempts have failed to demonstrate eye movements of velocities comparable with those evoked by angular accelerations of the head which stimulate the semi-circular canals (collated by Barnes 1980; Buizza et al 1980).

In contrast, in the preceding chapter we have seen that linear acceleration can provoke high velocity eye movements in normal subjects if angular and linear head movements are combined, as during natural head movements, by oscillating subjects in yaw with their head placed eccentrically from the axis of rotation such that a linear (tangential) lateral component of acceleration was derived. Thus, there is some doubt as to whether an OOR exists which can function in isolation and with similar power to the compensatory vestibular canal-ocular reflex. There is a possibility that compensatory OOR arise from a synergistic interaction between otolith signals and canal reflexes.

The prerequisite condition for an OOR to become necessary or manifest which has generally been ignored in the past, is that an eye movement which stabilises the eyes on a visual target in compensation for linear head movement is only required for targets closer than about 10m (see diagram A, previous chapter). Accordingly, any attempt to evoke otolith-ocular reflexes which are conducted in the dark to exclude visuo-motor reflexes should provide subjects with the "mental set" to imagine appropriate earth stationary targets. Alternatively, it should be theoretically possible to measure the OOR in the light. However, in order to separate the contribution of visually guided compensatory eye movements, linear velocities required to oscillate subjects in such experiments should be well above their range of action and this poses considerable technical difficulties.

Further problems in the investigation of otolith-oculomotor functions are that slow phase eye movements can be evoked by arthrokinetic and somatosensory stimuli which signal self motion (Brandt et al 1977; Bles et al 1983) which can be enhanced in some subjects by making imaginary constructions of relative movements of the visual world. The ability to generate eye movements via a mental construction of self motion may be of particular

importance in experienced subjects, when movement is predictable and for linear translation when somatosensory stimuli are particularly strong. In these respects many previous studies suffer the disadvantage that they have involved highly predictable motion.

Therefore, in the following experiments using purely linear acceleration the strategy adopted in order to minimise the several limitations discussed above will include: firstly, the use of relatively unpredictable stimuli; secondly, a requirement on the part of the subject to maintain imaginary fixation when assessing the OOR in the dark; thirdly, the investigation of OOR responses in the light in the initial 150 ms following the onset of linear acceleration, previous to the occurence of visually guided eye movements.

THE OTOLITH-OCULAR REFLEX IN THE DARK

The aim of these experiments was to attempt to evoke lateral eye movements by linear movements of the head along the inter-aural axis ("heave") in subjects instructed to imagine nearby targets and using relatively unpredictable stimuli. In the preceding chapter, involving combined angular and linear head movement, the motion stimuli used were based on measurements made on subjects during everyday activities. For comparison, the same stimulus parameters for linear motion will be used in the present experiments. In addition, in order to gain some impression of the threshold and amplitude linearity of the response, the eye movements evoked by stimuli at a constant frequency with varying magnitudes of peak linear acceleration will be studied.

METHODS:

Linear motion stimuli were provided by a cart which runs on a precision levelled track. The cart is driven by two linear motors (Lintrol TM) which generate thrust against a reaction plate fixed in the centre of the track. The motors are powered by a 3-phase thyristor drive (Davy Linear Motors, Davy Corporation PLC) which is controlled by velocity feedback from a tacho-generator driven by a friction wheel running on the track. Each motor provides greater than 1000 Newtons thrust with 20 ms rise time for a response to a velocity step of 1 m/s. The cart is capable of accelerating a 75 kg subject in excess of 1 g peak. The harmonic distortion of the stimulus waveform used in the present experiments was less than 0.5% (power). Subject's shoulders, hips, legs and feet were restrained with pressure pads. The head was restrained between two self moulding sacs of polystyrene balls

which were collapsed onto the head between pressure plates.

Recordings: Eye movements were recorded with DC EOG with leads secured to exclude microphonics. Head acceleration was recorded using precision, DC-accelerometers mounted with surgical tape over the forehead. Sled velocity was recorded from the tacho-generator. Signals were led from the sled via multiway, self-laying, cable track.

Linear motion stimuli: The stimuli consisted of windowed sinusoids (figure 1), the properties of which have been described in the preceding chapter. The stimuli were based on centre frequencies of 0.1, 0.5 and 1.2 Hz with peak accelerations in units of g of 0.02, 0.1 and 0.24 respectively. The compensatory eye velocity for a target at 60 cm (arms length) for these stimuli is 31 ^{o}/s peak. Each of the frequencies was presented twice, the first time commencing with either rightwards or leftwards motion and the second being in the reverse direction. Stimulus presentation was organised as a Latin square, scrolling the sequence, 1.2R, 0.5L, 0.1R, 1.2L, 0.5R, 0.1L (R is rightwards starting, L is leftwards starting).

Experimental conditions:

i) no instructions - The subjects were in the dark and given no instructions other than to keep alert. The trial stimuli were presented as described in the preceeding paragraph.

ii) instruction to imagine fixation on a near target - The trials without instruction were followed by similarly organised trials in which the subjects were presented with a visual target in the form of an 8 cm high toy monkey placed at a distance of 60 cm from the nasum and were told to imagine fixating upon this target through the trial. The lights were then extinguished and the

trials began immediately.

iii) increasing peak acceleration at a constant frequency - The stimulus frequency of 0.5 Hz was determined by the length of the track and problems with movement artefacts at higher frequencies. Peak acceleration was increased in octaves from 0.1g to 0.8g with the stimulus at each magnitude being applied in both the rightwards commencing and leftwards commencing direction. Since the previous experiments had shown no differences between the results of imagining a target versus no instruction at this frequency, the subjects were given no instruction other than to keep alert.

All trials were conducted in darkness and the eyes were calibrated on 20^{o} target markers placed at 1m distance. At the end of the experiment the eyes were calibrated dynamically by applying the 0.5 Hz, 0.1g stimulus in the light whilst the subject fixated the toy monkey.

Subjects: For experiments (i) and (ii), 6 naive normal subjects, 3 male and 3 female, age range 17-45, were tested. Similarly a further 6 subjects (3 male, 3 female, age range 21-35) were used in experiment (iii).

Measurements: Care was taken to distinguish between slow phase and fast phase eye movements. Hand measurements of peak slow phase velocity eye movement were taken during the central part of the stimulus pattern which comprises a pure sinewave. A coherent eye movement response was identified if the slow phase eye movement formed one complete sinusoidal cycle at the same frequency as the stimulus. For each subject the values for the peak slow phase velocity were averaged over the rightwards and leftwards stimuli if a coherent response in both directions could be identified. Peak chair velocity derived from the tachometer and peak head acceleration transduced by the linear accelerometer were in close agreement up to and including the 0.5 Hz stimulus. The 1.2 Hz stimulus provoked high frequency vibration transients in the

acceleration record. Digital integration of the acceleration trace which considerably smoothed the high frequencies produced velocities in agreement with the tachometer.

RESULTS:

Subjective sensations: The subjects reported that the experience was strange and disorienting and they had little idea of the amplitude or velocity of motion, nor of the whereabouts of the toy monkey when they were required to imagine its location. The most distinct sensation was of strong alternating lateral pushes.

Eye movements: The linear stimuli in the dark evoked poorly formed, low velocity slow phase eye movements interspersed with sporadic fast phases generally characteristic of vestibular nystagmus. It should be emphasised that making sense of the eye movements as responses coherent with the motion stimuli was difficult. At times, some subjects showed no systematic modulation of slow phase eye movements in relationship to the stimuli. At other times, responses were related to the stimuli for only part of the several cycles. Examples of reasonably well formed responses are shown in Figure 1. The data of all subjects are presented in Table 1 and are based on measurements of the parts of the traces where the shape of the slow phase eye movements clearly related to the shape of the stimulus.

The 1.2 Hz stimulus was the most effective in evoking high velocity eye movements and individual subjects produced responses with gains (gain calculated as: peak net angular eye velocity/peak relative angular velocity of cart with respect to stationary target) between 30% and 50% of the ideal unity gain required for fixation on the 60 cm target. The 0.5 Hz stimulus produced the second highest velocities with lowest velocities being provoked at 0.1 Hz.

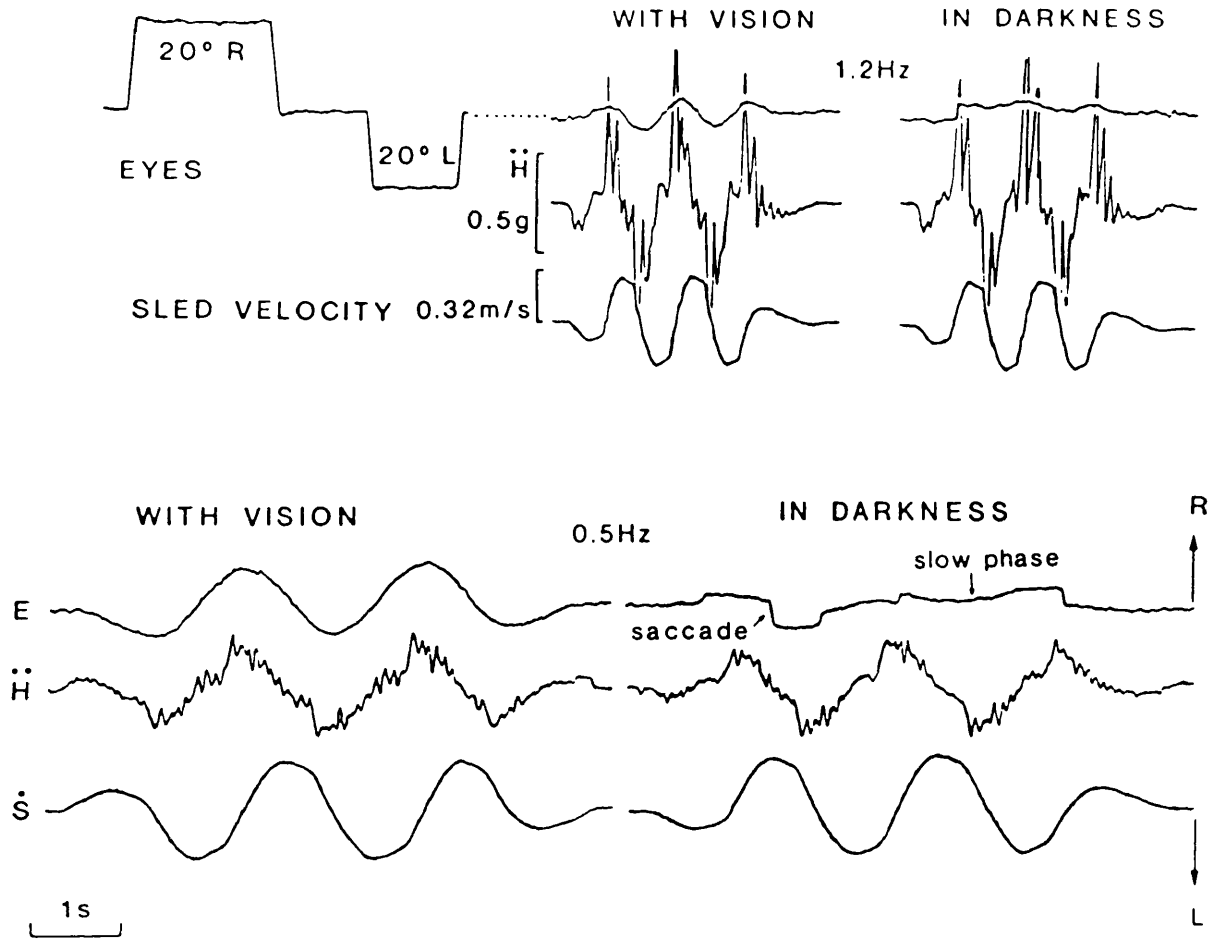

Figure 1. Raw data records from a subject who gave amongst the best formed responses to linear oscillation. Dark: subject is instructed to imagine the position of a target at 60 cm. With Vision: for comparison and calibration the subject is required to fixate a real target. H = linear head acceleration, E = eye displacement, S = sled velocity transduced by tachogenerator. Right = rightwards, L = leftwards.

The phase of slow phase eye movement responses at 1.2 Hz was more or less appropriate for compensatory responses. At the two lower frequencies phase shifted in the direction of phase advance of the response with respect to the stimulus (Table 1) with an average of 40° advance of peak velocity of eye movement with respect to peak velocity of chair movement at 0.1 Hz.

VELOCITY AND PHASE OF THE SLOW PHASE EYE MOVEMENTS OF SIX NORMAL SUBJECTS IN RESPONSE TO TRANSIENT SINUSOIDAL LINEAR OSCILLATION IN THE LATERAL DIRECTION.

	1.2 Hz °/s	0.24g phase	0.5 Hz °/s	0.1g phase	0.1 Hz °/s	0.02g phase
S1n	15.0	-117	7.4	-84	0.9	-68
S1i	9.0	-90	8.7	-90	3.8	-63
S2n	3.8	-90	2.9	-64	*	*
S2i	8.8	-90	6.1	-62	1.64	0, -159
S3n	10.3	-111	4.8	-81	*	*
S3i	13.0	-64	4.7	-73	1.3	-52
S4n	*	*	0	*	0	*
S4i	0	*	0	*	0	*
S5n	6.6	-65	3.9	-56	0.7	-27
S5i	*	*	3.1	-106	1.9	-86
S6n	9.0	-90	0	*	0.7	-30
S6i	6.0	-54	*	*	0.52	-34

Mean values (X) expressed as gain in °/s/g and phase

	°/s/g	phase	°/s/g	phase	°/s/g	phase
Xn	37	-95	32	-71	30	-42
Xi	31	-75	45	-83	76	-59

Mean values (X) expressed as % of unity gain for a target at 60 cm.

Xn	30%	10%	2%
Xi	25%	15%	5%

The responses of each subject at each frequency are averaged over two stimuli (commencing rightwards and commencing leftwards). Phase is taken as peak slow phase eye displacement with respect to peak head velocity, -90° is compensatory phase. The velocity for unity gain at each frequency would be 30 °/s. *: responses were not coherent with the stimulus (given value 0). n: no instruction condition. i: instructions were given to imagine fixation on a stationary target at a distance of 60 cm. Double values are given where subjects exhibited widely disparate responses.

Effects of imagery: No significant differences were found between the peak slow phase eye velocities evoked with or without instructions to imaging the nearby target at 0.5 ($t=-1.01$) and 1.2 Hz ($t=-0.68$). On the hypothesis that imagery could raise slow phase velocities so that they should become more compensatory, a one tailed paired T-test indicated that the slow phase

velocities at 0.1 Hz were significantly higher when subjects imagined the near target ($t=-2.47$, $p<0.05$).

The gains of the eye movement responses averaged over all subjects and expressed as deg/s/g are shown in Table 1 and compared with previous results in Figure 2. Gains as percentages of ideal unity gain for a 60 cm fixation target are given in Table 1 and show a characteristic rising with frequency from 2-5% at 0.1 Hz to 25-30% at 1.2 Hz.

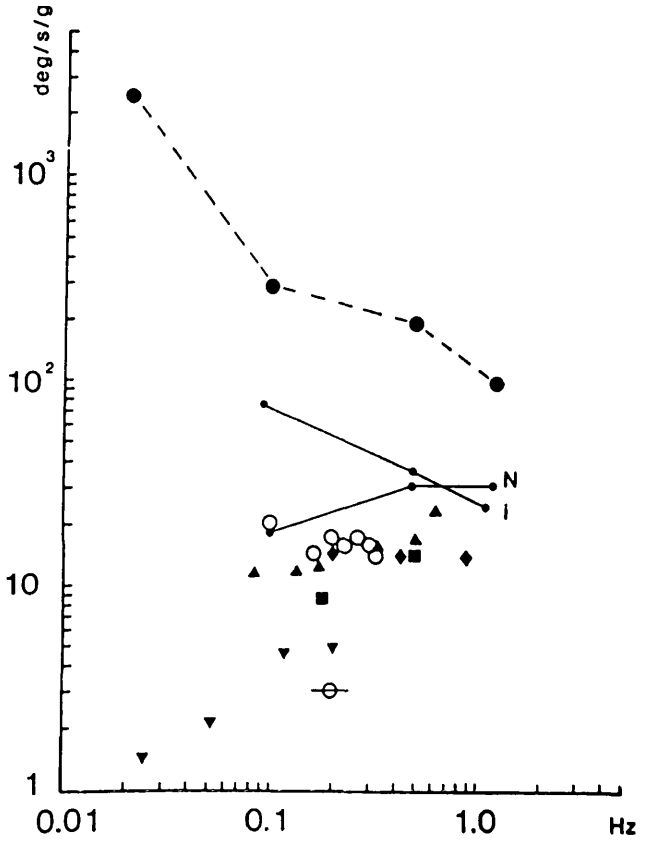

Figure 2. Gains of peak slow phase eye velocity with respect to peak "g" level at various frequencies of linear stimulation. The present ● results, i (instructed subjects) and n (uninstructed) are superimposed upon the results of previous studies for comparison (redrawn from Barnes 1980). The data points represent the means of six subjects. ▼ Benson, Bodin (1966); ■ Correia, Guedry (1966); -⊖- Stockwell et al (1971); ▲ Steer (1967) in Barnes (1980); ◆ Niven et al (1966); ○ Benson and Barnes (1973); ● responses to the linear component of combined angular and linear head movement, with instruction to fixate imaginary near target, from the preceding chapter.

In experiment (iii) in which acceleration varied and frequency was held constant (Table 2), despite individual differences in response magnitude, the averaged peak velocity of responses were found to be linearly related to peak acceleration (Figure 3) at a constant proportionality of $17^{o}/s/g$ ($r=0.92$, $p<0.01$). However, the velocities observed were low in comparison with those required for an ideal gain of unity for fixation at a distance of 60 cm (Table 2) and would only be sufficient to provide stable fixation on targets at a

TABLE 2

PEAK VELOCITIES OF EYE MOVEMENTS OF 6 NORMAL SUBJECTS IN RESPONSE TO TRANSIENT SINUSOIDAL LINEAR OSCILLATION IN THE LATERAL DIRECTION ("HEAVE") AT 0.5 Hz WITH INCREASING LEVELS OF PEAK ACCELERATION.

	PEAK ACCELERATION							
	0.1g		0.2g		0.4g		0.8g	
	°/s	phase	°/s	phase	°/s	phase	°/s	phase
S1	1.5	-76	2.9	-41	5.5	-10	12.0	-36
S2	0.8	-62	2.8	-45	4.9	-17	10.7	-30
S3	0	*	0	*	4.6	-62	17.7	-62
S4	1.0	-90	3.7	-83	7.1	-133	10.8	-84
S5	0	*	0	*	5.7	-17	15.2	-32
S6	0	*	1.9	-125	3.3	-41	7.6	-38
VC	30.0		60.0		120.0		240.0	°/s

VC is the theoretical eye velocity which would be compensatory for fixation on a visual panorama at 60 cm distance. Phase as peak slow phase eye displacement with respect to peak head velocity, would be compensatory at -90°. The responses of each subjects at each g level are averaged over two stimuli (commencing rightwards and commencing leftwards). *: response was not coherent with the stimulus (given value 0).

distance of between about 5 and 15 m. The phase of the responses was in advance (in the present convention -90° would be compensatory) and showed a trend to increasing advance with peak g level from -76° at 0.1g to -57° at 0.8g (Figure 3). The intercept on the x-axis of the regression line indicates that the threshold acceleration for evocation of eye movements at 0.5 Hz is 0.075g (Figure 3).

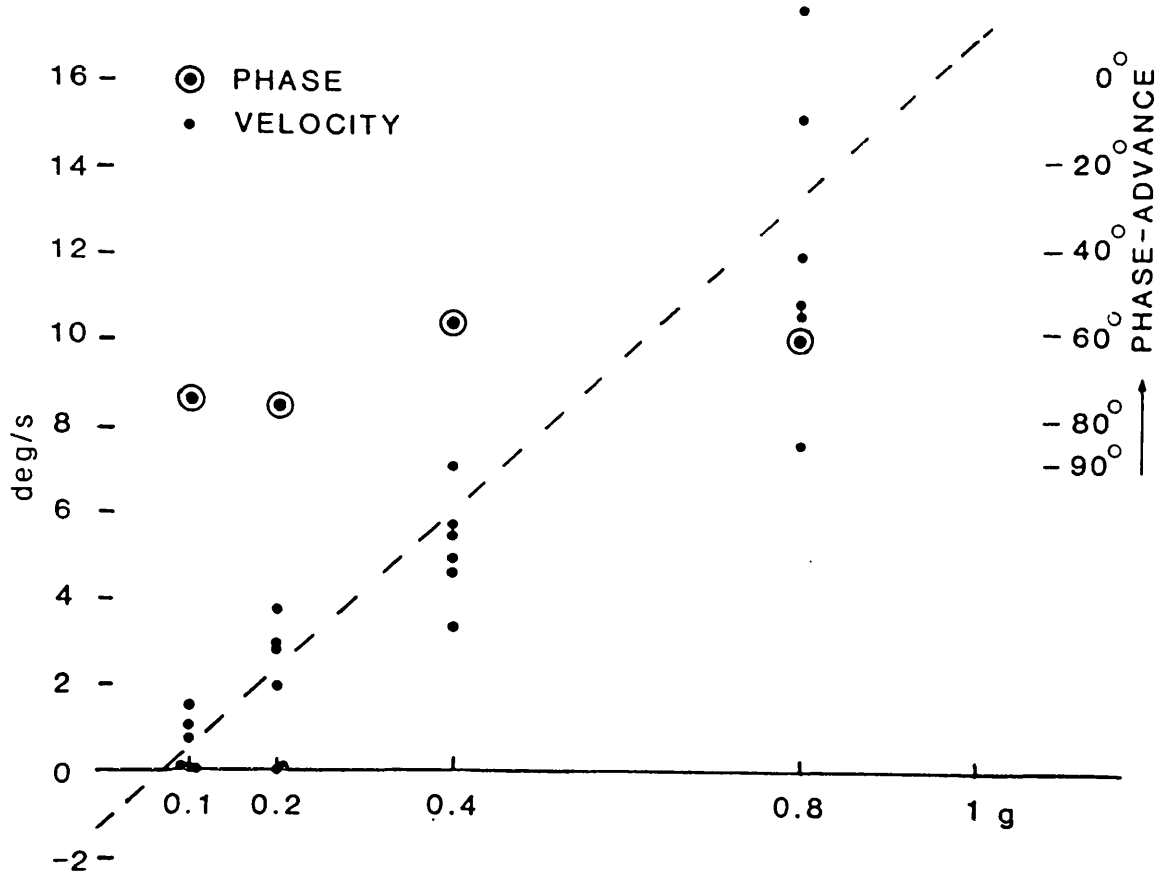

Figure 3. Peak slow phase eye velocity • and phase ◉ as a function of peak linear acceleration in g units at a constant frequency of oscillation of 0.5 Hz. Data from six uninstructed subjects. Phase points are averaged. The dotted line through the velocity points is a linear best fit showing a sensitivity of 17.01 °/s/g.

DISCUSSION:

The experiments have shown that the average eye movement responses to linear acceleration, operating at a gain of around 17°/s/g and in phase advance would be insufficient for compensatory stabilisation of the eyes on proximal targets. In these respects the results are in general agreement with those of previous investigations (Figure 2). The important finding is that the low gain of the otolith-ocular reflex is not attributable to the absence or presence of the mental set of imagining fixating on nearby objects.

The velocities of the responses obtained with pure linear motion were only affected by imagining nearby targets at the lowest frequency of stimulus, which is, subjectively, the most predictable. This enhancement at 0.1 Hz is probably related to pursuit mechanisms which are effective at predictable low frequencies; it is unlikely to result from voluntary modulation of vestibular reflex gain which, for canal-reflexes, is effective across all frequencies regardless of predictability (McKinley and Peterson, 1985). The absence of enhancement by imagery at high frequencies is of importance because it has been proposed that the mental set of fixating on proximal targets might be the factor determining whether or not linear stimuli evoke compensatory eye movements (eg Barnes 1980). It would seem that regardless of mental set otolith signals are not coupled strongly enough to slow phase eye movement mechanisms to provide compensation during pure linear motion.

The weak eye movements evoked by pure linear stimuli stand in marked contrast to the high compensatory velocities of eye movements evoked by the linear component of motion which can be observed when linear and angular head movements are combined (previous chapter; see also Viirre et al 1986, in the monkey). The contrast is of particular significance since the magnitudes and waveforms of the linear stimuli were carefully matched in the present

experiment to those employed in the earlier ones. For example, when subjects were asked to imagine fixating a target at 60 cm in the dark during 0.5 Hz oscillation, the peak velocity slow phase eye movement evoked by linear acceleration of 0.1g peak, combined with an angular peak velocity of 60°/s was 13.5°/s. This value is some three times larger than that found in response to linear acceleration alone and would provide compensation for fixation on a target at 1.5 m distance. At 1.2 Hz the compensation for combined linear and angular head motion was complete for targets at 60 cm. For linear acceleration alone compensation would only be adequate for targets at 2.3 m. From these comparisons it would seem that the response to linear acceleration is enhanced in some way by the presence of concurrent canal signals and further by the appropriate mental set for fixating on nearby objects. Similarly, it has been reported by Harris (1986) that canal signals are needed to generate the full response to otolith stimulation by off vertical axis rotation. Interaction with another sensory modality has been shown by Buizza et al (1980) in that optokinetic nystagmus can be significantly modulated by simultaneous linear lateral head acceleration. It is difficult to believe that somatosensory nystagmus significantly contaminated the otolith responses observed because of its slow build up, long latency, low frequency sensitivity and dependence on the building of a mental image of subjective motion (Brandt et al 1977)

A further difference between the results using combined angular and linear motion and those with pure linear stimuli is that the gain characteristics of the eye movements expressed as °/s/g have very different slopes (figure 3). With the exception of the slightly enhanced gain at 0.1 Hz the gain plot for pure linear stimuli is almost flat or rises gently (present data and previous results plotted in figure 3), showing that eye velocity is proportional to head acceleration and, in keeping, shows phase advance. In

contrast, the gain of responses to the linear component of combined linear and angular motion shows a slope of approximately -1 indicating that eye velocity is matched to head velocity and is appropriately compensatory. To account for the rising gain characteristics of the eye movement response to linear motion it has been proposed, for example by Hain (1986), that the response is derived either from the "irregular", phasically sensitive units in the primary afferent fibres of the macula, as determined by Goldberg and Fernandez (1976), or from differentiation of the regular unit activity. The compensatory response to the linear component of combined angular and linear head motion would require an integration of the regular unit activity.

The implication of the above for modelling the otolith-ocular reflex is that one way in which the otolith signals become effective is in accompaniment with canal signals if tuned up by a requirement for proximal fixation. The model of Viirre et al 1986, proposes a summing of canal and otolith signals which implies that in the absence of canal signals an effective otolith ocular reflex should still be observed. This does not seem to be the case. The model of Hain (1986) proposes that the otolith signals interact multiplicatively with canal signals in the brainstem velocity storage mechanism and act to adjust storage gain and time constant. Although this model is attractive in simulating the eye movements produced by off vertical axis rotation and suggesting novel ways in which the otolith signal can access the canal pathway, it does not explain the responses produced by high frequency linear stimuli. The experimental findings indicate alternative types of model. One possibility is of a direct otolith-ocular pathway which is normally suppressed and becomes "switched in" in the presence of canal signals. If signals in this pathway are responsible for the weak eye movements evoked by pure linear stimuli then they would require integration and gain enhancement to produce an adequate head velocity signal during

natural head movement. An alternative possibility is that the otolith signals interact multiplicatively with, or enhance the gain of, canal signals to compensate for additional linear head motion.

The reason why robust "otolith-ocular reflex" eye movements are only manifest during combined linear and angular head movements is probably related to the problem of distinguishing between gravitational and acceleratory stimuli which affect the otoliths equivalently. It would be inappropriate to have a significant amount of lateral eye movement evoked by sideways head tilt which causes gravity to stimulate the otoliths in a similar way to lateral linear acceleration. The concurrence of other sensory information such as co-ordinated angular head movement, optokinetic stimulation and, one presumes, visual context allows otolith signals to be interpreted appropriately. This latter possibility will be investigated in the following section.

THE OTOLITH-OCULAR REFLEX IN THE LIGHT

As discussed in the preceding section, pure linear acceleration fails to elicit compensatory eye movements of significance in the dark, although they occur in the presence of simultaneous canal signals. This suggests the existance of a direct otolith-ocular reflex (OOR) which is normally suppressed and becomes "switched in" in the presence of canal signals and/or that the otolith signals enhance the gain of canal signals to compensate for additional linear head motion. The question therefore arises as to whether other concurrent sensory signals might also have similar effects on the OOR.

In this section an experiment designed to assess the interaction between otolith and visual inputs will be described. In the vestibular nuclei, neurons driven by linear optokinetic and head accelerative stimuli have been identified, which may provide the anatomical substrate for an otolith-visual interaction (Daunton and Thomsen, 1979). A suggestion that these sensory signals may play a significant role in the control of eye movements stems from experiments in which optokinetic nystagmus slow-phase velocity was modulated by concurrent linear head acceleration (Buizza et al, 1980) involving predictable, steady-state sinusoidal motion.

Thus, it has not been clearly established what role the purely linear OOR might play during normal viewing conditions, in response to more unexpected head movements. It might be possible that, visually guided, slow phase eye movements (VGEMs) might predominate in compensation for linear motion (Eckmiller, 1982). However, VGEMs movements have a long latency of 125 ms (Robinson, 1965; pursuit of small target) whereas two factors suggest that OOR might have a unique role at an earlier stage of head movement. Firstly, an OOR, like canal reflexes (Lisberger, 1984), should have a short latency. Secondly, because of the acceleration sensitivity of the responses, as shown

in experiments in the dark, the OOR should give strong responses at the onset of movement. Therefore, in order to detect an effective OOR, short latency eye movements evoked by linear head acceleration were sought. This approach provides the opportunity of looking at OOR responses before VGEMs come into action. Since compensation for linear relative motion is only required for viewing nearby targets an appropriate visual context was provided by presenting a visual target close to the subject.

METHODS:

The technique used to obtain linear acceleration of the subjects and recordings was described in the previous section, with the arrangement illustrated in figure 1. Motion stimuli were velocity ramps to the subject's left or right which rose from 0.0 m/s to 1.11 m/s in 423 ms. Because of

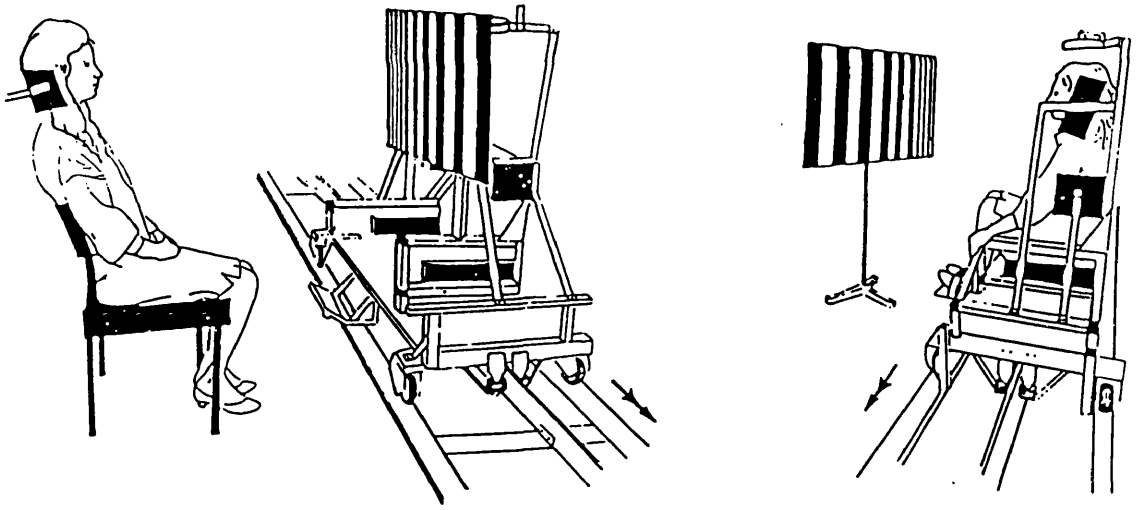

Figure 1. Diagram illustrating the experimental arrangement used to produce lateral linear acceleration of the subject or of the visual target.

servo delay and starting friction the initial acceleration to the head was approximately 0.35g peak reducing to approximately 0.25g within 40 ms (see figure 2). At the velocity of 1.11 m/s the angular displacement of the subject with respect to the visual target was 12° and its relative angular velocity, 53°/s. The stimuli were presented, randomised in direction, within a Latin square design using 6 normal subjects (age range 24 to 61 years) and the following conditions: i) motion of the subject on the car in total darkness; ii) motion of the subject whilst fixating the centre of a target at a distance of 110 cm. iii) the target was mounted on the car and was fixated from a distance of 110 cm by the subject, who was seated, earth stationary, with his head fixed (figure 1). In conditions ii and iii subjects were told to fixate the centre of the target and follow its motion. In the dark, subjects were only instructed to stay alert because the experiments reported in the previous section had shown that mental imagery had little effect on slow phase eye movement responses to linear motion.

The target used in the above experiments was a flat card subtending +/- 20° horizontally and +/- 15° vertically with a pattern of vertically oriented, black and white stripes (spatial frequency 0.5 cycles/°) having a circular centre point subtending 0.5° and which was viewed under normal room illumination. This was thought to be the optimal configuration for the possible development of the technique into a clinical test. However, in order to exclude the possibility that differences in the responses under the two conditions could result from different motion parallax cues with respect to the room background and/or relative target size, further investigations were made in two of the above subjects; a) using a similar target which subtended vertically and horizontally +/-100° of visual angle and, b) using a target consisting of a 0.5° black cross on a 1.0° luminous disk presented in

otherwise total darkness. The larger target provided central and peripheral retinal stimulation without significant motion parallax. The smaller target provided largely central retinal stimulation without motion parallax.

In addition to the normal subjects a 67 year old patient with significantly reduced labyrinthine function, but otherwise neurologically normal, was studied in conditions ii and iii. He had a 20 years history of severe Meniere's disease and underwent a right labyrinthectomy one year before being tested. His nystagmic responses to horizontal rotational velocity steps of +/- 40°/s in the dark were bidirectionally reduced to about 10% of normal slow phase velocities and durations.

Measurements were made on a Solartron Schlumberger 1200 signal processor using a flat frequency bandwidth of 200 Hz and temporal resolution of 3 ms. Data collection included 150 ms before and 600 ms after the onset of car motion. Averages of between 4 and 8 data records from individual subjects were taken separately for rightwards and leftwards stimuli when artefacts were rejected. Between 7 and 14 records were averaged for the experiments in which target size was varied. Measurements were made on the averaged records of each subject of the latencies of slow phase compensatory eye movements evoked by the stimuli. To measure latency, cursors were drawn through the maximum and minimum peak levels in the eye movement trace during the 150 ms preceeding stimulus onset. A response was identified when the post stimulus trace exceeded the bounds of a cursor and maintained a consistent trajectory. Latency was measured with a resolution of +/- 3ms as the time from stimulus onset to the point at which the cursor was intersected. It is estimated that because of noise in the recordings, response latencies could appear to be longer than they were by up to 15ms. In addition the time after stimulus onset required for eye velocity to match target velocity was measured. This was done by overlaying the eye displacement trace on an angular target

displacement trace (the latter was constructed by digitally integrating and scaling car velocity on the signal processor as shown by the target trajectory in fig 2). These traces were seen to converge as the slow phase eye movement homed into the target trajectory and the velocities were judged to match when the traces became congruent.

RESULTS:

Examples of raw data records of the eye movement responses to head acceleration are given in figure 2, LIN(light) and LIN(dark), showing that a slow phase eye movement response, without saccades, commences within 50 ms of the stimulus onset. On average, the responses to head acceleration during target fixation had a mean latency from the onset of acceleration of 34 ms, range 14 to 54 ms (5 subjects, rightwards and leftwards directions combined; one subject was excluded because his response was initiated by an unsuppressed blink). Eye velocity matched target velocity after a mean of 113 ms, range 52 to 246 ms (6 subjects). At this point in time, the mean relative angular velocity of the car and the velocity of the eyes were 15^{o}/s range 14 to 33^{o}/s.

In the dark, eye movement responses to the linear stimulus showed considerable intra and intersubject variability in magnitude. The mean latency of responses was 27 ms, range 15 to 60 ms (3 subjects combining rightwards and leftwards directions; the responses of 3 subjects were excluded because they were initiated by blinks).

For comparison, figure 2 also shows a raw data record of the eye movement response to motion of the target ("PURSUIT") which starts at a latency of 150 ms. On average, responses to motion of the target had a mean latency of 161 ms, range 101 to 197 msec (6 subjects). This was followed within 150 ms by a saccadic eye movement, also towards the target. Following

the saccade the eyes maintained a slow phase movement which matched target velocity, on average, after 264 ms, range 245 to 320 ms (6 subjects). The

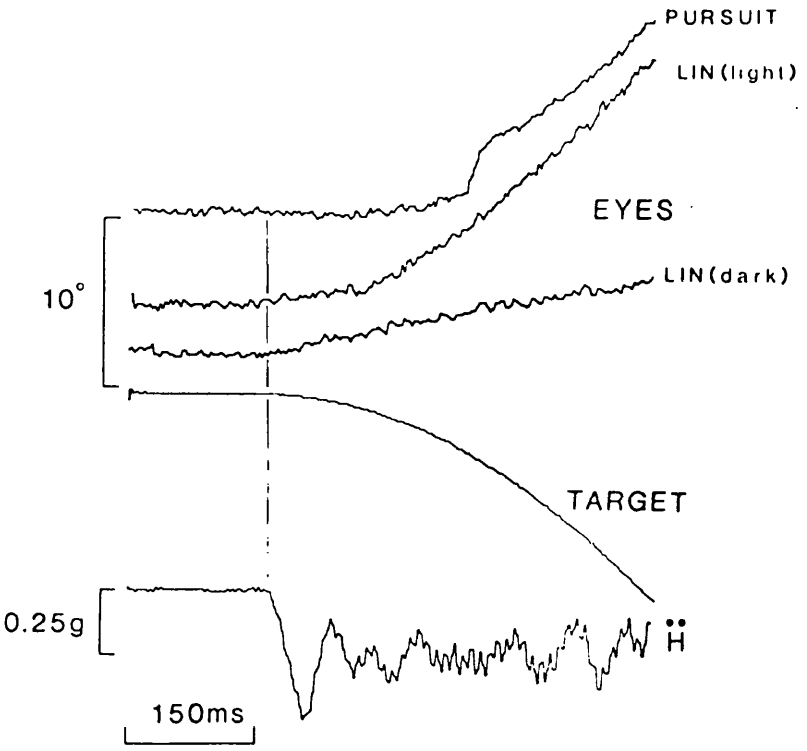

Figure 2. Raw data records from a normal subject showing angular eye displacement responses under the three experimental conditions: i) the subject rides on the car in total darkness "lin(dark)"; the car begins at rest and then moves to the subject's left with a velocity ramp, ii) the subject rides on the car whilst viewing an earth stationary target at 110 cm in the light "lin(light)" and, iii) the subject is seated, earth stationary, and views the target riding on the car. The relative angular motion of the subject and target is the same in conditions ii and iii and is shown by the "TARGET" trace. H: linear acceleration of the subject's head measured along the inter-aural axis. The vertical line indicates stimulus onset from which eye movement response latencies are measured. A position corrective saccade is seen as a stepwise eye movement in the pursuit trace at 225 ms latency.

mean relative angular velocity of the target and of the eyes at this point were 36°/s, range 33 to 43°/s. The latency of responses and time taken for

eye velocity to match target velocity for head acceleration with fixation were significantly shorter than those for target motion (Sign test: $p<0.001$). There was no significant correlation between latency of eye movements in response to subject and to target motion.

Some subjects blinked at a latency of 27 to 50 ms in response to the first few head acceleration stimuli. The blinks merged with the subsequent slow phase eye movement and except for two subjects, habituated. Blinking is probably a startle response (Landis and Hunt, 1939; Fox, 1978) to otolith stimulation (Halmagyi and Gresty, 1983) and is part of a generalised activation of body musculature which has a threshold for evocation of the order of 0.3g (Greenwood and Hopkins, 1976).

Effect of target size: for the two subjects, slow phase responses to motion of the large target commenced with mean latencies of 160 and 148 ms with times to match target velocity of 282 and 330 ms. Slow phase responses to motion of the small, luminous target in darkness were at mean latencies of 167 and 173 ms with times to match target velocity of 420 and 320 ms. Mean response latencies when subjects moved linearly viewing the stationary small target in darkness were 48 and 46 ms with times to match target velocity of 138 and 112 ms. For comparison, the latencies of these subjects responses to head movement viewing the medium size target were 44 and 48 ms.

Figure 3 shows the averaged responses of a normal subject and of the labyrinthine deffective patient. In contrast to the normal subject, the patient had no short latency eye movements to head motion. His responses to both target and head movement were identical, commencing at 190-200 ms.

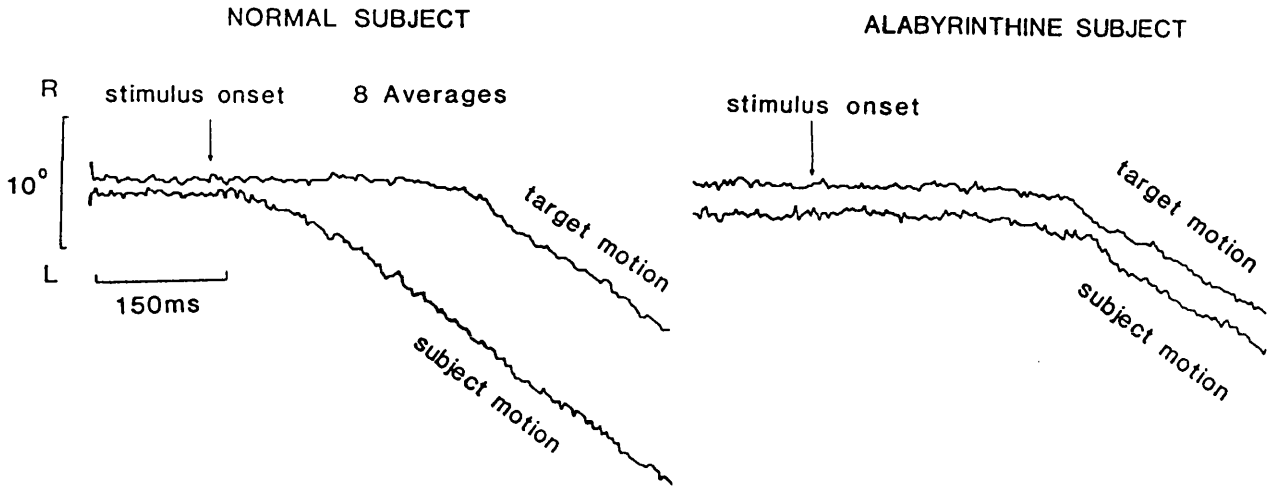

Figure 3. Responses of a normal subject and of a labyrinthine defective patient to experimental conditions ii) subject motion and iii) target motion. The traces represent averages of 8 responses for each condition. Note that the normal response to subject motion, beginning shortly after stimulus onset, is absent in the alabyrinthine subject.

DISCUSSION:

The experiments have shown that linear head acceleration evokes a short latency compensatory eye movement. It is unlikely that this response is a visuo-motor reflex because the latencies of eye movements to target motion were five times longer than the latency of responses to head acceleration. The latencies found for visually guided slow phase eye movements (VGEMs) in response to target motion are in agreement with those accepted for human

smooth pursuit (Robinson, 1965). VGEMs at a short latency of 50 ms have recently been reported in the rhesus monkey (Miles et al, 1986), however, there is no evidence in the present experiments or in the literature, that human subjects are capable of such short latency VGEMs. In particular, it has been impossible to shorten visual following latencies by manipulating the target in size from that of a large optokinetic field (100^{o}) to a central target (1^{o}).

In contrast, responses to linear head movement were evoked at short latencies, less than 50 ms, regardless of target size or whether the subject was in darkness. The latency of the response to linear head motion compares favourably with the latency of compensatory responses to angular (Lisberger, 1984) and combined angular and linear head motion (Virre et al, 1986) in the monkey. In addition, and perhaps of most importance, short latency responses were absent in the labyrinthine deffective subject. For these reasons the short latency response is almost certainly an otolith-ocular reflex (OOR).

The importance of this finding is in showing that there is a robust OOR in response to purely linear motion which provides stabilisation of the visual axis before visually guided eye movements become effective. Thus, within the context of an earth fixed visual frame of reference, the OOR is evoked with consistency and appropriate scaling. Similarly, it has been shown that robust OOR responses can be evoked in man by periodic motion in context with concurrent canal signals (previous chapter) or optokinetic stimuli (Buizza et al, 1980) (see appendix for comparative values). It may be possible that the need for an appropriate sensory context for strong OOR responses to manifest relates to the problem of resolving the ambiguities to which the otolith system is exposed: distinguishing gravitational from linear acceleratory stimuli, as discussed above, and conflicting angular-linear head motion, as exemplified in diagram B in the previous chapter.

The OOR provides compensation during the early stages of linear head movement up to around 150 ms. From this time on, VGEMs combine with or replace the OOR in maintaining the eyes on target (Buizza et al, 1980; Eckmiller, 1982). However, VGEMs alone do not become fully effective until around 250 to 300ms whereas the OOR provides early eye acceleration which leads smoothly into target following without corrective saccades. Since the eye movement provoked by linear head motion starts after the onset of movement it must have a higher initial acceleration than that of the stimulus in order that the eyes catch up with the target. This initial eye acceleration is possibly derived from the activity of the irregular otolith units in the primary afferents which respond to a partial derivative of acceleration, "jerk" (Fernandez and Goldberg, 1976). Jerk sensitivity would allow a prediction of future demands on eye velocity. This view is consistent with that exposed in the preceding section and with previous observations (see Barnes, 1980) on the dynamics of the OOR, showing a phase lead in the dark, which one would expect from the phase characteristic of irregular otolith units. Once on target, and before VGEMs commence (ie between 115 and 160 ms), eye acceleration is constant and could, therefore, be derived from the activity of regular otolith units which shows a constant proportionality to acceleration accross frequencies.

As stated in the general introduction, the aim underlying the work described in this thesis was to learn more about the way in which the various sensory inputs interact in the control of balance and eye movements so that new testing procedures could be incorporated for the investigation of the patient with disequilibrium. It is envisaged that some of the experimental techniques described can become useful clinical tests so that, in addition to the standard assessment of semicircular canal and optokinetic function,

information concerning for instance the cervical and otolith input can be available for diagnostic purposes.

APPENDIX: Comparative gain estimates of the OOR.

The high frequency (circa 0.8 Hz) gain of the OOR in the dark has previously been estimated as $17^{o}/s/g$ in terms of eye velocity or $85^{o}/s^{2}/g$ in terms of eye acceleration (summarised in Barnes, 1980). This represents a background level of sensitivity and does not take target distance into account. In the present experiments, eye acceleration could not be measured from the electro-oculographic records because the inherent noise in the signal would cause too much degradation of the data after double differentiation. However, the steady state eye acceleration after catching up with the target but before VGEMs become effective could be estimated from the acceleration of the stimulus velocity ramp, since eye and target displacement records were congruent, and was approximately $140^{o}/s^{2}$. In response to a head acceleration of 0.26 g this eye acceleration shows a gain of $540^{o}/s^{2}/g$ (at our target distance of 110 cm). This estimate compares well with the gain of $630^{o}/s^{2}/g$ for the response to the linear component of combined angular and linear head movement obtained from subjects imagining fixation on a target at 60 cm. These values are also the same order of magnitude as the estimate of $250^{o}/s^{2}/g$ for the sinusoidal modulation of optokinetic eye movements by linear head motion (calculated from Buizza et al, 1980).

SUMMARY

- In the first set of experiments the otolith-ocular reflex in response to pure linear acceleration in the dark was evaluated. One of the main interests was to evaluate the effects of visual imagery of a nearby target, as this aspect was frequently ignored in the past. Compensatory slow phase, eye movement responses were assessed in normal subjects exposed to linear acceleration of the head along the inter-aural axis. The linear acceleration was provided by a cart powered by linear motors and the stimuli waveforms consisted of relatively unpredictable windowed sinusoids centred on frequencies of 0.1, 0.5 and 1.2 Hz at maximum peak velocities of 0.32 m/s. Subjects were instructed either simply to keep alert or required to imagine fixating the target during the trials. In addition, as a test of linearity of response gain, using the 0.5 Hz stimulus, peak velocity was varied up to 2.56 m/s. Under both instructions the linear stimuli evoked weak slow phase eye movements interspersed with occasional fast phases. Imagining a target had a weak enhancing effect on slow phase velocity at 0.1 Hz with no enhancement at the higher frequencies. On average, the slow phase movements had a gain of 17^{o}/s/g accross the frequencies tested, which is too low to compensate for head movement relative to the proximal target. The average phase of response ranged between 30-95^{o} in advance. Slow phase velocity was linearly related to magnitude of acceleration with a threshold of 0.075g.

The present results contrast with findings reported in the previous chapter that, during combined linear and angular head movement, robust slow phase eye movements, which are enhanced by imagery, are evoked by the linear component of motion at gains adequate to compensate for head movement relative to nearby targets. It would seem that, unlike canal-ocular reflexes, the otolith-ocular reflex in isolation does not generally show voluntary

non-visual enhancement. The weak enhancement at 0.1 Hz may be related to pursuit mechanisms.

- In another set of experiments, second section of this chapter, normal subjects were exposed to 0.26 g linear acceleration steps along the inter-aural axis whilst they fixated an earth stationary target at 110 cm distance. The stimulus evoked slow phase eye movements at a mean latency of 34 ms which attained the relative target velocity in 113 ms. In contrast, visual following with head fixed, of identical relative target motion, had significantly longer latencies and time to match target velocity. The short latency responses to linear acceleration were absent in an alabyrinthine subject. It is concluded that the otolith-ocular reflex is responsible for the short latency responses to linear head movement and functions to stabilise vision during sudden head movement before visually guided compensatory eye movements take effect.

The experiments described in this and the preceding chapter provide evidence about the need of concurrent sensory stimulation for the otolith to generate powerful compensatory eye movements. Interaction of the otolith signals with other sensory modalities can occur with both canal and visual stimuli. The lack of an appropriate sensory context to investigate OOR function in the past, with experiments typically carried out without instructions in the dark, led to the erroneous impression that the vestibular system was unable to generate significant compensatory eye movements in response to linear head movements. It is suggested that the need of the otolith-ocular reflex for concurrent sensory signals may be related to the problems of distinguishing gravitational from linear acceleratory stimuli and resolving conflicting angular-linear head motion so that an appropriate eye movement is generated.

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APPENDICES

DECLARATORY NOTE:

Most of the experimental work described in the preceding chapters has already appeared in the specialized literature. It was felt important to include those articles in this volume because it is mainly in that form, as individual papers, that the work will become known to the international scientific community. The description of the material, methods and presentation of the results is virtually the same in the papers and in the thesis whereas the introductions and discussions have been carefully adapted for the specific requirements of each form of publication. I believe that such a change has allowed for a better cross referencing between different sections of the research and improved coherence and homogeneity of the work presented in the thesis.

Each paper has been labelled with a capital letter at the top so that they can be better identified when referenced in the text. These references to the appendices have been usually reserved for some technical details or additional processing of the data which might not have been essential for the main thrust of the thesis.

The specific research topics common to the papers (apendices) and the thesis are as follows:

- Appendix A: Chapter I, pages 13-32, "The cervico-ocular reflex in normal subjects and in patients with absent vestibular function".

- Appendix B: Chapter I, pages 33-44, "Compensation of oscillopsia of peripheral vestibular origin: The role of the cervical input".

- Appendix C: Chapter I, pages 33-44, referenced in the discussion in "Compensation of oscillopsia of peripheral vestibular origin: The role of the cervical input".

- Appendix D: Chapter II, pages 52-60, "Vestibular contribution to head stability".

- Appendix E: Chapter II, pages 61-69, "Vestibular involvement in Spasmodic Torticollis".

- Appendix F: Chapter II, pages 70-81, "Spasmodic Torticollis following vestibular lesions".

- Appendix G: Chapter II, pages 82-92, "Further investigations on the interaction between head posture and the vestibular system in Spasmodic Torticollis: The VOR before and after botulinum toxin injections".

- Appendix H: Chapter II, pages 47-51, "Review and introduction", and pages 82-92, referenced in the discussion in "Further investigations on the interaction between head posture and the vestibular system in Spasmodic Torticollis: The VOR before and after botulinum toxin injections".

- Appendix I: Chapter III, pages 102-106, "Eye movement responses to combined linear and angular head movement".

- Appendix J: Chapter III, pages 107-120, "Combined linear and angular acceleration: The effects of unpredictable stimuli and target imagery".

- Appendix K: Chapter III, pages 121-133, "Rotation with the head eccentric. Preliminary clinical applications".

- Appendix L: Chapter IV, pages 152-162, "The otolith-ocular reflex in the light".

SUPPORTING PAPERS:

The following is a list of the supporting papers, included as appendices to this thesis, found at the end of this volume:

Bronstein, A.M. and Hood, J.D. (1986) The Cervico-Ocular Reflex in Normal Subjects and Patients with Absent Vestibular Function. Brain Research 373: 399-408.

Bronstein, A.M. and Hood, J.D. (1987) Oscillopsia of Peripheral Vestibular Origin. Acta Otolaryngol (Stockh) 104: 307:314.

Bronstein, A.M. (1986) Suppression of visually evoked postural responses. Experimental Brain Research 63: 655-658.

Bronstein, A.M. (1988) Evidence for a Vestibular Input Contributing to Dynamic Head Stabilization in Man. Acta Otolaryngol (Stockh) 105: 1-6.

Bronstein, A.M. and Rudge, P. (1986) Vestibular involvement in spasmodic torticollis. J. Neurol. Neurosurg. Psych. 49: 290-295.

Bronstein, A.M., Rudge, P. and Beechey A.H. (1987) Spasmodic torticollis following unilateral VIII nerve lesions: neck EMG modulation in response to vestibular stimuli. J. Neurol. Neurosurg. Psych. 50: 580-586.

Stell, R., Bronstein, A.M. and Marsden, C.D. (1989) Vestibulo-ocular abnormalities in spasmodic torticollis before and after botulinum toxin injections. J. Neurol. Neurosurg. Psych. 52: 57-62.

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The Cervico-Ocular Reflex in Normal Subjects and Patients with Absent Vestibular Function

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The role of the cervico-ocular reflex (COR) has been studied in 12 patients with absent vestibular function and 13 normal subjects. Ramp and sinusoidal displacement stimuli were applied with trunk on head and head on trunk movements. In all patients, trunk on head movements evoked a marked slow-phase compensatory COR while in normal subjects it was weak and variable in direction. Fast components of the COR induced gaze shifts in the direction of the relative head movement ('anticompensatory' direction) which could be suppressed by imagining an earth fixed targed. No tonic component could be identified instead, in the case of ramp stimuli, a residual eye deviation was noted which was significantly enhanced in the patients and resulted from activity dynamically generated during the course of the trunk movement and not from its final angular displacement. Head on trunk ramp displacements in the dark evoked initial anticompensatory saccades followed by slow compensatory components, a pattern of eye movements remarkably similar to that seen during active head–eye target seeking. Thus, in the absence of labyrinthine function, the COR appears to take on the role of the vestibulo-ocular reflex in head–eye coordination in (a) the initiation of the anticompensatory saccade which takes the eyes in the direction of the target, and (b) the generation of the subsequent slow compensatory eye movements. Central pre-programming, as revealed by comparing the effect of different instructions and active versus passive neck-induced eye movements, has a profound influence on COR functioning.

INTRODUCTION

Most active head movements occurring in everyday life are step or ramp movements, normally associated with eye movements as part of a strategy designed to shift gaze in space in response to visual or auditory stimuli[8,25]. This type of eye–head coordination consists of an initial fast offset of the eyes in the direction of the object of interest (refoveating saccade), followed, after a few milliseconds, by a head movement in the same direction. During this head movement fixation upon the target is supported by the vestibulo-ocular reflex (VOR), which induces what has come to be termed a compensatory slow eye movement because it occurs in the opposite direction to that of the head. Although the initial anticompensatory saccade was originally thought to be visually elicited there have been more recent suggestions that, at least in certain circumstances, it may be generated by way of the VOR[3,22], its function being to contribute to target acquisition in the direction of the ongoing head movement[18].

Patients with absent vestibular function typically suffer from imbalance and oscillopsia. The latter results from loss of the VOR and manifests itself as a disturbing illusion of movement of the environment[7]. Some patients, however, are much less disabled than others and this can be attributed to the development of a number of compensatory mechanisms which take over the stabilizing role of the slow component of the VOR[15]. Prominent among these is the cervico-ocular reflex (COR) which, although virtually non-existent in normal monkeys, has been shown in labyrinthectomized animals to become increasingly instrumental in restoring the slow compensatory eye movements which accompany active head movements[11]. To date,

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however, information is lacking on the relevance of these findings to the possible role the COR might play in other circumstances such as gaze transference.

The existence of a COR in man has been recognized since Barany's early observations[1b] but its function remains a matter of some controversy. This may be attributed in part to the technical difficulty of examining the reflex in isolation which involves restraining the head in space while rotating the trunk. Surprisingly, the limited studies available using this technique have, without exception, been confined to the effects of sinusoidal trunk rotation. This selective interest in the dynamic components of the COR contrasts with the early observations of Barany[1a,1b], Magnus[17], De Kleyn[10] and Frenzel[12], who invariably included descriptions of a tonic deviation of the eyes on sustained neck torsion.

The results of recent studies of the neck–eye reflexes in humans with absent vestibular function are by no means as clear cut as those in the monkey. Only one of two patients studied by Barnes[4] had an enhanced COR and although 3 cases presented by Kasai and Zee[15] were reported to have increased COR gain, normative data were not available. By contrast, a later study of 5 normal subjects and 5 patients with absent vestibular function concluded that the latter had normal neck–eye reflexes and that the COR did not seem to compensate for loss of labyrinthine function[16].

The issues involved are clearly of clinical and theoretical importance which calls for further clarification. In the investigation to be described the COR has been studied in 12 patients with absent labyrinthine function and in 13 normal subjects. Specific questions to which we have addressed ourselves are: (a) Does a tonic component of the COR make any contribution to the maintenance of eccentric gaze? (b) Is the COR enhanced in patients with absent vestibular function? (c) What is the COR influence in target acquisition and retention during head movements?

MATERIALS AND METHODS

The 12 patients were aged 22–73 years and the 13 normal subjects 24–60 years. The patients had either absent or grossly reduced nystagmic reactions to caloric tests with water at 30 °C, 44 °C and occasionally 20 °C in the light and dark and to impulsive rotation of at least 60°/s in the dark. They had sought medical advice because of variable degrees and combinations of deafness, tinnitus, oscillopsia, imbalance and dizziness. In 8 cases ototoxicity by aminoglycoside antibiotics was the proven or possible cause, alone or in combination with meningitis (3 cases). One patient had Von Recklinghausen's disease with bilateral VIIIth nerve neuromas and another had lost VIIIth nerve function during a subacute illness with uveitis and skin lesion, thought to be Vogt–Kyanagi–Harada disease. In two patients with markedly reduced vestibular responses no cause was found. The duration of loss of vestibular function ranged between 5 months and 30 years. All the experiments to be described were carried out in total darkness.

Studies with head fixed in space

In order to examine the role of the neck reflexes in isolation it is necessary to rotate the trunk while maintaining the head immobile. To this end the subjects sat in a rotating chair which could be moved manually and were required to bite on a dental plate attached to a rigid frame mounted on the wall. A closed circuit TV display using an infrared camera directed at the subject's head testified to the absence of any inadvertant head movement. Some subjects who experienced difficulty because of dental prosthesis were assisted manually. Following preliminary trials during which the subjects were encouraged to relax their neck muscles few problems were encountered. In the following it is convenient to refer to these as trunk on head movement.

Ramp stimulation — trunk on head. In the case of ramp displacement stimuli the chair was moved randomly from left to right or vice versa over varying angular displacements between 10 and 50° at peak velocities ranging between 10 and 20°/s. A target light mounted in line with primary gaze was presented about 2–8 s following the termination of each discrete trunk movement. In this way it was possible to measure any residual deviation of the eyes from the primary position of gaze. All the subjects were required to fixate the target when it was switched on, but, in complementary experiments, some subjects were instructed to look straight ahead during the trunk movement, as if the target light was on all the

time (imaginary target). This imagining task was always performed following the routine test and did not affect the subjects' ability to maintain their neck muscles relaxed.

Sinusoidal stimulation — trunk on head. Sinusoidal trunk on head movements were applied manually over a range of frequencies from 0.07 to 0.4 Hz with amplitudes of approximately ± 25° and peak velocities ranging between 10 and 50°/s. Additionally, a 0.3 Hz stimulus (in synchrony with a metronome) with an amplitude of about ± 25° and peak velocity of approximately 45°/s was also applied. Repeated enquiry was made as to the subjects' ease and, if any discomfort developed, the highest frequencies were not used.

Studies with head free

Ramp stimulation — head on trunk. By way of comparison the effect of neck torsion during active head movements (head on trunk) was also studied. For this purpose the subjects wore a light helmet connected to a low torque potentiometer which monitored horizontal head position. To its front was attached a 50 cm long rigid rod with a target light attached to its distal end which moved with the subject's head. Subjects were instructed to make discrete random head movements to the right and left over variable amplitudes. About 2–8 s following the termination of each movement the target light was lit so that, following refixation, measurements could be made of any residual deviation of the eyes from the primary position of gaze. Additionally, in the case of the patients, in order to exclude any role played by volition, rapid ramp angular displacements of the head were passively and unpredictably delivered by the experimenter in darkness. The head and the helmet were securely and firmly held by the experimenter in order to avoid any inadvertant slippage during the execution of this manoeuvre.

Adopting the same experimental set-up, target seeking strategies were also examined by requiring the subjects to locate target lights presented randomly on a tangent screen 1.5 m to the front and covering visual angles between ± 10 and ± 50°.

Sinusoidal stimulation — head on trunk. As a counterpart to the studies of sinusoidal trunk on head movements, sinusoidal head on trunk movements were studied by asking the subjects to move their head from side to side at a frequency of 0.3 Hz in time with a metronome over amplitudes of approximately ± 25°. Those subjects who found this difficult were guided manually by the experimenter in order to induce smooth movements. In the circumstances it cannot be claimed that these head movements were exclusively active or passive. Eight patients undertook this test, the two with some residual vestibular function being excluded. Nine normal subjects served as controls.

In addition to the above studies the VOR in darkness was recorded in the same 9 normal subjects in response to whole body (i.e. trunk with head) sinusoidal oscillation at 0.3 Hz over ± 25° while they were performing mental arithmetic. In order to exclude any interference from the COR their heads were rigidly clamped to the chair. As an additional enquiry of the influence of neck torsion upon the VOR 3 normal subjects were rotated sinusoidally with their heads turned as far as comfortably possible (usually about 75°) to the left, care being taken to ensure that their eyes were in the primary position of gaze.

Eye movements were recorded with bitemporal direct current electro-oculography (EOG) after the subjects had been adapted to the dimly lit room for at least 15 min. Chair, helmet and eye position, together with a target light signal, were displayed on an inkjet recorder (ELEMA Mingograph).

Data analysis

For the ramp tests (trunk on head and head on trunk) the amplitude of the residual eye deviation was plotted against the angle of neck torsion and a regression line fitted to the data, usually comprising some 15 measurements. The slope of the line will be referred to as amplitude gain.

Velocity gain is defined as the ratio between peak slow component velocity of nystagmus and either trunk or head movement peak velocity for both ramp and sinusoidal tests. Gaze shift amplitude gain was taken as the ratio between peak eye displacement and peak trunk displacement, during sinusoidal COR. The recordings were analyzed by hand. In the case of sinusoidal stimuli, measurements were carried out over 20–30 s periods which included 2 and 8 cycles, respectively, of the lowest and highest frequencies.

RESULTS

Studies with head fixed in space

Ramp stimulation — trunk on head. In normal subjects trunk movement initiated a somewhat irregular combination of fast and slow eye movements. In 9 of the 13 subjects the saccadic movements were predominantly in the direction of the head movement relative to the trunk while in 4 they were in the opposite direction. Slow phases were generally weak and ill-defined and irregular in direction. In no instances was a regular pattern of vestibular-type nystagmus detected. Presentation of the target light at the termination of trunk movement revealed a persistent or residual deviation of the eyes from primary gaze (Fig. 1). In 5 subjects it was in the same direction of the relative head movement and in 8 subjects in the opposite. The VOR elicited in darkness has been shown to be markedly modified by requiring subjects to fixate upon an imaginary earth-fixed target[6,23]. Interestingly, a similar modification can be demonstrated with

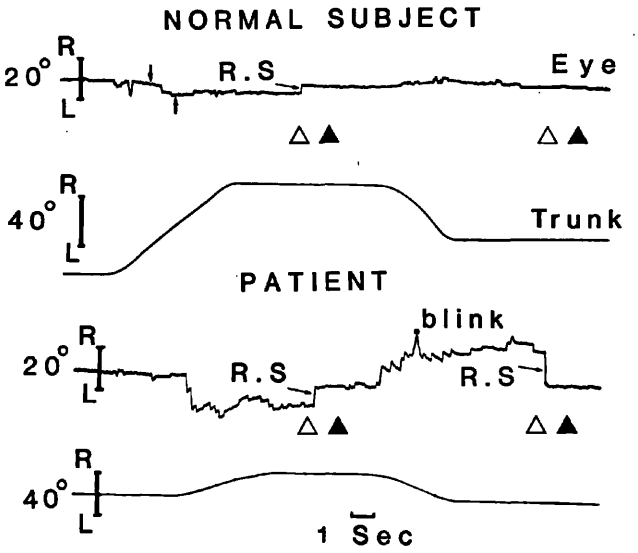

Fig. 1. Eye movements elicited during ramp trunk displacement with the head fixed. Normal subject: during rotation to the right (R) (relative head movement to left), very weak slow eye movements were elicited, which changed direction (vertical arrows) during the course of the stimulus. A small residual eye deviation to the left (L) persisted for several seconds at the termination of movement as is evident from the recentering saccade (RS) required to bring the eyes on to the target light (open triangle). Closed triangles indicate target light off. Rotation in the opposite direction elicited equally irregular but weaker response. Patient: trunk rotation from centre to right and vice versa induced marked nystagmus and gaze shift in the direction of the relative head movement. The residual eye deviation persisted until its cancellation by presentation of the target light.

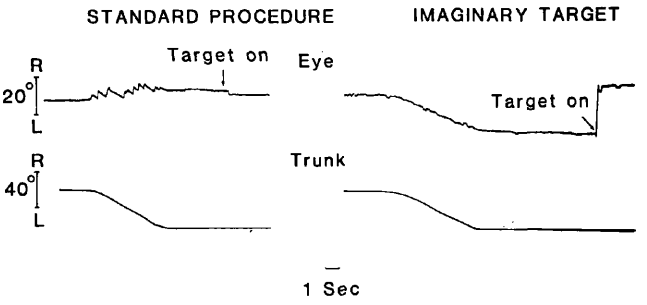

Fig. 2. Effect of instruction to a patient upon eye movements elicited during trunk ramp displacement with head fixed. In the standard procedure the subject was required to look at the target when presented. With imaginary target the patient was instructed to look straight ahead 'as if the target light was on all the time'.

the COR. Thus, 3 subjects, two of whom had consistently deviated in the direction of the relative head movement, were instructed to imagine a visual target to their front. Under these circumstances saccadic activity was reduced and the eyes executed low velocity slow-phase movements mainly in a direction opposite to that of the neck torsion.

In the lower tracing of Fig. 1 is shown a response to trunk on head ramp movement highly characteristic of the patients with absent vestibular function. The striking feature is the appearance of a sawtooth nystagmus during trunk movement with the fast component beating in the direction of the relative head movement. The effect of imagining a fixed target in the case of a patient is shown in Fig. 2. This procedure resulted in a marked suppression of fast phases and the eyes deviated in a direction opposite to the relative head movement. Visual fixation abolished all eye movements elicited by neck torsion in normal subjects and patients.

The results shown in Fig. 3 illustrate the typical re-

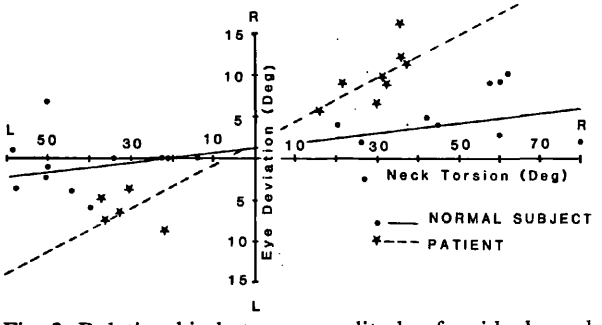

Fig. 3. Relationship between amplitude of residual eye deviation and neck torsion angle following ramp trunk displacement with the head fixed. Slopes (amplitude gain) of the regression lines; normal subject, 0.05; patient 0.26.

TABLE I

Results of ramp trunk on head stimulation

	Amplitude gain (slope)	*Symmetry of response (y intercept)*	*Cases showing anti-compensatory responses*[a]	*Velocity gain*
Normal controls	0.06 (S.D. 0.03)	0.98 (S.D. 0.98)	38%	0.05 (S.D. 0.07)
Patients	0.16 (S.D. 0.11)	3.84 (S.D. 2.64)	66%	0.51 (S.D. 0.26)

[a]Residual eye deviation in the direction of the relative head movement.

lationship between amplitude of trunk rotation and residual eye deviation in one normal subject and one patient in whom the deviation was in the same direction as the relative head movement. Findings in respect of patients and normal subjects are summarized in Table I where it will be seen that the amplitude gain (slope) of the former is almost 3 times that of the latter. In 8 out of 12 patients the residual eye deviation was in the direction of the relative head movement due to a prevalence of quick over slow eye movement components.

In order to establish whether the residual eye deviation was a function of a tonic or dynamic neck input some subjects, following the initial target fixation, were kept in total darkness with neck torsion sustained before the target was re-presented. Under these circumstances in neither the patients nor the normal subjects did the residual deviation reappear once it had been cancelled by the previous target presentation. It follows, contrary to the expectation which motivated the design of the experiment, that the residual eye deviation is a balance of activity dynamically induced during trunk movement and not a manifestation of neck tonus. This is further supported by the fact that trunk movements from centre to lateral positions or from excentric to centre positions were equally effective in inducing eye deviation; an example of the latter is shown in the recording of the patient in Fig.1.

Interestingly, in a few patients, vestibulo-ocular asymmetries established at neuro-otological examination were matched by similar asymmetric responses of the COR.

Sinusoidal stimulation — trunk on head. As with the ramp stimuli, marked differences were apparent in the responses of normal subjects and patients to sinusoidal trunk movement as exemplified in Fig. 4. Whereas in the former eye movements were feeble, variable in direction and frequently difficult to correlate with the stimulus, in the patients the slow movements were always clearly identifiable as compensatory insofar as they were consistently in a direction opposite to that of the relative head movement. In Fig. 5 is shown the velocity gain of the COR in 9 patients successfully studied over a range of frequencies and of 5 normal controls from whom reliable responses were elicited. The remaining patients were incompletely studied but they also manifested a hyperactive COR. The velocity gain of the reflex consistently decayed with increase in stimulus frequency.

Gaze shift amplitude gain was slightly increased in the patients (Mann–Whitney test; $Z = 1.97$, $P = 0.05$) but was not consistently related to frequency of stimulation, and considerable variation was present in both groups (Table II). This gaze shift, which occurred in the direction of the relative head movement

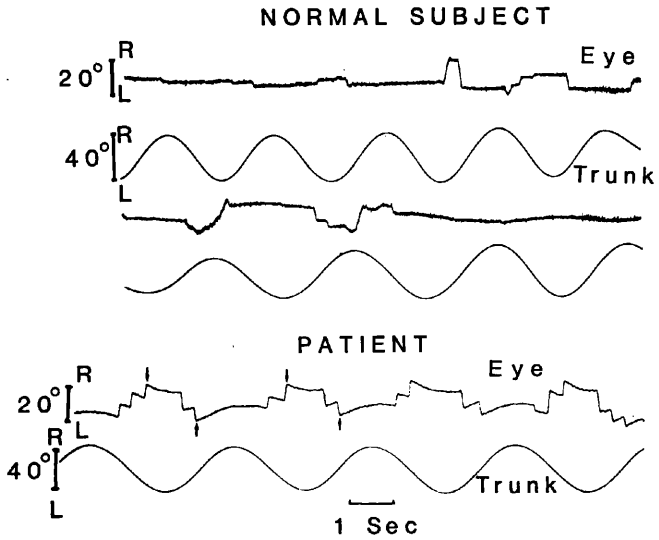

Fig. 4. Sinusoidal trunk displacement with the head fixed. A consistent nystagmus pattern is apparent only in the patient. Slow components are opposite in direction to and approximately in phase with relative head movement. Peak gaze displacements, brought about by saccadic components and indicated by arrows, are in the same direction as relative head movement and 90° phase-advanced.

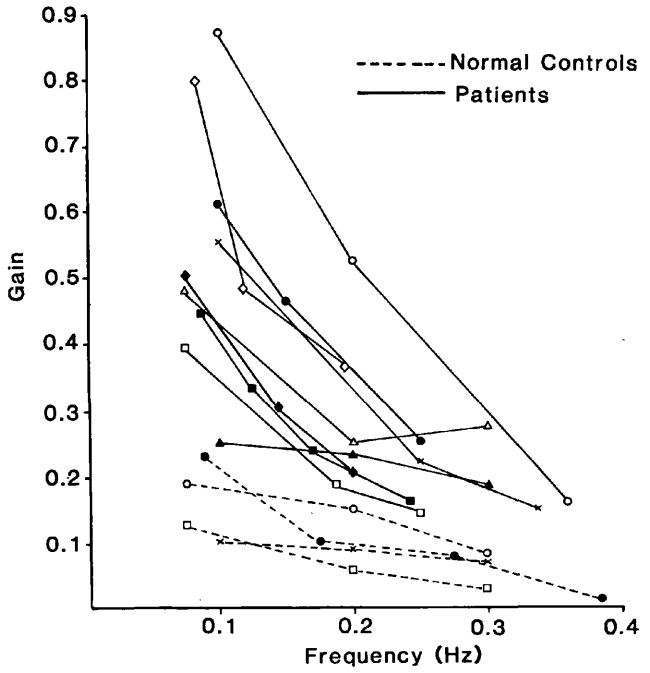

Fig. 5. COR velocity gain (peak slow-phase eye velocity/peak trunk velocity) during sinusoidal stimulation. Individual data on 9 patients and 5 normal subjects.

in both groups, was brought about by saccadic components. In the case of the normal subjects, however, gaze shifts had variable phase relationships and lagged the stimulus by 32° ± 48 (S.D.). By contrast, in the case of the patients it occurred characteristically 90° in advance of trunk displacement, i.e. at zero trunk displacement and maximum stimulus velocity presumably triggered by acceleration (Fig. 4).

Studies with head free

Ramp stimulation — head on trunk. The pattern of eye movements evoked by active head turning in the dark was remarkably similar in both normal subjects and patients (Fig. 6). It consisted of one or more saccades in the direction of head movement followed by a slow return of the eyes in the opposite direction, i.e. towards the centre of the orbits. Saccadic activity tended to prevail in the accelerative and slow eye

TABLE II

Gaze shift amplitude gain during sinusoidal COR (median and range)

	0.1 Hz	*0.2 Hz*	*0.3 Hz*
Normal controls	0.14 (0.09–0.63)	0.18 (0.10–0.60)	0.17 (0.03–0.60)
Patients	0.32 (0.15–0.54)	0.23 (0.13–0.50)	0.26 (0.10–0.42)

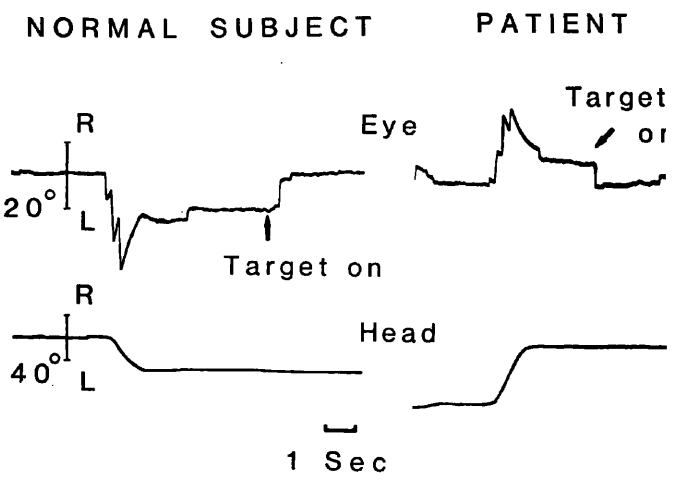

Fig. 6. Active ramp head on trunk displacement. Note similarity of eye movements in normal subject and patient (same subjects as in Fig. 1) and sustained eye deviation in the direction of head movement, revealed by presentation of target light.

movements in the decelerative phase. On cessation of head motion a residual eye deviation persisted in the same direction. Its magnitude, assessed in terms of the recentering saccade required to bring the eyes on to the target light, was a function of head deviation and comparable in both groups (amplitude gain or slope: normals, 0.22 ± 0.13 (S.D.), patients 0.18 ± 0.15 (S.D.)).

Eye movement responses to rapid ramp angular displacement of the head passively and unpredictably

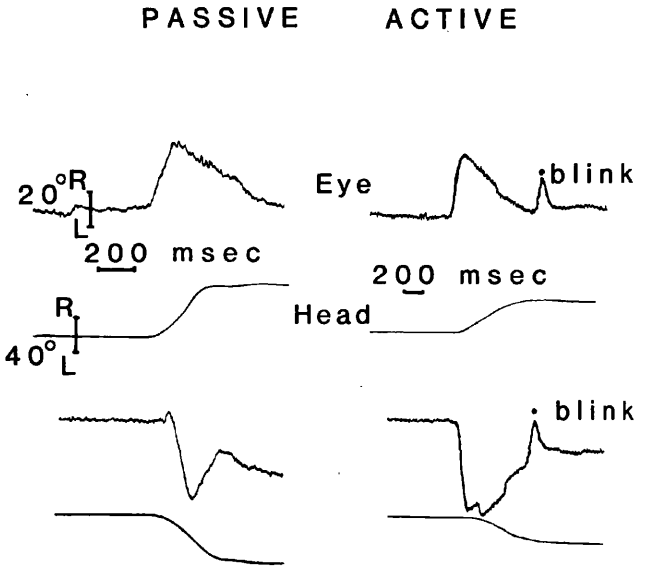

Fig. 7. Left: eye movements elicited in a patient by sudden and passive rapid ramp head on trunk displacement in the dark. The pattern of eye movements is essentially similar to that elicited when the patient actively directed his eyes and head towards a visual target, randomly presented to the right or left of primary gaze (right).

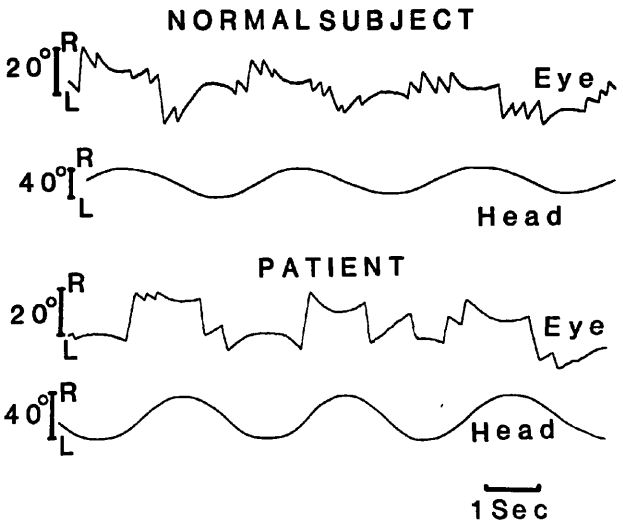

Fig. 8. Sinusoidal head on trunk rotation in the dark. Nystagmic pattern is similar in normal subject and patient but slow-phase velocities are slower in the former.

delivered, together with eye and head movement responses during active target seeking in a patient are shown in Fig. 7. Both are characterized by an initial saccade followed by a slow movement of the eyes in the opposite direction to head movement and similar to the eye movements shown in Fig. 6 resulting from active head movements in the dark. The latency of the eye movements elicited by passive head turns had a mean value of 50 ms ± 33 (S.D.) in 8 patients tested. This short latency is clearly indicative of the reflex nature of the response.

Sinusoidal stimulation — head on trunk. Sinusoidal head on trunk movements in the dark gave rise in all subjects to a consistent nystagmic reaction in the direction of head movement (Fig. 8). In the patient group, as a result of absence of the VOR, slow component velocity was much reduced as is reflected in the velocity gain measurements shown in Table III in which are included, for comparison, the gains for COR and VOR. However, it is of particular note that the gain for head on trunk 0.37 was significantly higher than that for trunk on head 0.24 (paired t-test; $t = 2.52$, $P < 0.05$). By the same token sinusoidal head on trunk movements in normal subjects induced velocity gains (0.82) significantly higher than those found with the head rotated en bloc with the body (0.60) (paired t-test; $t = 4.53$, $P < 0.01$). Sustained neck deviation to one side (left) did not consistently induce any asymmetry in the VOR as shown in Table IV.

TABLE III

Velocity gain at 0.3 Hz sinusoidal stimuli in darkness

	VOR	*Head on trunk*	*COR*
Normal controls	0.60 (S.D. 0.21)	0.82 (S.D. 0.13)	0.02 (S.D. 0.03)
Patients	–	0.37 (S.D. 0.16)	0.24 (S.D. 0.09)

DISCUSSION

The main topics of interest that have emerged from our studies concern the tonic properties of the COR and the role of the COR in target acquisition and gaze stability. For convenience of discussion these will be addressed separately.

Tonic COR. The studies using discrete ramp trunk movements with head restrained have shown that in normal subjects and patients with absent vestibular function a residual eye deviation was induced (markedly so in the case of the patients), the ampli-

TABLE IV

VOR in darkness with head centered or turned left (normal subjects)

Movement	*Velocity gain*				*Phase error**			
	Head center		*Head left*		*Head center*		*Head left*	
	Right	*Left*	*Right*	*Left*	*Right*	*Left*	*Right*	*Left*
Subject 1	0.58 (S.D. 0.10)	0.67 (S.D. 0.09)	0.53 (S.D. 0.12)	0.57 (S.D. 0.21)	3.10 (S.D. 1.80)	2.30 (S.D. 0.98)	3.40 (S.D. 1.20)	4.70 (S.D. 1.40)
Subject 2	0.99 (S.D. 0.15)	1.02 (S.D. 0.05)	0.73 (S.D. 0.09)	0.71 (S.D. 0.05)	1.10 (S.D. 0.30)	0.60 (S.D. 0.40)	2.30 (S.D. 0.70)	0.50 (S.D. 0.20)
Subject 3	0.83 (S.D. 0.06)	0.95 (S.D. 0.20)	0.80 (S.D. 0.12)	0.95 (S.D. 0.14)	5.40 (S.D. 2.0)	-3.10 (S.D. 4.00)	6.80 (S.D. 4.80)	4.00 (S.D. 3.00)

Values represent the difference (degrees) between slow component eye position and head position; (–) indicates phase lag.

tude of which appeared to be linearly related to the angle of neck torsion. The evidence as it stands, however, indicates that it was dynamically induced and not the result of tonic activity associated with sustained neck torsion.

It seems, therefore, that tonic neck and labyrinthine postural reflexes differ from the tonic neck/eye reflexes. In the case of the former, according to the classical descriptions of Magnus[17], the reaction is tonic in the sense that it is produced not by the movement of the head, but by the new position imposed upon it, and that it persists as long as this is maintained. Although more recent studies have added qualification to this view[27], it contrasts strikingly with the nature of the COR as revealed by the present studies.

The COR in target acquisition and retention

'Anticompensatory' role of the COR. There is evidence, derived from studies involving both ramp and sinusoidal head movements, that in man and animals compensatory and anticompensatory eye movements are subserved, respectively, by the slow and fast components of the VOR. Ramp step head movements in total darkness initiate, in normal subjects, saccadic components in the direction of head turn followed by a slow return of the eyes in the opposite[2,3]. Since this pattern of eye movements is identical to that found during active target seeking it implies that in certain circumstances the initial saccade may be vestibularly induced[3,22]. To this can now be added our own observations that in the chronic absence of vestibular function passive and unpredictable head movements, as well as active head turning in the dark, all essentially reproduce the pattern of eye movements found during active target seeking. Similarly, during whole body sinusoidal rotation in the dark normal subjects present, in addition to the slow compensatory eye movements, a shift in eye position into the quick phase direction (anticompensatory gaze shift) 90° phase-advanced[19]. This too has its counterpart in our observations upon the COR in the patients and, in the circumstances, it would seem that in the absence of vestibular function the COR is able to take over the so-called anticompensatory properties of the VOR, inducing gaze shifts of the appropriate direction, velocity, phase relationship and amplitude such as to project the eyes in advance of an ongoing head movement. Presumably this is subserved by the neck muscle spindles responsive to the accelerative components of stretch[21].

Compensatory role of the COR. The trunk on head experiments in normal subjects confirm the findings of others that neck-induced slow eye movements make little if any contribution to retinal stability during head movement[1c,5,11,13,14,24]. This is evident from the very low gain and extreme variability in direction of the slow components of the COR. It follows that the increased gain during sinusoidal head on trunk movement, compared to that of the VOR alone, cannot have resulted from a simple addition of COR and VOR. Instead, it seems more likely that an element of pre-programming is involved. This certainly accords with the reduction in intra- and interindividual variance encountered in head on trunk movements.

The striking enhancement of cervically induced slow eye movements in patients has its parallel in similar findings in monkeys and cats following bilateral labyrinthectomy[11,20]. As to its functional significance it is presumed that it serves to stabilize gaze during head movements, although it has to be admitted that there is as yet no direct evidence for this. Such evidence as there is derives from the obvious similarities between the COR in patients and what we know of the VOR. Thus under all experimental conditions including the unusual trunk on head movement the cervically induced slow eye movements were consistently compensatory, that is to say in a direction that would be expected to summate with the visuomotor reflexes (optokinetic and pursuit), thereby aiding retinal stability during ordinary head movements. Counter to this view would be the marked decrease in slow-phase gain of the COR with frequency (Fig. 5), which indicates that the COR is not particularly effective within the frequency range of normal head movements, i.e. above 0.2 Hz[26]. It is, however, worth recalling that head on trunk gain was significantly higher than that of trunk on head. This implies the existence of a pre-programmed mechanism of the kind already referred to and for which there is experimental evidence[11,15], cooperating with the COR to stabilize retinal images in the patients during head movements.

Finally some comment is called for on the finding that instruction to imagine a stationary target exerts

such a marked effect both in normal subjects and patients upon the COR. Comparable effects are now well documented in respect of the VOR[6,23] and it is of some interest that the COR can be shown to be susceptible to similar central control.

Although our experience is that this calls for a considerable conscious effort on the part of the subject and in its absence the COR reverts to its unmodified form, it does direct attention to possible influences operating upon the COR other than those from peripheral mechanisms. The cerebellum in particular is a case in point and has been shown to exert an inhibitory effect upon the COR similar to that which it is known to have upon the VOR[9]. How significant these various central influences are remains to be determined, but they would appear to merit further attention in any future studies of the COR.

In summary our findings show that: (a) the COR makes no significant contribution to eye movements in the normal subject; (b) a tonic component of the COR could not be identified; instead, in the case of ramp stimuli, a residual eye deviation was noted which was significantly enhanced in patients and resulted from activity dynamically generated during the course of trunk movement and not from its final angular displacement; (c) in patients with bilateral vestibular loss the COR takes on the role of the vestibulo-ocular reflex in head–eye coordination, in (1) the initiation of the anticompensatory saccade which takes the eyes in the direction of the target, and (2) the generation of the subsequent slow compensatory eye movements; (d) an increased gain found during active head movements both in normal subjects and patients can only be accounted for in terms of an element of pre-programming.

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Oscillopsia of Peripheral Vestibular Origin

Central and Cervical Compensatory Mechanisms

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Bronstein AM, Hood JD. Oscillopsia of peripheral vestibular origin: central and cervical compensatory mechanisms. Acta Otolaryngol (Stockh) 1987; 104:307–314.

Eight patients with absent vestibular function categorized into four grades according to the disability they suffered from oscillopsia have been studied with a view to correlating its severity with the development of gaze stabilizing compensatory mechanisms. Eye movements were recorded while the following sinusoidal rotational stimuli were delivered: 1) trunk *on* head oscillation in the dark (COR); 2) head *on* trunk oscillation in the dark; 3) head *on* trunk and whole body (head *and* trunk) oscillation in the light in the presence of optic fixation. The COR was potentiated in all the patients regardless of their clinical status. Velocity gains (peak slow phase eye velocity/peak head velocity) during whole body rotation were significantly lower than head on trunk gains in the light in the better compensated patients. Since in the absence of vestibular function whole body rotation involves only the otokinetic system (OKN), this finding implies a depression of the OKN in these patients which can be corrected during head on trunk movements by virtue of a dynamic input from the neck. The results suggest that the processes of recovery from oscillopsia are dependent, in the main, upon the development of central mechanisms by means of which undesirable image movement across the retina is perceptually suppressed. Depression of OKN may be secondary to this perceptual rearrangement.

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The vestibulo-ocular reflex (VOR) normally serves to stabilize the eyes in space during head movements by generating compensatory eye movements, i.e. of equal velocity and in the opposite direction to those of the head. Derangements of the reflex may take the form of hypo or hyper activity; in either event the resultant mismatch can give rise to a disturbing illusion of movement of the visual surroundings, termed oscillopsia, caused by images of the environment traversing the retina (1). Of these, hypo-activity caused by loss of vestibular function is by far the more disturbing and subjects typically complain of objects "bobbing", "jumping", "moving to and fro" or of "blurred vision" whenever they walk or move. Some, however, are appreciably less disabled than others and this may be due to the development of certain compensatory mechanisms involving in particular the cervico-ocular reflex (COR).

The COR, which is only minimally active in normal animals and man, becomes hyperactive after bilateral vestibular damage (2, 3, 4). Its phase and direction, variable and unstable in normal circumstances, becomes systematically compensatory such that slow eye movements are generated in a direction opposite to that of neck torsion, suggesting that the COR may assume the role of the VOR in the absence of vestibular function.

The present study has been undertaken to determine if any correlation exists between the degree of clinical disability produced by oscillopsia due to the absence of vestibular function on the one hand, and the development of compensatory gaze stabilizing mechanisms on the other.

MATERIALS AND METHODS

Eight patients were studied. All lacked nystagmic reaction to caloric irrigation with water at 30°C and 44°C in the light and in darkness, and to rotational velocity steps 40°/s in the dark. Two patients (nos. 3 and 6, Table I) had a few isolated nystagmic beats during the first 2–3 s after velocity steps of 80°/s in the dark; the remainder showed no response. All suffered from varying degrees and combinations of deafness, oscillopsia and imbalance.

From the history they were classified according to the clinical severity of oscillopsia from grade 0 to III as follows:

Grade 0–Oscillopsia denied by the patient.

Grade I–Oscillopsia not described spontaneously. On questioning, the patient admitted it was present in certain circumstances such as running, but was not troubled at all by the symptom.

Grade II–Oscillopsia was a presenting symptom but was well tolerated and did not appear to impart any disability affecting the patient's mobility.

Grade III–Oscillopsia of disabling severity with gross interference in the patient's daily activities.

The relevant clinical data are included in Table I. Age at onset and progression of symptoms could not be established with certainty in patients 1 (grade 0) and 2 (grade I). Patient 1, presented in an earlier paper (5), had received a long course of treatment with streptomycin 30 years ago for a gangrenous wound due to Buerger disease. Neuro-otological symptoms and absent labyrinthine responses were documented for the first time 14 years before our current investigations. Patient 2 had von Recklinghausen's disease with bilateral slow growing tumours of the VIII nerve; the estimated age at onset refers to the first presentation of VIII nerve symptoms.

A full clinical neuro-otological examination was carried out, including tests for spontaneous, gaze-evoked and positional nystagmus. Doll's head manoeuvre was executed in the horizontal, vertical and coronal planes; head movements in the latter plane usually produce torsional compensatory eye movements and nystagmus (ocular counter-rolling) indicative of the functional state of the vertical canals and the otoliths (6, 7). Vertical and horizontal saccades and smooth pursuit movements were also studied.

Table I. *Clinical findings*

Oscillopsia grade	Patient no.	Sex	Age at onset (years)	Duration (years)	Aetiology	Deafness	Ocular counter-rolling	CNS signs
0	1	♂	34	30	Aminoglycoside ATB	–	Weak asymmetric	–
I	2	♂	17	7	Bilateral VIII nerve tumours	Severe	Weak	Cerebellar
II	3	♂	29	3	Meningitis Aminoglycoside ATB	Severe	Absent	–
II	4	♀	35	20	Meningitis Aminoglycoside ATB	Severe	Normal	–
II	5	♂	20	35	Meningitis Aminoglycoside ATB	Severe	Weak	–
III	6	♀	71	1	Aminoglycoside ATB	–	Absent	Alternating nystagmus in the dark
III	7	♀	73	0.5	Aminoglycoside ATB	–	Normal	–
III	8	♀	50	0.5	Aminoglycoside ATB	Moderate	Absent	–

Horizontal eye movement recordings (DC EOG) were carried out under four experimental conditions:

1. *Head/eye co-ordination in target acquisition*

By way of an examination of target-seeking strategies, subjects were required to locate in the dark, target lights positioned at 10° intervals on a bar 1 metre to their front and subtending ±50°. The lights were presented randomly and the subjects were encouraged to endeavour to make as natural a head movement as possible. Head position was monitored with a light adjustable helmet connected to a low-torque potentiometer.

2. *Sinusoidal trunk movements in the dark (COR)*

With the subject seated on a rotating chair and the head fixed by means of a bite plate mounted on a rigid frame attached to the wall, the chair was moved by hand in synchrony with a metronome at frequencies between 0.07 to 0.3 Hz. with amplitudes of approximately ±25°. In this way the COR is studied in isolation from the VOR. All tests were carried out in the dark and subjects were instructed to relax their neck during the rotation. Thirteen normal subjects, age range 24 to 60 years, constituted the control group.

3. *Sinusoidal head movements in the dark*

In this test the patients were instructed to relax their neck muscles and let the experimenter make passive sinusoidal head movements as regularly and smoothly as possible in time with a metronome at frequencies of 0.3 and 1 Hz. with amplitudes of approximately ±25°.

4. *Sinusoidal head movements in the presence of fixation*

In order to study the contribution of neck input to gaze stability in the light, compensatory eye movements were measured and compared in two different conditions: head clamped and free. In the first, the subject seated in a rotating chair to which his head was firmly secured, was rotated sinusoidally at 1 Hz while fixating upon an earth-fixed target to his front at a distance of 5 metres. Peak velocity was varied between 80 and 140°/s. Body movements were suppressed by means of head, hip and leg clamps. In the second condition the head was freed and the helmet fitted. The subject was then instructed to relax his neck as much as possible and allow the examiner to move the head freely while fixating the target, care being taken to avoid any slippage of head and helmet. Frequency was kept constant at 1 Hz in synchrony with a metronome and the amplitudes of the oscillations were adjusted so that they matched those obtained during the head-clamped experiment as monitored on the recording.

In the interests of comparability, eye movement measurements under the two conditions were carried out on those recordings which did not differ from each other by more than 5% in respect of frequency, amplitude and velocity of the stimulus. Patient 5 was not available for the head-clamped experiment. For both procedures, in addition to the routine eye calibration with targets 10° apart, simultaneous head–eye calibrations were obtained by turning the head or chair slowly in the presence of optic fixation. These normalized values served as a baseline (gain=1, see below) for the analysis of the results.

Eye, chair and helmet position were recorded upon an ink-jet polygraph (ELEMA Mingograph). The recordings were analysed by hand. Gain was defined as peak slow phase eye velocity/head (or trunk) peak velocity; measurements were made on each individual half-cycle and a minimum of 8 were included.

RESULTS

The relevant clinical findings are presented in Table I. It will be seen that Grade III is characterized by three older patients with a relatively short history of oscillopsia.

Ocular counter-rolling was normal in patients 4 and 7. The remainder of the subjects had considerable weakness, asymmetry, or absence of the reflex. These derangements did not relate to the patient's clinical status however, nor did the presence of a minimal residual nystagmic response during high velocity rotational steps in patients 3 and 6 (see Material and Methods).

No additional CNS involvement could be called in to account for the severity of the oscillopsia. Patient 6 (group III) was found to present bouts of alternating nystagmus in the dark, thought to be of central origin, which was accentuated by high velocity impulsive rotation in the dark. Patient 2, however, who had clear CNS damage as evidenced by mild cerebellar signs, exhibited only minimal oscillopsia.

Head–eye co-ordination in target acquistion

Head velocity was measured during eye–head co-ordinated movements aimed at fixating randomly presented targets. It is well established that peak velocity of the head increases linearly with the amplitude of target displacement (8). Accordingly, a linear regression curve was fitted to the amplitude–velocity data of each subject (typically comprising 15 data points) and the velocity value at 50° target amplitude established for each subject (see Table II). From this and the curves displayed in Fig. 1 it will be seen that patients in group III showed a tendency to move their heads more slowly than normal controls or patients less severely affected, presumably in order to avoid oscillopsia. This difference in head speed cannot be explained in terms of age, since patient 8, who had the slowest head velocity, was younger than 2 patients in grade II and the patient in grade 0. Similarly, 16 normal subjects between 22 and 70 years of age were studied; they showed no relationship between age and head velocity.

Sinusoidal trunk movements in the dark (COR)

The striking finding was a marked enhancement of gain in all the patients which decayed consistently with frequency of stimulation (Fig. 2). There appears to be no obvious

Table II. *Test results*

Patient no.	1	2	3	4	5	6	7	8
Target acquisition								
Head velocity at 50° (°/sec)	98	79	100	106	112	52	61	30
Sinusoidal rotation (gain)								
Darkness								
0.3 Hz	0.44	0.17	0.21	0.45	0.72	0.35	0.36	0.35
1 Hz	0.55	0.11	0.51	0.13	0.59	0.51	0.36	0.21
Fixating (1 Hz)								
Head clamped	0.59	0.62	0.71	0.51	–	0.71	0.74	0.76
Head free	0.73	0.87	0.98	0.81	0.74	0.69	0.67	0.73
[a]Clamped/free (%)	−20	−29	−28	−38	–	+11	+10	+4

[a] Refers to percentage reduction or increase in gain with head clamped relative to that with head free.

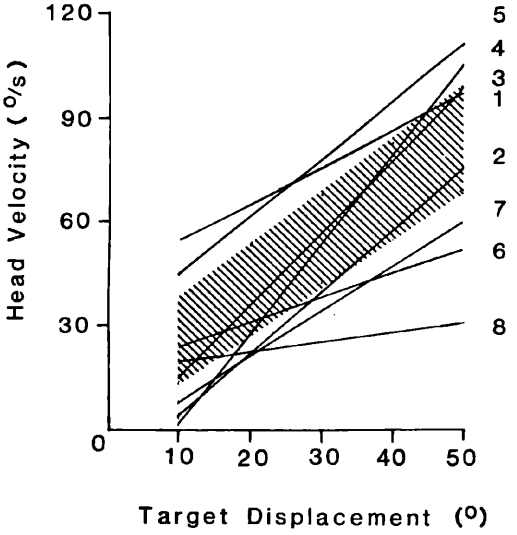

Fig. 1. Relationship between amplitude of target displacement and peak head velocity during head–eye coordinated movements. The regression lines shown are from each individual patient; patients 6, 7 and 8 belonged to group III. The shaded area represents mean ± SD of 16 normal controls.

relationship between gain values and clinical status. More detailed consideration of these findings is given in a separate publication (4).

Sinusoidal head movements in the dark (Table II)

During head upon body movements in the dark at 0.3 Hz the mean velocity gain of the slow compensatory eye movement was 0.38 SD 0.16 and 0.37 SD 0.19 at 1 Hz, indicating no consistent change with frequency. No obvious relation was apparent with the degree of oscillopsia.

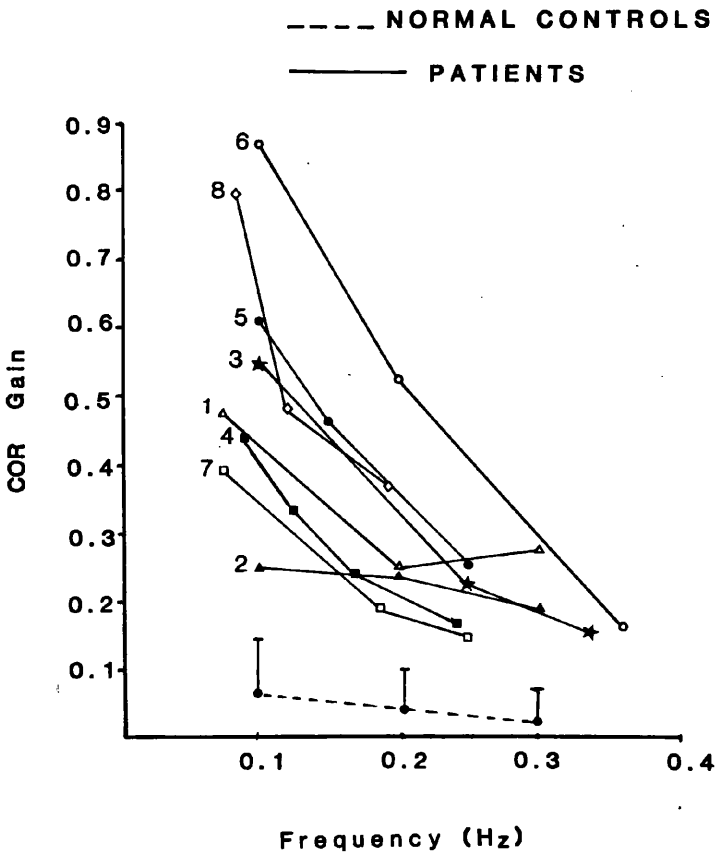

Fig. 2. COR gain in the dark with sinusoidal trunk rotation about the head. Amplitude of oscillation was approximately ± 25° degrees. Individual values of each patient (1–8) are presented, together with the mean +1 SD of 13 normal controls. Although the COR is considerably enhanced in the patients, this did not correlate with the degree of oscillopsia.

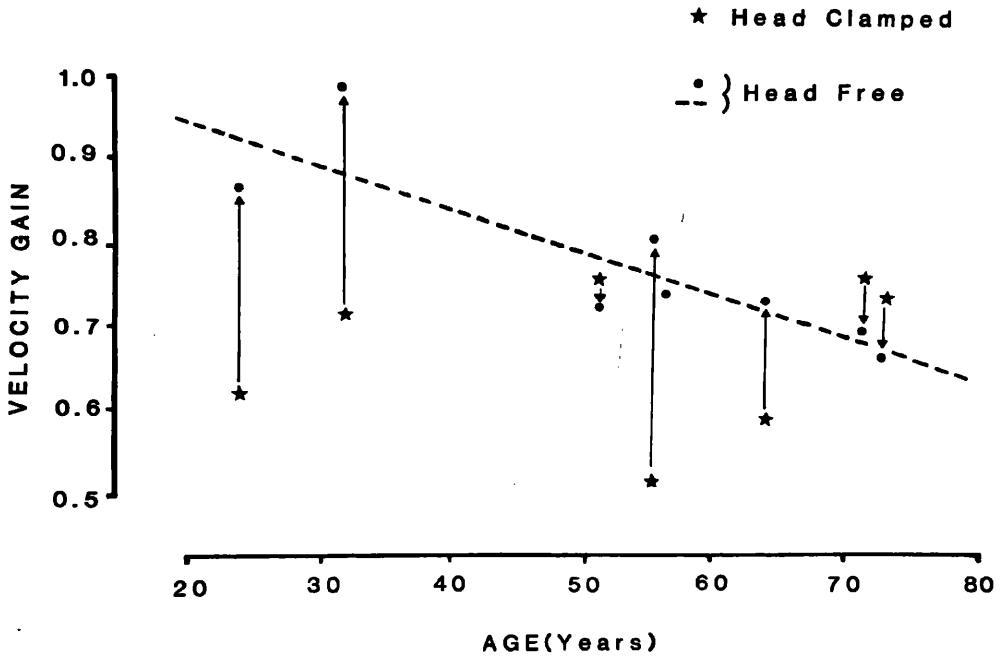

Fig. 3. Relationship between age of patients and gain during sinusoidal rotation in the presence of optic fixation with head clamped and free. The regression line refers to gain with the head free. The 3 patients showing inversion of the two gains (downward pointing arrows) had grade III oscillopsia, relative to the 4 patients with less oscillopsia (upward pointing arrows).

Sinusoidal head movements in the presence of optic fixation

It is apparent from Table II and the data presented in Fig. 3 that gain values either with head free or clamped were not related to the degree of oscillopsia. However, it is clear that in the patients with little or no oscillopsia, gain values with the head clamped were depressed by 20–38% vis-à-vis those with the head free; by contrast, patients with severe oscillopsia had gains with head clamped either marginally increased or within the range of those with the head free. An analysis of variance and covariance with repeated measures (BMDP2V, Univ. of California) showed that the interaction between the gains with head clamped and free and the mild (0–II) and severe (III) oscillopsic groups was highly significant (f=42.20, p=0.001). This did not hold for the two groups and the respective gains treated in turn (f=0.04, p=0.847), implying no direct effect of gain values with either head free or head clamped.

In view of the possibility that age of the patients and gain values may be associated, Kendall's rank correlation coefficient was calculated. A significant negative correlation was present between age and gains with the head free:

(tau coefficient = -0.62, $p = 0.03$, $n = 7$)

but not with the head clamped

(tau coefficient = 0.42, $p = 0.12$).

Although this showed that head-free velocity gain decays with the age of the patients, the precise form of the relation between the two variables cannot be inferred from this particular analysis. This in fact is more appropriately exemplified by the linear regression shown in Fig. 3. ($r = -0.87$, $p<0.01$), which implies a linear relationship.

DISCUSSION

The marked potentiation of the COR found in our patients with absent vestibular function has been noted earlier and held to contribute to the restoration of gaze stability during head movements (2, 3, 4). Since during the development of this potentiation (which in the monkey takes several months (2)), more general symptoms usually diminish, it might be assumed that the two are related. It might therefore appear surprising that we have been unable to establish any obvious correlation between the degree of oscillopsia and COR gain as assessed by rotation of the trunk around the head fixed in space.

This, however, involves an unnatural test situation designed to elicit the COR in isolation from the VOR and it is noteworthy that although the gains observed were appreciable they are most apparent at low frequencies where optokinetic reflexes could by themselves provide adequate gaze stability during head movements (5). In this context, however, it must be recalled that during head on trunk movements in the dark, these gains were further increased and extended well into the frequency range of normal head movements (Table II). Since both trunk on head and head on trunk rotation produce identical peripheral cervical stimulation it must be presumed that, in the absence of vestibular function, the additional ocular-motor activity found during head on trunk rotation is pre-programmed in origin. This notion is not new and has in fact been invoked in the past to account for similar observations in normal subjects which have shown that although in isolation COR gain is minimal, the apparent VOR gain elicited by head on trunk movement is greater than that obtained by movement of head and trunk en bloc (4, 9).

Of perhaps greater relevance in this respect are the findings embodied in Fig. 3 concerning the gains obtained during head-free (head on trunk) oscillation in the presence of optic fixation. These showed a remarkably good negative correlation with age and it will be noted that gain values approach unity amongst the younger, well compensated members of the group. This seems clear enough evidence that when evoked by head on trunk rotation the COR, in conjunction with its associated pre-programmed activity and optokinetic reflexes, is capable of taking on the role of the VOR in stabilizing gaze during head movements. Latencies of eye movements mediated by the COR are considerably shorter than those of the optokinetic and smooth pursuit system (4, 10) and would be well suited to initiate this compensatory response.

In contrast, during whole-body oscillation with head clamped, the stimulus, in the absence of both VOR and neck torsion, is solely optokinetic and the response showed no correlation with age. Since there is good evidence that optokinetic gain deteriorates with advancing age (11, 12, 13, 14), the question arises: why was such a correlation so conspicuously absent in our findings?; instead, the gains in the patients relatively free from oscillopsia were markedly depressed, whereas in the case of the 3 patients in grade III the gains were marginally greater than those with head free and the highest in the group despite their advanced age.

The most likely explanation for these somewhat paradoxical findings rests in the fact that since the illusory movement of the environment in oscillopsia is consequent upon retinal slip it is possible that certain perceptual rearrangements might be engendered whereby image movement, unpleasantly interpreted as movement of the visual world, is in some way neglected or ignored as presumably occurs in congenital nystagmus and at least partially in down-beat nystagmus (15) and oculo-motor palsies (16). Viewed in this light, it is to be concluded that depression of the optokinetic responses may be an inevitable consequence of the development of those compensatory mechanisms which bring about a reduction of the perceived oscillopsia and material to this is Zee et al's observation of just such a depression in three patients with long-standing lack of vestibular function (17).

Unfortunately these conclusions were arrived at after the completion of the study and data are not available from direct observations of the optokinetic responses of the patients in our group.

In summary, therefore, the two factors which have been identified here as contributing to the alleviation of oscillopsia are the potentiation of the neck–eye loop and the development of an ability to neglect the undesirable effect of image motion across the retina, though both seem to be interdependent. Provocation of vertigo is an essential element in rehabilitation procedures applied to patients with acute vestibular failure (18) so that by analogy the avoidance strategy adopted by patients with severe oscillopsia of moving their heads more slowly during head–eye coordinated movements may not be in their best interests—at least in respect of the development of compensatory mechanisms.

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Experimental Brain Research

Research Note

Suppression of visually evoked postural responses

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Summary. Normal subjects standing on an earth-fixed force platform inside a movable room displaced at velocities comparable to those accompanying spontaneous body sway, exhibit a visually evoked postural response (VEPR) some 600 ms after the start of the room movement. It consists of a displacement of the centre of force of the body in the direction of the stimulus (primary component), followed shortly by a corrective displacement in the opposite (secondary component). On second presentation of the stimulus VEPR is markedly reduced, but only if full proprioceptive information from the lower limbs is available to the subjects. A patient deprived of this information showed much enhanced VEPR which he was unable to suppress, in contrast to a patient with absent vestibular function who presented normal VEPR. The results show that in the presence of conflict between different sensory clues, vision is initially dominant in sway control, although adaptive processes can quickly rearrange this hierarchy.

Key words: Vision – Posture – Motor control – Vestibular system – Proprioception

Introduction

Clear evidence of the dominant role of vision in the control of posture has been advanced in a variety of studies in which the visual stimulus was manipulated in such a manner that the information relating body movement to the environment was in conflict with that supplied by the vestibular and proprioceptive systems. These have involved the analysis of body sway in response to moving visual surrounds occupying large areas of the visual field, the assumption being that the stimulus is misinterpreted as self-displacement and thereby induces postural adjustments. In this context vision was found to prevail over other sensory inputs and a characteristics body tilt in the direction of the visual stimulus occurred (Lee and Lishman 1975; Lestienne et al. 1977; Clement et al. 1985; Hufschmidt et al. 1980). It is surprising, however, that in spite of the fact that visuo-postural responses induced experimentally by linear displacement of visual scenes are unstabilizing with respect to an earth-fixed vertical, little or no habituation or suppression of the responses has been reported (Lestienne et al. 1977; Clement et al. 1985). Since this implies a somewhat inflexible visual control of posture, the following experiments were designed by way of clarification.

Methods

The displacement of the centre of force of the body was measured by means of a force platform. The platform was placed on an earth-fixed floor and located inside a floorless room, measuring 2.50 m long, 2.20 m high and 1.80 m wide, mounted on pneumatic wheels. It could be displaced smoothly and quietly by hand. Its walls and ceiling consisted of a red and pink chequered fabric attached by its edges to the room's frame. The subject stood facing one of the lateral walls at a distance of about 38 cm so that movement of the room produced full field linear stimulation along the y axis (coronal plane). The stimuli consisted of discrete movements of the room, with a sigmoid time-course, lasting approximately 12 s, over a fixed distance of 30 cm with a peak velocity of 2 to 3 cm/s (average peak angular velocity at the level of the eye = 3.76 °/s). Three to nine stimuli were delivered regularly, from right to left and vice versa, with variable interstimuli intervals between 8 and 16 s. Room displacement was monitored with a potentiometer attached to one of the wheels. Nine normal subjects, 4 male and 5 female, aged between 18 and 54 years took part in these experiments under two conditions: first standing shoeless on the platform and then, in order to reduce lower limbs proprioceptive information, on two pieces of foam, the lower one of polystyrene, 5 cm high and the upper one of rubber 2.5 cm high. Two patients were also tested. One was a 68 year old male devoid of proprioceptive function below the knees, due to tabes dorsalis,

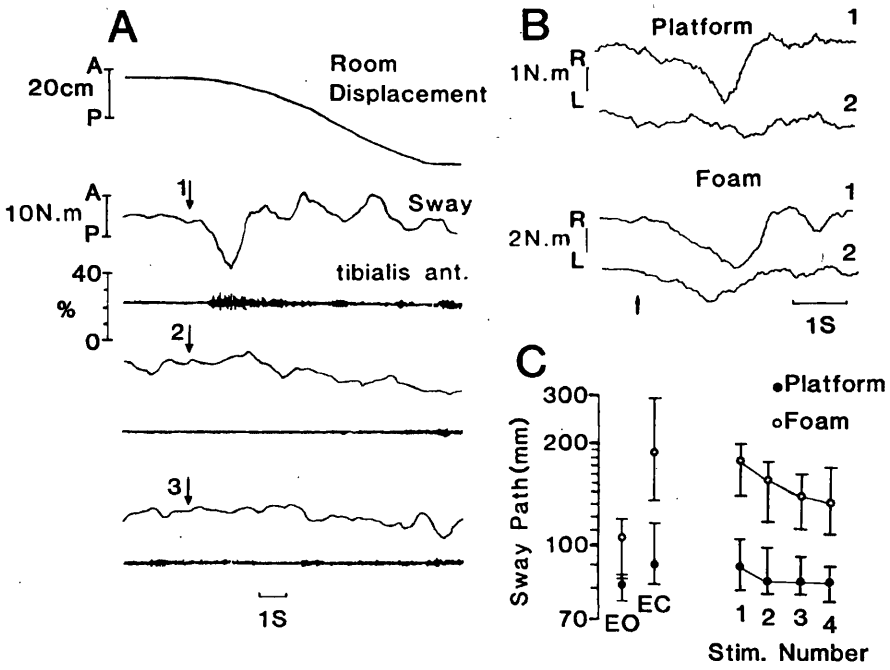

Fig. 1A–C. Habituation of visually evoked postural responses (VEPR). **A** Raw records at the start of 3 successive backward room displacements (arrows 1, 2, 3) in a normal subject. The first stimulus elicits, at a latency of 600 ms, a displacement of the centre of force in the direction of the room movement (primary component) which is absent on subsequent trials. EMG calibration refers to % of maximal voluntary contraction. Sway calibration is in Newton metres. **B** Averaged VEPR of 9 normal subjects at the start of room displacement to the left (arrow) during the 1st and 2nd trial on platform and foam. A primary component during the 2nd stimulus is present only on the foam. Note different calibrations used for platform and foam. **C** Sway path with eyes open without stimulation (EO), closed (EC) and during successive room displacements along the y axis (1–4). Each stimulus number combines room movements to the right and left. Medians and interquartile ranges for 9 normal subjects are presented

whose vestibular function, assessed clinically and by rotational tests, was within normal limits. He was not tested on the foam. The other patient was a female aged 47 years, with acquired absence of vestibular function but otherwise normal on neurological examination. Body sway in the coronal and sagittal planes plus the room displacement signal were recorded on paper with an ink jet polygraph (Elema mingograph) and on magnetic tape and thereafter subjected to further analysis as follows. Visually evoked postural responses (VEPR) were averaged with a signal processor (Solartron 1200) triggered at the start of the room displacement; a window of 6 s was set, the first 15% of which was prestimulus analysis. Since this procedure is dependent upon reproducible stimuli, the distance traversed by the room was mechanically limited to 30 cm, and the stimuli were always delivered by the same experimenter. Under these conditions the mean duration of 25 consecutive displacements was 11.80 s with a SD of 0.82 s, a variance considered adequate for the purpose of this study in the light of the long duration responses. Each individual stimulus was expanded in time (× 4) and amplitude (up to × 100) in order to check that the signal processor was actually triggered at the start of the movement; a tolerance limit of ± 35 ms was set, representing ± 5% of a typical latency of 700 ms to the beginning of the postural response (Lestienne et al. 1977). A second analysis involved measurements, in the normal subjects, of the "sway path" along the y axis over periods of 12 s, using a computer program similar to that described by others (Hufschmidt et al. 1980). In brief, the force signals from the subject standing on the platform were normalised to represent the force exerted by a 70 kg mass. During body sway the signals from the platform behave as if the force is moving across the surface of the platform. The computer program samples the momentary position of the centre of force and sums differences between successive positions to calculate the total length of the path of sway. A minimum of 4 periods with eyes open, facing the stationary room, and eyes closed were analysed and compared to the periods during which visual stimuli were applied. Experiments were also carried out with similar room displacements along the x axis (sagittal plane) by placing the platform in the centre of the room with subjects facing the front wall. Four female and one male normal subjects, aged 17 to 54 years, were tested standing shoeless on the platform. Surface EMG was recorded from soleus and tibialis anterior. In all experiments, prior to any stimulation all subjects were informed that the room, but not the platform, would move and were encouraged to keep a natural upright posture. Following the experimental session all subjects were asked to report any sensations induced by the room displacement and in particular if they experienced an illusion of movement in a direction opposite to that of the visual stimuli (linear-vection).

Results

Results from normal subjects are shown in Fig. 1. Following stimulation, the first or primary response was a postural displacement in the same direction as room movement, with a latency of some 600 ms (Fig. 1A). This was followed by a burst of EMG activity in the muscle antagonist to the primary component thus bringing about a corrective displacement in the opposite direction (secondary component). Thereafter, during the remainder of the stimulus, the tracings revealed a general non-specific instability. Strikingly, however, on repetition of the stimulus, the primary component was conspicuously absent.

Table 1. Amplitude of primary component of VEPR (N.m) during the 1st and 2nd stimuli. The responses to the first stimulus in each direction were averaged for all normal subjects. The procedure was repeated for the second stimulus

	Lateral stimuli platform	foam	Backward stimuli platform
1st stimulus	1.81	4.54	7.87
2nd stimulus	0.64	3.76	2.57
%	35	82	32

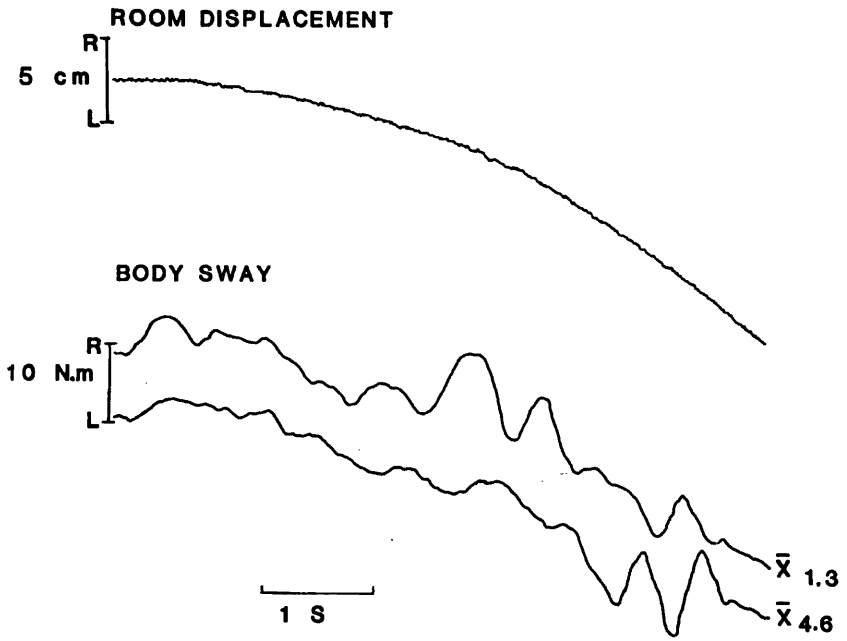

Fig. 2. Body sway induced by room movement to the left in a patient devoid of lower limbs proprioceptive information due to tabes dorsalis. The first three (1.3) and second three (4.6) averaged responses are shown

The responses to the initial room displacement both on platform and on foam were averaged and compared to those obtained during the second, in the same direction (Fig. 1B and Table 1). In respect of the platform responses, although the absolute amplitude of sway was larger in the sagittal than in the coronal plane, the attenuation of the responses referred to above was much the same in both. By contrast, on the foam, the amplitude of the primary component was considerably larger and attenuated only minimally during the second stimulus.

The aggregate sway path length to the first stimulus on the platform was comparable to that with the eyes closed, and decreased thereafter during successive trials to a level intermediate between eyes closed and open without stimulation (Fig. 1C). However, the median values of sway at the second test on the platform fell within the interquartile range of those with eyes open and the room stationary, whereas the values on the foam remained high. Concerning the sensations evoked, although slight "giddiness" or unsteadines was reported, none of the subjects experienced an illusion of self-displacement in the opposite direction to room movement (linear-vection). Some subjects felt as if they moved in the direction of the stimulus but this could have reflected their actual bodily displacement.

The results from the patients with absent proprioceptive or vestibular function contrasted markedly. The maximum torque exerted in the direction of the stimulus during the first 6 s of its occurrence was measured by hand from the tracings. The mean value of the combined first stimuli to right and left was 33.15 Newton metres (N.m) for the tabetic patient, and 0.42 N.m for the labyrinthine defective patient. The range for normal subjects lay between 0 and 4.74 N.m (median: 1.60). On foam, the value for the patient without vestibular function was 14.85 N.m, the normal range being 0.8 to 24.89 N.m (median: 6.87). At the second test on the labyrinthine defective patient these values fell to 0 N.m on the platform and 6.85 N.m on the foam indicating a VEPR within normal limits and unimpaired suppression. The tabetic patient, on the other hand, swayed markedly in the direction of room movement with no effective secondary component present. As a result, he repeatedly fell off the platform and had to be caught by two observers standing to his rear. After 3 stimuli in each direction, however, he learnt to avoid falls with a conscious strategy, maintaining "if I didn't want to fall I had to move the other way as soon as the room started to move". Although useful in preventing falls, this voluntary response failed to introduce any modification within the 6 s of analysis of the VEPR (Fig. 2). Neither of the patients had significant modifications of the latency values of the VEPR.

Discussion

This study has shown that novel linear movement of a visual surround along the x or y axis initiates a postural displacement in the direction of the stimulus (primary component), followed shortly afterwards by a corrective (secondary) displacement in the opposite direction. This sequence is almost completely suppressed on subsequent stimulation. In marked con-

trast to this, earlier studies have reported either absence of habituation during linear visual stimulation along the x axis or its relatively slow development in the coronal plane with a disc rotating around the visual axis (Lestienne et al. 1977; Clement et al. 1985). An essential difference, however, is that the stimuli utilized here were discrete, short in duration, did not elicit vection illusions in the opposite direction and, perhaps more importantly, were within the linear velocity range of normal body sway. The VEPR, occurring during the accelerative phase of the stimulus, susceptible to rapid habituation and counteracted by a corrective component within 1 s of its initiation, seems appropriate to the execution of visuo-postural adjustments during the recurrent small changes in posture present in spontaneous body sway. The ease with which habituation occurs probably reflects the fact that, not infrequently, vestibulo-proprioceptive clues take over the normally dominant role of vision in sway control in the presence of diminished or inappropriate visual information. On the other hand, postural changes induced by rapid and long-lasting visual stimuli, associated with vection illusions, probably mediate balance adjustments to significant body displacements occurring, for instance, during locomotion or vehicular travel. It is arguable that in these situations, habituation would be undesirable since vision, once the accelerative phase of movement has ended, is the main sensory channel for body motion. The similarity in the latency values of these two types of visuo-postural responses, however, could indicate that common pathways are involved.

The studies with normal subjects on foam and with the tabetic patient indicate that, in the absence of reliable visual information, proprioceptive clues take precedence over vestibular. This is probably due to the fact that the range of frequencies and velocities present in ordinary body sway and in the stimuli applied in this study are too low to be effectively detected by the vestibular apparatus. Similarly, as shown by the impaired habituation of VEPR in the normal subjects tested on foam and in the tabetic patient, conscious efforts to "neglect" a known unstabilizing visual stimulus were not successful in the absence of an alternative source of reliable sensory information.

The rapid habituation of VEPR illustrates the remarkable plastic properties of the mechanisms detecting and correcting spontaneous body sway, and supports the concept formulated by Talbott and Brookhart (1980) of modifiable effectiveness of the visual input in the control of balance in different environmental contexts. The suggestion is that the fine sensory control of body sway is hierarchically organised; vision normally dominates over proprioceptive information from the lower limbs, but this arrangement can be quickly reversed depending upon the changing conditions in the environment. The role of volitional and vestibular activity to this end is comparatively much less effective.

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Evidence for a Vestibular Input Contributing to Dynamic Head Stabilization in Man

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Bronstein AM. Evidence for a vestibular input contributing to dynamic head stabilization in man. Acta Otolaryngol (Stockh) 1988; 105: 1–6.

Horizontal head movements in response to unpredictable horizontal oscillations of the trunk were studied in 6 patients lacking vestibular function and in 6 normal subjects. In order to obtain compensatory (i.e. stabilizing with respect to earth) head movements, all subjects were required to look at an earth-fixed target, using their eyes *and* head. The turning points (maxima and minima) were determined from head and trunk position records. It was found that normal subjects reversed the direction of head movements in advance of trunk movements (mean lead = 82 ms) whereas the patients reversed head direction after the trunk (mean lag = 169 ms). The coherence function between head and trunk movements, measured with a spectral analyser in an additional labyrinthineless patient, was considerably lower than in normal controls. It is concluded that patients lacking vestibular function have impaired stabilization of the head in space, which can be taken as indirect evidence of the existence of active dynamic vestibulo-collic reflex (VCR) mechanisms in normal man. The lead found in normal subjects, notwithstanding the unpredictability of the stimuli, may reflect the detection of early acceleration signals by the vestibular apparatus to organize compensatory head movements. *Key words: vestibulo-collic reflex, head posture, absent vestibular function, movement.*

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The mechanisms intervening in the control of head posture in man are largely unknown. Despite the fact that neurological disease can affect these mechanisms (1) basic questions such as "Is normal human head stability in space dependent upon vestibular information?" have only rarely been addressed (2, 3, 4).

In animals, unilateral labyrinthine lesions are known to provoke asymmetric head posture (5), a feature much less striking and only occasionally encountered in human clinical practice (6, 7). Bilateral labyrinthine lesions to the best of our knowledge do not have any effect on head static posture in man. However, it will be shown here that when assessed in dynamic conditions patients with absent vestibular function show abnormal head stability during whole body movements. This in turn implies the existence of functioning vestibulo-collic reflexes (VCR) contributing to head posture in normal humans.

MATERIAL AND METHODS

Six patients with clinically absent vestibular function were tested. Their ages ranged between 32 and 73 years and the cause of the vestibular loss was aminoglycoside antibiotic toxicity; in 3 of them these drugs had been administered for meningitis and thus a combined peripheral/VIII nerve aetiology is possible. The duration of the vestibular loss ranged between 1 and 35 years. Absent vestibular function was confirmed with bithermal caloric tests in the light and dark together with rotational tests in the dark with impulsive rotation of 60°/s or greater. Apart from the VIII nerve damage they were neurologically normal. Six normal subjects aged 18 to 62 years served as a control group.

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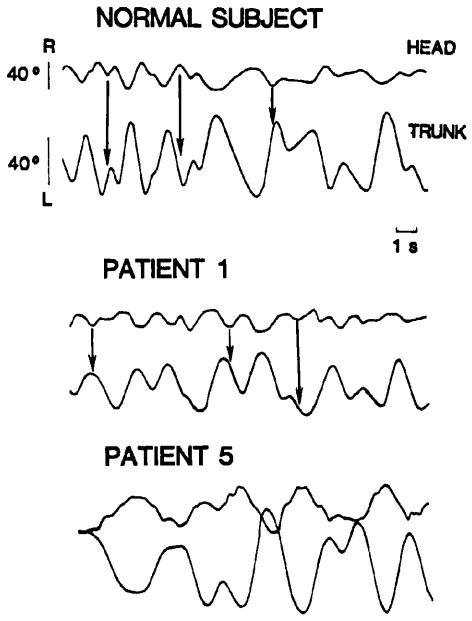

Fig. 1. Compensatory head movements in response to horizontal oscillation of the trunk in a normal subject and in 2 patients lacking vestibular function. Arrows indicate that in the normal subject the head reverses direction in advance of the trunk (lead) whereas in patient 1 the head reverses direction after the trunk (lag).

The experimental strategy consisted of assessing the stability of the head in space during whole-body oscillation. This strategy is analogous to that used in determining gaze stability in space by measuring eye movements in response to head oscillation (Vestibulo-Ocular Reflex).

The subjects sat on a rotating chair with the head free to move in a well lit room. They wore a light helmet connected to a low torque potentiometer which monitored horizontal head position with respect to chair (trunk) position. Leg and hip clamps were fitted. The stimuli were delivered by hand by the author in all cases but one, when he acted as a control subject. They consisted of horizontal unpredictable sinusoidally shaped oscillations in which frequency, amplitude, velocity and direction of movement were constantly changed (see Fig. 1). Maximum amplitudes were of approximately 70°. Peak frequency of the stimulus was 0.8 Hz (see below and Fig. 2). The inertia of the chair with the subject on it determined a jolt-free, smooth stimuli. Chair and helmet position signals were recorded with an ink-jet recorder (Mingograph).

The subjects were required to look at a real tridimensional object 5 metres to their front; 4 patients and 2 control subjects had simultaneous d.c. EOG recording to monitor their visual fixation. However, pilot studies had shown that normal subjects and patients frequently restrained their head movements voluntarily during stimulation so that head and trunk rotated *en bloc* and only the eyes moved in a direction counter to that of the stimuli. Subjects were therefore encouraged to direct their eyes *and* head at the visual target and example stimuli were delivered so that they familiarized themselves with the requirements of the experiment. This dependence on a relevant instruction in some subjects in order to obtain a head movement renders measurements of the amplitude of the response of doubtful value. Accordingly, measurements were made by hand of the time difference between the points of peak amplitude at which the chair and head reversed direction (maxima and minima). The first 10 s interval was not measured. Automatic techniques of spectrum analysis were available to compute data on-line from 3 of the originial 6 controls, at the same time that the paper recordings were obtained, and from 2 additional subjects (a 31-year-old normal subject and a 26-year-old patient lacking vestibular function). The power spectrum of the stimulus and the coherence function between head and chair movements were measured with a signal processor (Solartron 1200). The coherence function measures the degree of association between two signals; its formula is:

Table I. *Time delay between maxima and minima (turning points) for the head with respect to trunk movements*[a]

	Mean (ms)	Range (ms)
Patient 1	156	80/240
Patient 2	Not measurable	
Patient 3	202	80/280
Repeat test	236	100/360
Patient 4	188	40/440
Patient 5	Not measurable	
Patient 6	130	40/280
Mean (n=4)	169	
Control 1	−130	0/−250
Control 2	−153	50/−250
Control 3	−157	−100/−220
Control 4	54	0/100
Control 5	−58	0/−200
Control 6	−49	100/−160
Mean (n=6)	−82	

[a] A negative value indicates a lead of head over trunk.

$$\text{Coherence between } x, y = \frac{(\text{Cross Spectra of signals } x, y)^2}{\text{Power Spectra } x \cdot \text{Power Spectra } y}$$

Coherence varies, at each frequency of stimulation, between 0 (the two signals are totally unrelated) and 1 (the system output, i.e. the head movement is due entirely to the input). The stimuli were delivered over a period of about 100 s until 50 averages were obtained on the signal processor, set with a baseband between d.c. −200 Hz and a frequency resolution of 0.4 Hz.

RESULTS

Typical head movements were compensatory to that of the chair's motion, i.e. in a direction counter to that of the stimuli and fairly sinusoidal in shape (Fig. 1). Comparison of the points where the direction of the movement reversed (maxima and minima) revealed consistent differences between the two groups of subjects studied. Normal subjects reached turning points with head in advance of the chair, whereas in the patients the converse occurred (Fig. 1, normal subject and patient 1). Table I summarizes the time delay measurements between turning points of head and chair movements. In normal subjects there was a mean lead of head over chair of 82 ms, whereas in the patients there was a mean lag of 169 ms. Considerable intra- and inter-subject variability was present, as shown in the ranges in the table. In 2 patients the head moved less consistently, with irregularities in the trace which precluded time delay measurement due to the difficulty in determining maxima and minima (Fig. 1, patient 5).

In the 5 cases subjected to Fourier analysis, the frequency of the stimulus was less than 1.2 Hz, with a peak spectrum in the 0.8 Hz band (Fig. 2, below). The results of the coherence function indicated that in normal subjects at least 50% of the power present in the head movement was linearly related to the chair's movement (coherence values between 0.50 and 0.82) whereas in the patient studied the values were considerably smaller (Fig. 2, Table II). Gain (in decibels), also shown in Table II, show great variability and for the reasons given earlier are of questionable interest. However, a point to note on the amplitude of the re-

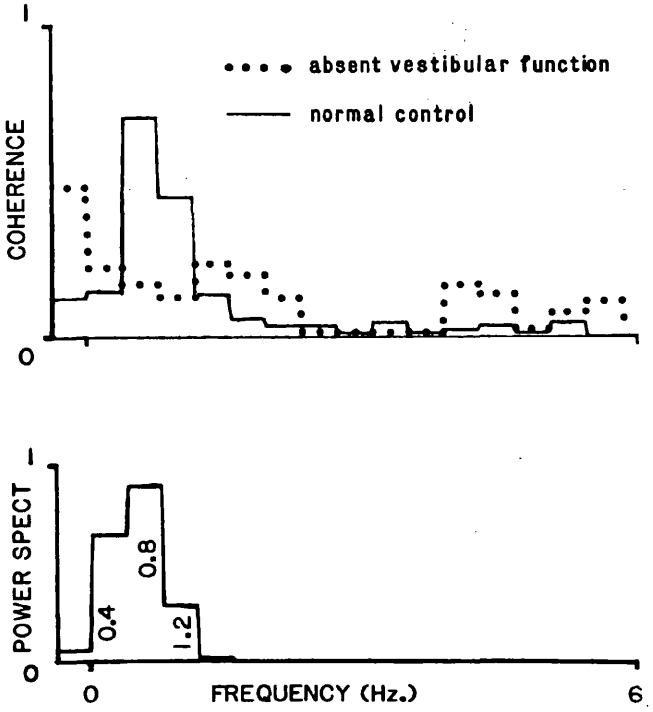

Fig. 2. (*Above*) Coherence between head and trunk movements in a patient lacking vestibular function and in a normal subject. (*Below*) Power density of the stimulus (arbitrary units) showing the typical frequencies present (0.4, 0.8, 1.2 Hz).

sponse, as assessed from the raw records (Fig. 1) is that the compensatory head movements were always of smaller amplitude (usually by about 40–50%) than that of the chair oscillation. This in turn implies that the semicircular canals were always subjected to net head acceleration in the direction of the chair's rotation.

DISCUSSION

These studies have shown that during angular horizontal whole-body movements, labyrinthineless patients differ from normal subjects in their ability to stabilize their head in space as evidenced by the presence of a time delay between peak head–chair displacements and a low coherence between head and chair motion.

Normal subjects, on the other hand, presented negative time delays, that is, anticipated the reversal of chair direction. With ordinary sinusoidal stimuli, such a time relationship between stimulus and response could be attributed to a 'high order' predictive response but,

Table II. *Coherence and gain*[a] *of head movements elicited by trunk oscillation*[b]

	Coherence	Gain (dB)
Control 4	0.68	−4.7
Control 5	0.82	−10.6
Control 6	0.68	−8.5
Control 7	0.50 (0.4 Hz)	−10
Repeat test	0.50	−4.8
Patient 7	0.22 (0.4 Hz)	−11.7
Repeat test	0.34	−7.7

[a] Amplitude head movement/amplitude trunk movement.
[b] Maximum values of coherence are given, usually at 0.8 Hz, unless otherwise stated. Gain values are at 0.8 Hz.

under our experimental conditions, this would not be likely because the stimuli were randomly delivered and unpredictable. More likely, the compensatory head movement followed a derivative of head in space displacement (i.e. acceleration) sensed by the vestibular system, thus giving the head/trunk position recordings an anticipatory or predictive appearance. It is known that the vestibular system detects early head acceleration signals and provides the ocular-motor system with an estimate of final head position (8); such an estimate could also be used by the neck muscles to generate compensatory head movements.

In partial agreement with these data is the recent work of Guitton et al. (4), assessing head stability during random body oscillation in subjects who had to make a spot of light, which originated in a projector fixed to the head, coincide with another earth-fixed target light. They reported that normal subjects achieved good head stability in these conditions, or when blindfolded while trying to stabilize an imaginary head-mounted light, whereas labyrinthineless patients performed significantly worse. Since their estimated delay values in normal subjects (mean 137 ms) were considerably larger than those reported here and than the latencies found in neck muscles (50 ms, unpublished results) or lower limbs (9, 10, 11) during free fall, these delayed responses were interpreted as 'long loop' vestibulo-spinal mechanisms under voluntary control. However, the prolonged delay may represent the additional time required by their subjects to process the visual feed-back of head position provided in the experiment.

In the absence of vestibular function the head can be stabilized in space by following the relative displacement of visual scenes in the direction opposite to that of the body. Thus, it is probable that our patients' strategy during the experimental session may have been analogous to following with the eyes and head a slowly moving visual target while sitting stationary. It is noteworthy in this respect that similar time delays between target and head were seen in normal subjects required to pursue a target in an unpredictable manner within a comparable frequency range (12).

The amplitude of the response was not measured systematically, since it was under strong voluntary control. This is not surprising, since animals require two opposing strategies in different circumstances; on the one hand to stabilize the head with respect to the environment and, on the other, to stabilize the head with respect to the trunk. It has been shown in animal experiments that two reflexes, the vestibulo-collic reflex (VCR) and the cervico-collic reflex (CCR), subserve respectively these requirements (13, 14). Accordingly, a central gating mechanism appears to be needed in the behaving animal in order to re-weigh one or the other during different movement strategies. The existence of such a mechanism could account for the dependence on a relevant instruction needed to obtain compensatory head movements in some of our subjects. It would also help explain the variability which Outerbridge & Jones (3) demonstrated in the head movement responses of normal subjects to angular velocity steps in the dark; some subjects did not respond at all, whereas others displayed nystagmoid head movements synchronous with eye nystagmus. It is interesting that these gating mechanisms also seem to be present in lower mammals since, in the absence of normal viewing conditions, dynamic VCR responses elicited by trunk rotation are absent in the guinea pig and in the rabbit (15, 16).

Limitations of VCR responses seem also to be imposed by the frequency of the stimulus. Thus, with trunk oscillation at much higher frequencies and accelerations than those used here, no active VCR could be identified and the resulting head stabilization was attributed to the inertial–mechanical properties of the neck–head system alone (2).

To sum up, the experiments described here have shown that during whole-body oscillation, labyrinthineless patients have impaired stability of the head in space when required to direct their eyes and head towards a stationary object in the environment. This suggests that VCR responses, gated by central mechanisms, operate in normal man.

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Vestibular involvement in spasmodic torticollis

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SUMMARY Vestibular findings in a group of 35 patients with spasmodic torticollis without other otological or neurological symptoms were reviewed. The most consistent abnormality, present in more than 70% of cases, was a directional preponderance of vestibular nystagmus in the dark in a direction opposite to the head (chin) deviation. Rigidly clamping the head to a rotating chair did not abolish the directional preponderance. In the presence of optic fixation the directional preponderance was less frequent and its severity tended to diminish as a function of the duration of the disease. Smooth pursuit and optokinetic nystagmus were only occasionally affected. The results are indicative of primary involvement of the vestibular system in spasmodic torticollis and are discussed in terms of a break-down of the central mechanisms conveying sensory information responsible for head and eye orientation.

Spasmodic torticollis is a motor disorder comprising involuntary activation of the neck muscles resulting in intermittent or persistent deviation of the head. Although the underlying pathophysiology is unknown, the disorder is usually considered to be one of the extra-pyramidal system particularly involving the basal ganglia. On the other hand, in animals vestibular lesions cause striking postural derangement of the head position[1] and in man there are sporadic reports of vestibular abnormalities in patients with spasmodic torticollis.[2–6] Indeed operations on the vestibular system have been used as a treatment for spasmodic torticollis in man.[4,6] It is not clear, however, whether the vestibular abnormalities found in patients with spasmodic torticollis are primarily causative or the result of the abnormal head posture or the result of abnormal interaction with other sensory-motor systems.

In an attempt to clarify this we have looked at two groups of patients with spasmodic torticollis in whom extensive vestibular investigations were undertaken. The first included all the patients with spasmodic torticollis referred to the MRC Neuro-Otology Unit at the National Hospital, whose results will be discussed here. The second group comprises three patients each of whom developed spasmodic torticollis in association with an 8th nerve disturbance and will be considered in a separate paper.

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Material and methods

Clinical records of 71 patients with torticollis seen in the MRC Neuro-Otology Unit at the National Hospital between 1957 and 1984 were reviewed. As it was intended that abnormalities found on vestibular testing should be strictly related to spasmodic torticollis, all cases with additional neurological signs were excluded (28 cases). Most of these 28 patients had focal or generalised dystonic features, writer's cramp, Parkinsonism, tremor, pyramidal lesions or cerebrovascular disease. Five patients with otological diseases were also excluded as were six additional patients. Of these latter six, two had pure retrocollis, two had psychogenic torticollis, one had incomplete medical records and one had tuberculosis of the cervical vertebrae. Three patients had more than one condition resulting in their exclusion.

The clinical material thus comprises 35 patients (18 female and 17 male). The mean age at the time of the neuro-otological examination was 46 years (24 to 70 years) with a mean duration of spasmodic torticollis of 4 years (10 weeks to 19 years). The head could be rotated or tilted in a tonic or spasmodic manner; the most frequent abnormality was a combination of these four conditions. The direction of the torticollis was specified by the chin position relative to the mid line, that is chin to the right is right torticollis.

Clinical neuro-otological evaluation included assessment of the Romberg test and gait (eyes open and closed). Any nystagmus in primary position or with gaze deviation to right, left, up and down was noted. The Hallpike manoeuvre was used to produce positional nystagmus. Optokinetic nystagmus (OKN) was elicited with a small black and white striped drum rotated in the vertical and horizontal planes.

Smooth pursuit eye movements were assessed clinically in 15 patients. Caloric tests were performed in the presence of visual fixation with the head held in the primary position in 31 patients. Methods and criteria used to establish abnormalities of the various caloric patterns were as in Fitzgerald and Hallpike;[7] nine patients had, in addition, caloric testing in the dark while their eye movements were observed either with an infra-red viewer or with Frenzel's glasses. Four patients did not undergo caloric testing.

In 24 patients electro-nystagmography (ENG) had been obtained with bitemporal electrodes and direct current amplification. The paper recordings were available and re-evaluated. All the recordings included traces on primary gaze and on 30° deviation to the right and the left both in the presence of visual fixation and in darkness. OKN was investigated either with a small drum or full field stimulation in 18 patients. Smooth pursuit was assessed in 13 cases. OKN and smooth pursuit were inspected visually from the paper recordings and, when in doubt, slow phase velocity was measured by hand. Labyrinthine responses to an impulsive rotation to a velocity of 40°/s were assessed in 13 patients and the duration of the nystagmic response to the start and the stop impulse was measured. During ENG recording attempts were made to restrict head movement as much as possible by providing the subjects with a chin and a head rest. However, as this was not always entirely satisfactory, five patients were additionally tested on another revolving chair in which, by means of a head rest and bi-auricular head clamp, complete head immobility was achieved. These patients underwent sinusoidal rotation in the dark at a frequency of 0·3 Hz and peak velocity of approximately 50°/s.

Results

(a) *Clinical assessment*

Body balance was largely preserved in spasmodic torticollis; Romberg's test was negative in all 35 patients and gait was normal in 31. There was minimal lateropulsion in four patients (11%) on walking with the eyes closed. This body deviation was in the same direction of torticollis in one case and opposite in the other 3.

A summary of the vestibulo-oculomotor findings and their relation to the side of the neck torsion is presented in table 1. Spontaneous nystagmus on primary gaze (2nd°) was never found and 1st° nystagmus was exceptional. When present, however, it was of vestibular type and was usually apparent when the patients looked in the opposite direction to their torticollis. Positional nystagmus was seen in only two cases; it was in the direction opposite the torticollis. Of some interest were the five cases whose torticollis was markedly influenced by positional changes being more prominent in the upright position in two patients and while lying down in three. OKN was essentially normal although in 23% of cases a slight directional preponderance in the direction opposite the torticollis was found. Smooth pursuit was normal in the 15 patients examined.

(b) *Electronystagmography*

The results are summarised in Table 2. In 11 out of 24 cases (46%) a vestibular nystagmus in the direction opposite to that of the torticollis was clearly seen in the dark. In eight out of these 11 cases it was found on both eccentric and primary gaze (2nd°); in the other three the nystagmus was of 1st° only. The nystagmus was usually abolished on fixation. Less frequently ipsilateral or bilateral nystagmus was found. Although

Table 1 *Abnormalities in clinical vestibular testing*

	Spontaneous nystagmus n = 35	*Positional nystagmus n = 35*	*OKN DP n = 35*	*SP n = 15*	*Caloric test (Fixation) n = 31*		*Caloric test (Darkness) n = 9*	
					DP	*CP*	*DP*	*CP*
Ipsilateral	3%	0%	6%	0%	3%	13%	0%	11%
Contralateral	11%	6%	23%	0%	39%	19%	78%	0%
Bilateral	0%	0%	0%	0%	0%	0%	0%	0%
Normal	86%	94%	68%	100%	26%	26%	11%	11%

n = number of patients examined.
Ipsilateral-contralateral = abnormality in the same-opposite direction of torticollis in this and subsequent tables.
OKN = optokinetic nystagmus.
DP = directional preponderance of nystagmus.
CP = canal paresis.
SP = smooth pursuit.

Table 2 *ENG abnormalities*

	Spontaneous nystagmus n = 24		*OKN DP n = 18*	*SP n = 13*	*Rotation n = 13*
	Light	*Dark*			
Ipsilateral	0%	12%	5%	0%	23%
Contralateral	0%	46%	39%	15%	76%
Bilateral	4%	17%	0%	0%	0%
Normal	96%	25%	55%	85%	0%

in more than half of the cases OKN was normal, a directional preponderance opposite to the torticollis was encountered in 39%. Smooth pursuit was normal in most patients tested; in two out of 13 (15%) patients pursuit was moderately broken (saccadic) in the direction opposite to the torticollis.

(c) *Rotational and caloric testing*

Labyrinthine function assessed by the caloric test or rotation was usually abnormal. Only eight of 31 patients (26%) in whom caloric test was performed in the presence of fixation and one of the nine patients (11%) who were also assessed in the dark had normal responses to irrigation. There was a caloric directional preponderance in the direction opposite to the torticollis in 33% of the patients in the light and 78% of patients in the dark. Other abnormalities, listed in table 1, were less frequent.

None of the 13 patients in whom rotational tests were done had a normal symmetrical response (table 2). 76% of the patients had a clear directional preponderance in the direction opposite the torticollis, a figure in good agreement with that obtained with caloric testing in the dark (78%).

An attempt was made to correlate the degree of asymmetry found in the vestibular tests with features of the disease. Unfortunately we had no reliable way of assessing the severity of spasmodic torticollis. However the duration of the disorder seemed to be inversely related to the degree of asymmetry found on caloric testing. Since the duration of caloric and rotational nystagmus was available in all cases a directional preponderance index was calculated using the following formula:

$$\frac{\text{Duration of induced nystagmus in the direction of torticollis } (d_s)}{\text{Duration of induced nystagmus in the direction opposite to the torticollis } (d_o)}$$

From this it can be seen that if, $d_s/d_o < 1$ the directional preponderance was opposite to torticollis while if $d_s/d_o > 1$ the directional preponderance is in the same direction of torticollis; $d_s/d_o = 1$ indicates symmetric responses.

The directional preponderance indices of 29 out of 31 cases who had caloric testing in the light were calculated; two cases had to be discarded because in one of them the caloric test had been repeated with contradictory results and, in the other, only one of the four irrigations induced nystagmus. The directional preponderance indices of caloric test in the light of spasmodic torticollis patients with less than a year's duration were 0·77, SD = 0·17 (n = 10), between 1 to 5 years = 0·92, SD = 0·13 (n = 11) and more than 5 years = 0·97, SD = 0·11 (n = 8) (fig 1). There was a

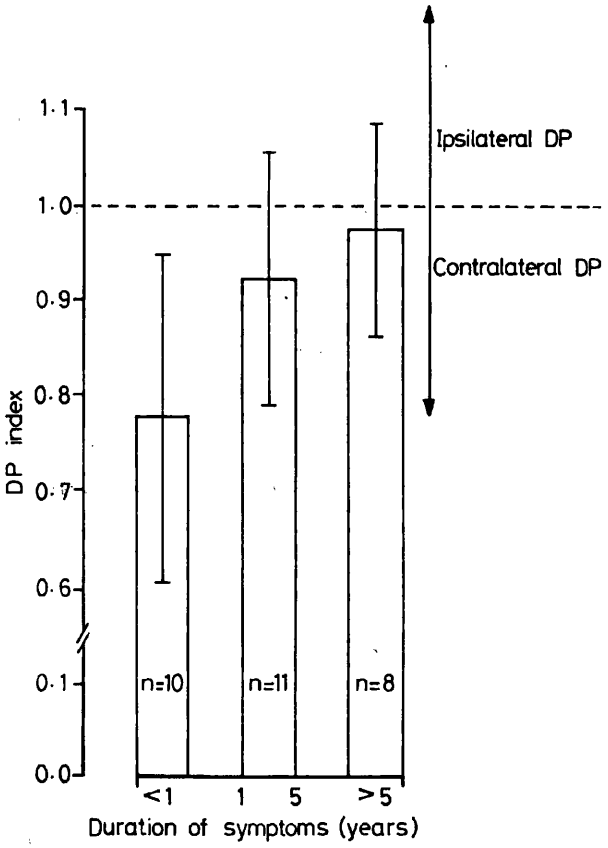

Fig 1 *Relationship between duration of torticollis and directional preponderance (DP) indices of caloric test in the light. Means and SD are shown.*

positive logarithmic correlation between the duration of the illness and directional preponderance index ($r = 0·55$; $p < 0·01$). This indicates that spasmodic torticollis patients show a tendency to have more active nystagmus (directional preponderance) in a direction opposite to the torticollis and that this asymmetry, in the presence of optic fixation, tends to decrease with time.

Further analysis of these data was undertaken. If only those patients who had rotational or caloric directional preponderance in the direction opposite to torticollis are considered (17 of the original 31) a better inverse correlation between the duration of the torticollis and the directional preponderance is found $r = 0·75$ $p < 0·01$ (fig 2). On the other hand, in the same group there was no correlation between the directional preponderance obtained on caloric testing in the dark or on rotational testing and the duration of the illness (fig 3). These data indicate that although directional preponderance in the presence of fixation shows a progressive reduction with time, the directional preponderance in the dark remains unchanged.

In order to establish whether the directional preponderance was a trivial consequence of the head movement or posture five patients (plus one with ad-

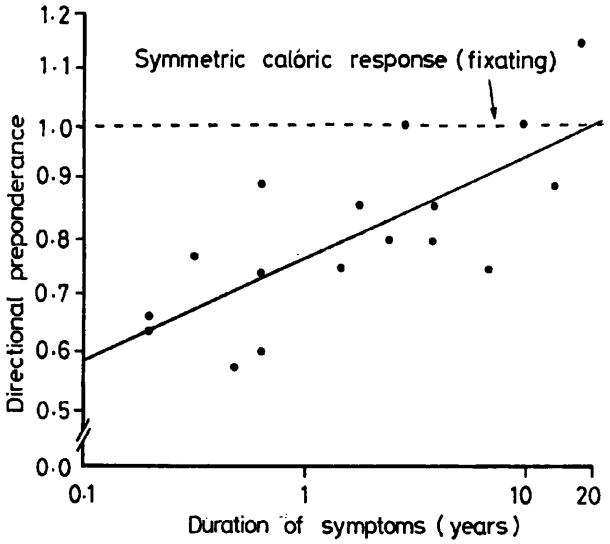

Fig 2 *Relationship between duration of torticollis and directional preponderance indices of caloric test in the light. Only the patients who had a rotational or caloric directional preponderance contralateral to the torticollis are presented.*

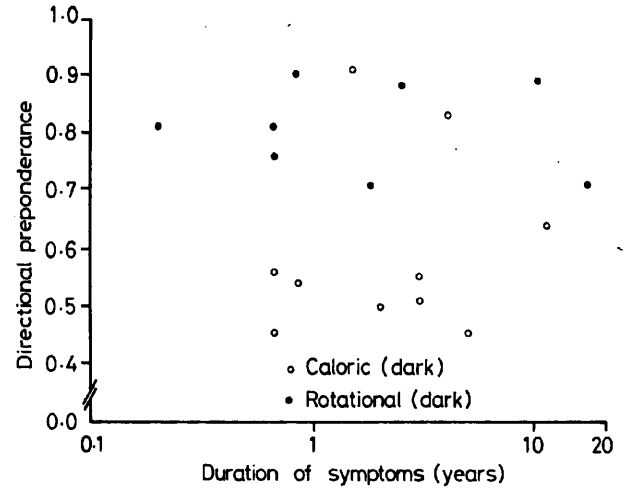

Fig 3 *Relationship between duration of torticollis and directional preponderance indices in the dark in patients with caloric or rotational directional preponderance contralateral to the torticollis.*

ditional mild unilateral upper limb dystonia who was not included in the present series) were subjected to sinusoidal rotation in darkness with the head completely immobilised in the central position. The gain of the vestibulo-ocular reflex (slow phase eye velocity/chair velocity) was measured separately to right and left. From fig 4, a case with left torticollis, it can be seen that nystagmus to the right was more active and of longer duration than in the opposite direction. All the other cases behaved similarly, VOR gain being higher during the half cycle in which the chair moved in a direction opposite to that of the torticollis.

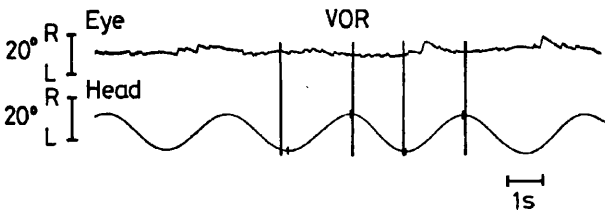

Fig 4 *Eye movements in the dark during sinusoidal rotation with the head clamped (vestibulo-ocular reflex, VOR) in a patient with left torticollis. The short and long vertical lines indicate respectively the points at which the head and the slow component of the eye movement reverse direction. During rotation to the left the eyes are advanced relative to the head (phase lead indicated by the larger gap between short and long vertical lines). Thus, hemicycles of right beating nystagmus are of greater magnitude and duration than those to the left.*

Discussion

Our results show that there are neuro-otological abnormalities in patients with spasmodic torticollis. The most consistent finding is the directional preponderance of vestibular induced nystagmus opposite to the direction of the torticollis. Since the directional preponderance is specified by the fast phase of the nystagmus the vestibular induced slow phase is greater in the opposite direction to the directional preponderance and thus in the same direction as the torticollis. The same trend was noted, although not emphasised, by Matthews *et al.*[8] Such a finding is consistent with the hypothesis that there is tonic imbalance of muscle activity both in the neck and the extra-ocular system which tends to deviate the head and the eyes in the same direction. That this directional bias of the vestibularly elicited eye movements is not a trivial consequence of the head movement is supported by three observations.

Firstly, in normal subjects, forced rotation of the head does not result in a directional preponderance of the rotational response (unpublished observations). Secondly, if the head is fixed during vestibular stimulation in a patient with torticollis the directional preponderance persists. Thirdly, if the directional preponderance were a consquence of the position of the head it might be expected to remain constant or even increase with time. In fact the reverse occurs in spite of the torticollis persisting. For these reasons we think the directional preponderance of induced nystagmus is more fundamentally related to the torticollis.

From the available evidence the type of neuro-otological abnormalities found indicate that the vestibular system itself, rather than other ocular-motor sub-systems, is affected. This is suggested by the much higher incidence of directional preponderance or

spontaneous nystagmus in the dark than in the light, indicative of a preserved capacity to compensate for vestibular asymmetry by fixation, and by the relative integrity of the more purely visuo-motor tests such as smooth pursuit and to a lesser degree OKN.

It might be argued, based on some isolated reports in the clinical literature, that the torticollis and directional preponderance stem from a vestibular end organ, 8th nerve or vestibular nuclear disturbance. Although this is a superficially attractive hypothesis, it is unlikely to be true since the vast majority of cases of spasmodic torticollis have no overt 8th nerve symptomatology.

It is more likely that the neuro-otological abnormalities are due to a central disturbance of posture which also affects the tonus balance of the vestibulo-ocular system. In Parkinson's disease, for instance, abnormalities of caloric,[9] rotational[10] and tilting reactions[11] have been reported which could be explained on a similar basis. Unfortunately, however, unilateral cases were not presented separately in order to determine whether basal ganglia diseases other than torticollis are able to produce a directional preponderance in the vestibular tests.

The vestibular system has complex connections within the brain stem, thalamus and cortex where interaction with other sensory modalities can occur.[12–17] It is possible that the abnormality in spasmodic torticollis is a break down of these central connections and particularly their interaction with other modalities signalling posture of the somatic musculature controlling head and eye position. Such a break down is consistent with a perverted or exaggerated response to sensory stimuli in patients with spasmodic torticollis and would account for the observations that patients are able to control their head position by cutaneous stimulation, have increased sensitivity to proprioceptive input[18] and for the effect of position with respect to gravity seen in five of our cases. The possibility that in some cases an abnormal peripheral labyrinthine input might play a role in the genesis of this break down is, however, an open question currently being investigated.

It is apparent from the present series that the directional preponderance in the direction opposite to the chin deviation, although frequently found, is not a constant feature of the disease. We suggest two possible reasons for this. Firstly, there is evidence from stereotaxic surgery that different forms of spasmodic torticollis (jerky, tonic, rotational, tilted) have a distinctive anatomical basis.[19] It is thus possible that different vestibular pathways are involved in various types of spasmodic torticollis. Secondly, the type and degree of compensation of the vestibular derangement could vary. Although this is entirely speculative there is no doubt that such compensation mechanisms are active in patients with spasmodic torticollis at least as far as the vestibulo-ocular system is concerned, in that removal of fixation in our study, resulted in an asymmetry of the vestibular ocular reflex in many patients. The exact nature of these complex derangements and corrective processes, however, remains as obscure as when Barre[2] proposed a similar mechanism over sixty years ago.

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Spasmodic torticollis following unilateral VIII nerve lesions: neck EMG modulation in response to vestibular stimuli

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SUMMARY Three patients with spasmodic torticollis following VIII nerve lesions (VIII-ST) underwent quantitative assessment of their sternomastoid EMG during vestibular (otolith and semicircular canal) stimulation. The results were compared with a normal control group and with six patients with idiopathic spasmodic torticollis (ST). Backwards tilt of the VIII-ST patients resulted in a marked increase in the EMG, especially in the more affected sternomastoid, whereas this manoeuvre did not have a significant effect in normal subjects, or had a variable effect in the ST group. These results suggest that those with torticollis following VIII nerve lesions are a distinct group. Since there was no relationship between the side of the VIII nerve lesion and the direction of the torticollis a direct aetiological link between the two is, however, unlikely. The unusual EMG/tilt responses are explained on the basis of peripheral imbalance of utricular signals (maximal in the supine position) in the presence of central deranged processing of information concerning head posture.

The CNS relies on visual, proprioceptive and vestibular information to generate appropriate output to the cervical muscles controlling head position. For this reason damage to peripheral or central vestibular pathways gives rise to serious derangements of head posture in animals and occasionally in man.[1–4] These abnormal head postures, it must be stressed, do not show the massive EMG discharge which characterises the head deviation seen in spasmodic torticollis (ST).[5] However, recently we presented data from patients with spasmodic torticollis who did not have a previous history of vestibular disease, showing that a significant proportion of them had abnormal vestibular function.[6] In brief, caloric and rotational tests frequently disclosed as asymmetric vestibulo-ocular reflex, the slow component of the nystagmus being more active in the direction of the head (chin) deviation. Since there have been other reports on the association between spasmodic torticollis and vestibular lesions[7–10] we studied three patients in whom torticollis followed an insult to the vestibular system (VIII-ST) in an attempt to clarify a possible aetiological relationship between the two.

In addition to routine neuro-otological assessment neck EMG was recorded whilst various types of vestibular stimuli were delivered. It was expected that if there was a connection between the torticollis and the neuro-otological lesion some common clinical features should be present and the EMG activity from the dystonic muscles might be modulated by vestibular stimulation in a consistent way.

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Materials and methods

Case reports

Case 1 A 57 year old man who, at the age of 24, suddenly developed severe vertigo, unsteadiness, nausea, vomiting, tinnitus and hearing loss in the left ear. These symptoms settled over 24 hours. During the next 4 years he had occasional vertigo but more frequent feelings of unsteadiness and pulsion to the left. The tinnitus and hearing loss remained unchanged. At 37 years of age he noticed progressive weakness of the left leg. A left acoustic neuroma was removed at the age of 52 years and at the time the patient noticed that his head was rotated to the right.

On examination there was in addition to the deafness a

left lower motor neuron facial weakness, moderate pyramidal weakness on the left and a mild ataxia bilaterally. The head was turned to the right due to tonic contraction of the left sternomastoid which was hypertrophied. The right splenius and the left trapezius were also hypertrophic though to a lesser degree.

Case 2 A 62 year old man who had suffered from chronic bronchitis for many years. Five years before being seen he had a single episode of headache in the right parieto-occipital region following which he developed trigeminal neuralgia in the right cheek and jaw. This was partially controlled with carbamazepine and phenytoin. He occasionally had blurred or double vision and a vague sensation of dizziness and unsteadiness but did not report rotational vertigo or hearing troubles. In the year before assessment he noticed that the head involuntarily turned towards the left, especially on lying in bed.

On examination the right sternomastoid was moderately hypertrophic and there was a bilateral exophoria. Jerky torticollis to the left, which clearly increased in the supine position, was present. A CT scan showed the basilar artery looping into the right cerebello-pontine angle.

Case 3 A 52 year old man who, at the age of 15, developed involuntary movements of the face in which he screwed up his eyes and twisted the corner of his mouth. At the age of 45 he suffered attacks of vertigo with right sided tinnitus and progressive hearing loss. A right vestibular neuronectomy was carried out. This operation abolished the vertigo and the facial movement but he had moderate hearing loss with tinnitus and right facial weakness; the latter resolved over two months. Six months after the operation he developed head turning towards the right associated with neck pain.

On examination he had right torticollis with hypertrophy of the left sternomastoid. Both splenii and the right trapezius were mildly hypertrophic. There was a mild right facial weakness more marked around the mouth than the eye and a mild right pyramidal weakness.

Control groups

Two groups of subjects were used as controls. The first consisted of six normal male subjects, aged between 21 and 55 years, and the second of six patients with idiopathic spasmodic torticollis. The latter group comprised three males and three females aged between 32 and 59 years, with no previous history of otological disease; two had previously undergone a full neurootological investigation and had the typical directional preponderance of vestibular nystagmus in the direction opposite to the chin deviation.

Electro-myography

Surface Beckman silver cup electrodes were used to record the EMG from the sternomastoid on both sides of the neck. Raw EMG was displayed on-line by means of an ink jet recorder and collected on magnetic tape for subsequent processing on a Fourier analyzer (Solartron 1200) which displayed the power spectra and calculated the energy dissipated by the signal (power in band between 10 and 500 Hz) in volts^2. The frequency limit of the system was either 313 or 625 Hz according to the tape speed used. The periods analysed were approximately 30 s and usually included 30 averages. The first 10 seconds of EMG after each new vestibular stimulus was applied was not analysed to allow for stabilisation of the recording. Abnormally high peaks of activity at 50 Hz were deducted from the total power because this was always correlated with clearly identifiable noise on the paper recordings.

Vestibular stimulation

Vestibular modulation of the neck EMG was studied in response to tilt with respect to gravity (otolith stimulation) and to horizontal rotation (semicircular canal stimulation). In order to obtain quantifiable body tilt a bi-axial gymbal was used; the patients sat on a chair which restrained their arms and pelvis. The trunk was strapped in with an "X" shaped seat belt; the legs and feet were also fitted with belts. The head rested backwards and was fixed, when required, with a binaural clamp. The position of the chair was monitored with a potentiometer. The subjects were tilted backwards in steps of 30° up to a maximum of 90° in the sagittal plane with the head resting freely. Then the head was clamped and the patients tilted 45° backwards-forwards (sagittal plane) and right-left (coronal plane). These displacements were smooth and slow; the subjects stayed in the new position for at least a minute before being moved again. The effect of vision upon the EMG was assessed by obtaining records with eyes open and closed.

Rotational stimuli were delivered in the dark with a revolving chair which rotated around the vertical axis at a constant acceleration of 2 to 3°s^{-2} up to a maximal velocity of 100°/s. This velocity was then maintained for about 2 minutes during which the room lights were turned on and off for periods of about 45 seconds in order to assess the role of optokinetic stimulation. The procedure was carried out at least twice to the right and twice to the left resulting in a total constant acceleration duration in each direction of least 132 s. During rotation the head was in contact with an occip-

Table 1 *Clinical and neuro-otological summary*

	VIII lesion	*Torticollis (chin)*	*Spontaneous nystagmus*	*OKN*	*SP*	*Caloric test*	*Rotational test*
Patient 1	L	R	2° R	R DP	Saccadic R > L	L CP R DP	R DP
Patient 2	R	L	Nil	R DP	Saccadic	R DP	Not available
Patient 3	R	R	Nil	Normal	Normal	R CP L DP	Hypoactive bilaterally

OKN = Optokinetic nystagmus
SP = Smooth pursuit
DP = Directional preponderance of nystagmus
CP = Canal paresis

Table 2 *Resting EMG*: sternomastoid*

NC	=		n = 11	$1{\cdot}03 \times 10^{-2}$ SD $1{\cdot}86 \times 10^{-2}$
ST	=	Affected	n = 5	$1{\cdot}27 \times 10^{-1}$ SD $9{\cdot}82 \times 10^{-2}$
		Unaffected	n = 4	$3{\cdot}48 \times 10^{-1}$ SD $3{\cdot}79 \times 10^{-1}$
VIII-ST	=	Affected	n = 3	$1{\cdot}06 \times 10^{-1}$ SD $8{\cdot}43 \times 10^{-2}$
		Unaffected	n = 3	$1{\cdot}71 \times 10^{-2}$ SD $2{\cdot}04 \times 10^{-2}$

*Expressed as the ratio: resting EMG/EMG during forced voluntary head turn. NC = normal controls. ST = idiopathic spasmodic torticollis controls. n = number of muscles satisfactorily studied. Affected = more affected sternomastoid; contralateral to the chin deviation. Unaffected = least affected sternomastoid; ipsilateral to the chin deviation.

ital rest but was not clamped. The subjects were instructed to relax and keep their eyes open.

Results

A summary with the main clinical and neuro-otological findings of the VIII-ST patients is presented in table 1. There was no consistent relationship between the side of the vestibular deficit and that of the torticollis. In cases 1 and 3 the neuro-otological findings, apart from the saccadic pursuit in the former, can be explained on the basis of the VIII nerve section. In contrast, in patient 2 the marked directional preponderance of caloric nystagmus in the direction opposite to that of the chin deviation is typical of idiopathic spasmodic torticollis; although there was no unequivocal indication of peripheral involvement in the vestibular tests, the patient's symptoms and the radiological findings provide good evidence of unilateral vestibular impairment.

The results of EMG while the subjects were sitting up relaxed with the head unrestrained are presented in table 2. As expected these resting values, expressed as a proportion of maximal voluntary contraction, are increased in both patient groups by an order of magnitude. Owing to this difference in the resting EMG, it was necessary to normalise the data of all the subjects in order to compare the effects of vestibular stimulation. Thus, for each tilt and rotation experiment the mean of all the EMG activity values in the upright, resting position was calculated for each individual muscle and subject and this was taken as basal value. The effects of tilt upon this basal value are shown in tables 3 to 5. Two main difficulties were encountered during data analysis, namely that the VIII-ST group was small and that there were important individual variations within both patient groups. As the latter produced considerable skewing of the data, the medians and interquartile ranges were plotted to give a clearer picture of the trends present in all patient groups (fig 1).

The greatest difference between the three groups tested was found during backwards tilt with the head free. In normal subjects the effects were negligible but in the VIII-ST patients a marked increase of EMG activity usually occurred. This was related to the degree of tilt and was maximal in the muscle most affected clinically (fig 2). Two of the three patients were tested on more than one occasion with similar results. In no case did a spasmodic torticollis patient have a comparable enhancement of the EMG in the more affected muscle. On the contrary, two spasmodic torticollis patients had a significant reduction

Table 4 *EMG during tilt back and forward; head clamped*

		45B	*45F*
NC	n = 11	1·02 SD 0·29	1·39 SD 0·75
ST			
Affected	n = 6	3·17 SD 3·50	1·74 SD 1·97
Unaffected	n = 6	1·07 SD 0·46	1·02 SD 0·57
Patient 1			
Affected		8·93	7·25
Unaffected		1·02	4·74
Patient 2			
Affected		2·97	0·79
Unaffected		2·83	3·31
Patient 3			
Affected		1·94	2·6
Unaffected		1·53	2·59

Table 3 *EMG* during tilt backwards; head resting freely*

		30°	*60°*	*90°*
NC	n = 11	0·99 SD 0·19	1·04 SD 0·19	1·11 SD 0·38
ST				
Affected	n = 6	0·64 SD 0·33	0·64 SD 0·34	0·93 SD 0·82
Unaffected	n = 6	1·02 SD 0·44	1·44 SD 1·64	1·98 SD 2·29
Patient 1				
Affected		8·27	10·13	26·02
Unaffected		4·27	4·5	5·87
Patient 2				
Affected		3·63	3·76	3·14
Unaffected		1·6	1·99	3·25
Patient 3				
Affected		0·92	0·87	4·13
Unaffected		0·04	0·06	0·10

*Expressed as a ratio: EMG during tilt/EMG at 0° of tilt.

Table 5 *EMG during coronal tilt at 45°; head clamped*

		Side down	*Side up*
NC	n = 11	5·53 SD 9·36	3·71 SD 7·65
ST			
Affected	n = 5	10·73 SD 12·13	3·99 SD 7·53
Unaffected	n = 5	1·29 SD 0·53	1·19 SD 0·20
Patient 1			
Affected		5·15	0·29
Unaffected		1·09	0·13
Patient 2			
Affected		4·88	1·68
Unaffected		2·10	1·67
Patient 3			
Affected		4·40	24·12
Unaffected		1·39	1·46

Side down = left sternomastoid during left tilt or right sternomastoid during right tilt. Side up = left sternomastoid during right tilt or right sternomastoid during left tilt.

of muscle activity as they were tilted backwards (fig 3). Activity in the clinically less affected muscle activity was not altered by this manoeuvre in five of the six spasmodic torticollis patients.

During 45° tilt backwards or forwards with the head clamped, neck EMG usually increased in the VIII-ST patients. This effect was also commonly seen in the spasmodic torticollis group but not in the normal control group. Since spasmodic torticollis patients did not show EMG enhancement during sagittal tilt with the head free it is impossible to say how much of this effect was due to the tilt and how much due to the forced fixation of the head. Eye opening or closure did not affect the sagittal tilting responses.

Tilt in the coronal plane also had to be carried out with the head clamped. During this experiment all groups produced a similar pattern of EMG responses. Thus when the subjects were tilted to the right it was mainly the right sternomastoid which was activated as if opposing the tendency of the head to turn passively in that direction and vice versa on tilting to the left. This response was more prominent in both patient groups than in normal subjects and specially in the clinically more affected muscles. Although the subjects were encouraged to relax it is not clear whether this EMG modulation was the result of voluntary or involuntary activity.

During rotational tests on consistent modulation of the EMG was found in the normal subjects or the VIII-ST patients. Some spasmodic torticollis patients, however, did have a rotational modulation of their muscle activity. From what is known of the vestibulo-ocular and vestibulo-cervical reflexes, it is conceivable that during acceleration say to the right, the head would turn to the left. Thus, it was considered that EMG modulation consistent with stimulation of the horizontal semicircular canals occurred either when the muscle ipsilateral to the direction of the acceleration increased its discharge or the activity in the contralateral muscle diminished (table 6). If a change of 10% is considered significant a consistent EMG modulation occurred one in eight instances (12%) in the normal subjects, one in six (16%) in the VIII-ST cases and six in 11 (55%) in the spasmodic torticollis patients. There was no systematic optokinetic modulation of the EMG in any group nor were there any consistent differences in the frequency content (power spectra) of the EMG in the various groups. Highest levels of activity were in the region between 50–90 Hz with minimal power beyond 200 Hz.

Discussion

The possible existence of a link between spasmodic torticollis and the vestibular system has interested neurologists for a long time[6–12] and, not infrequently, isolated cases of otogenic spasmodic tor-

Table 6 *EMG* during horizontal rotation*

		Ipsilateral	*Contralateral*	*Cases with corresponding modulation of EMG*
NC	n = 8	1·08 SD 0·21	1·16 SD 0·28	1 — (12%)
ST				
Affected	n = 5	1·23 SD 0·71	1·02 SD 0·60	3 — (60%)
Unaffected	n = 6	1·13 SD 0·32	1·16 SD 0·42	3 — (50%)
Patient 1				
Affected		1·20	0·33	Yes — (33%)
Unaffected		0·77	1·31	No
Patient 2				
Affected		0·46	0·73	No
Unaffected		0·93	1·56	No
Patient 3				
Affected		0·03	0·21	No
Unaffected		1·02	1·19	No

*Expressed as the ratio: EMG during acceleration/EMG during periods of no acceleration. Ipsilateral = right sternomastoid during rotation to right or left sternomastoid during rotation to left. Contralateral = right sternomastoid during rotation to the left or left sternomastoid during rotation to the right.

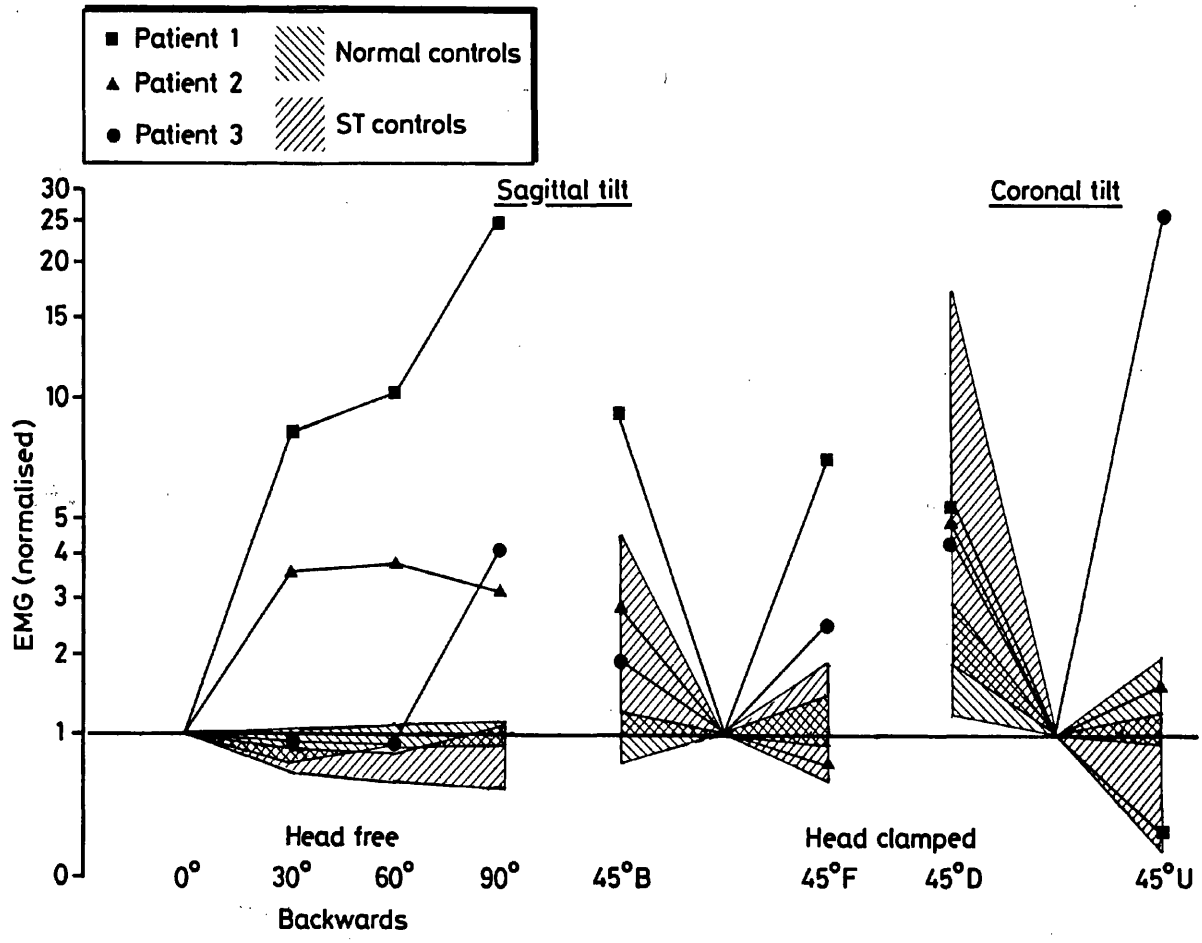

Fig 1 *EMG of the more affected sternomastoid in response to tilt backwards (B) forwards (F) side down (D) or side up (U). Shaded areas represent the interquartile range in the normal and ST control groups. Median values are presented for the VIII-ST patients. EMG was normalised for each subject and test condition so that a value of 1 represents the upright position.*

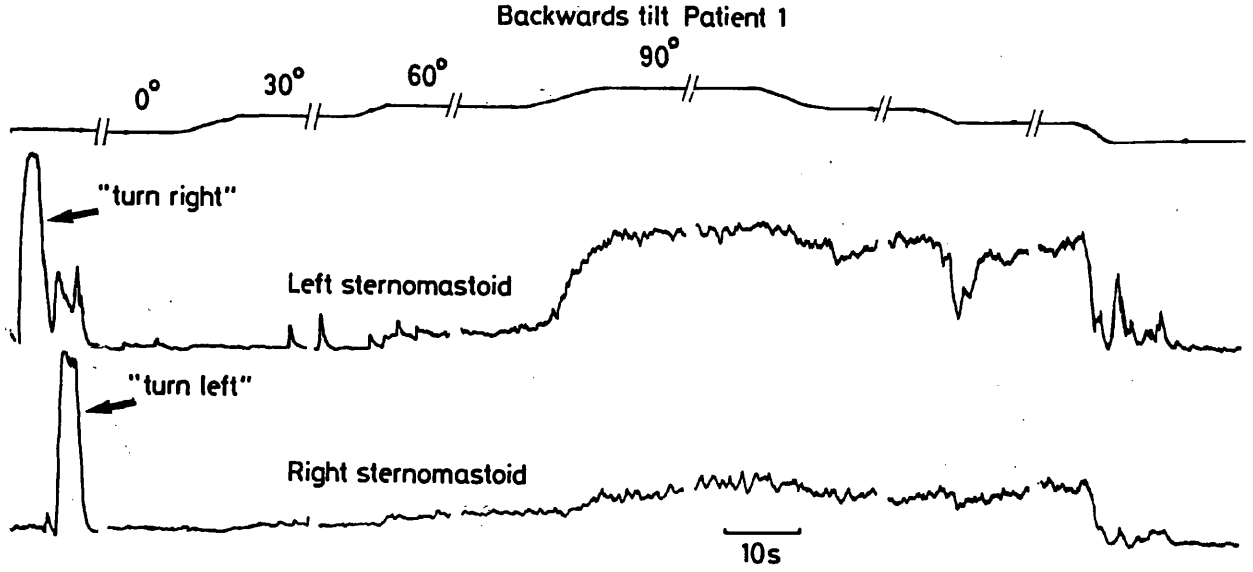

Fig 2 *Rectified and integrated EMG in a patient with a left acoustic neuroma removed and ST with chin rotation to the right. The patient was tilted backwards with his head freely resting. "Turn right" and "turn left" are voluntary forced head turns used as calibration. Records interruption, shown with parallel lines, were between 10–40 seconds.*

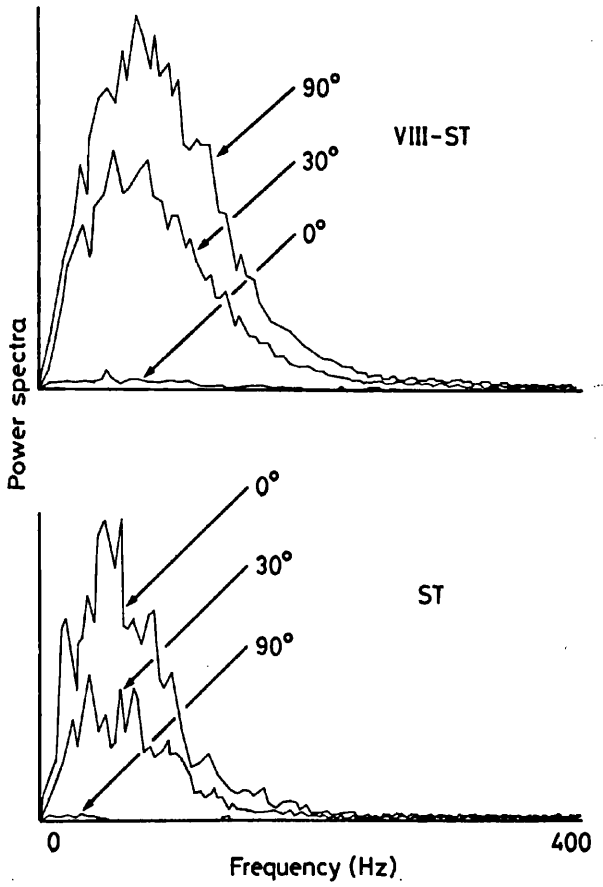

Fig 3 *Power spectra of EMG from the more affected muscle in patient 1 and in a ST control patient at various angles of tilt backwards with the head free. Power was measured in V^2 and normalised to 0° of tilt.*

ticollis have been reported.[7-10] Some of the cases in the literature had irritative labyrinthine lesions with marked fluctuations of the symptoms in whom a precise topographic diagnosis was difficult to establish. In contrast to this, in the present series two of the three patients undoubtedly had unilateral destructive lesions (nerve division in cases 1 and 3). The torticollis in these two patients was towards the right in both cases in spite of the nerve section being on the right in one case and the left in the other, arguing strongly against the tempting, but simple view, that unilateral vestibular lesions can produce spasmodic torticollis by virtue of an asymmetric vestibulo-collic reflex. This does not necessarily mean, of course, that the vestibular system and spasmodic torticollis do not influence each other.

The present investigations show that the three VIII-ST patients differed in their postural control from the cases of idiopathic spasmodic torticollis and normal subjects. In particular the response of the cervical muscles to backwards tilt with the head free was consistently different in the three groups of subjects studied. In the normal controls this manoeuvre did not modify the resting EMG and in the spasmodic torticollis group either it did not change the activity significantly or reduced it. In the three VIII-ST patients neck EMG was markedly enhanced especially that from the more affected sternomastoid. It is known from animal studies that these effects are probably dependent upon otolith macular activity. Magnus[1] described static vestibular reflexes in which maximal tonus in the decerebrate preparation occurred in the supine position and minimal tonus while prone. More recent studies have indicated that it is in these positions that macular units reach their maximal and minimal firing frequencies respectively.[13 14] Since the utricular macula is approximately horizontal when the animal is standing this position is also the point of optimal sensitivity, that is maximal change of discharge frequency per angle of head deviation relative to gravity.

It is reasonable to expect that during backward tilt macular discharge will activate both sternomastoids in order to keep the head upright or at least, in the absence of a supporting surface, to keep it aligned with the trunk. Clearly, if one VIII nerve is sectioned, tilt backwards will produce a maximal imbalance of macular input to the CNS since one macula will greatly increase its activity while the other is silent. Such a patient who also has spasmodic torticollis may be reasonably compensated in the upright position because the remaining utricle is in its optimal position for signalling changes of linear acceleration and is discharging at a moderate rate.

The situation is different in the supine position. In these circumstances the utricular macula will be at its maximal firing frequency and minimal sensitivity. Unilateral absence of vestibular function in otherwise neurologically normal subjects does not seem to produce a significant increase in the EMG; in three such patients tested sternomastoid EMG increased by a factor of 1·22 in the muscle contralateral to the vestibular loss and 1·09 in the ipsilateral one (median values) when tilted from 0 to 90° (unpublished observations). However, in the presence of deranged processing of head/eye position information such as occurs in spasmodic torticollis, this could well lead to a pathological enhancement in the neck EMG discharge. Thus, it is likely that the abnormal tilt/EMG reaction present in the VIII-ST group is due to the unique combination of two different factors: imbalance of peripheral macular signals and perverted central processing of the information concerning head orientation. Evidence for this latter factor stems from two sources. First there is a high incidence of vestibulo-ocular abnormalities as shown in a previous review of patients with spasmodic torticollis.[6] Secondly spasmodic torticollis patients are reported to have perverted or exaggerated muscle responses to

extero-proprioceptive stimuli and semicircular canal stimulation,[11 15] the latter also being suggested by the rotational experiments in the present study.

In summary, the cases presented here do not indicate that a peripheral labyrinthine disorder can be held directly responsible for the clinical picture of spasmodic torticollis. However, there is some evidence that an VIII nerve lesion can modify, aggravate and perhaps precipitate spasmodic torticollis by inducing further disruption in the processing of sensory information about head position. It follows from this that operations on the vestibular system in idiopathic spasmodic torticollis are unlikely to be therapeutically effective; indeed aggravation of the torticollis might well occur.

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Vestibulo-ocular abnormalities in spasmodic torticollis before and after botulinum toxin injections

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SUMMARY In order to establish whether vestibular abnormalities often found in spasmodic torticollis are secondary to the abnormal head posture, the vestibulo-ocular reflex (VOR) was studied in eight patients before and after correction of head posture with botulinum toxin. Eye movements were recorded in the dark during sinusoidal and velocity step rotation. Four patients showed a significantly asymmetric response, with the slow phase of the VOR more active ipsilateral to the torticollis (chin). Despite significant improvement of the head posture in all patients for up to 10 weeks following treatment, no correction of the vestibular asymmetry occurred. This suggests that the VOR abnormalities are not caused by the head posture itself. We interpret the findings as evidence of primary involvement of the vestibular system in torticollis and we postulate a widespread derangement of the sensory-motor mechanisms controlling head posture in this disease.

Spasmodic torticollis (ST) is a focal dystonia characterised by involuntary movements and postures of the head consisting of either horizontal rotation or tilt in the sagital or coronal planes, or any combination of the above. No convincing pathology has been demonstrated,[1-3] but it may be that torticollis, like other forms of dystonia, is due to a functional abnormality of neurotransmitter action in the basal ganglia.[4]

The condition has long been thought to be associated with abnormalities of vestibular function.[5] Indeed some authors have used techniques to suppress vestibular function as a method of treatment.[6] Central and peripheral lesions of the vestibular system and its projections are known to cause abnormal head postures, although in humans this is exceptional.[7-9] In a review of 35 patients with ST studied in our vestibular laboratory, about 70% had a directional preponderance of caloric/rotational nystagmus contralateral to the side to which the chin pointed.[10] More recently, measurements of ocular counter-rolling evoked at low frequency rotation have suggested abnormalities of otolith function in patients with spasmodic torticollis.[11] However, the significance of these vestibular abnormalities is uncertain. In particular, it is not clear whether they are a reflection of an underlying abnormality responsible for the torticollis, or whether they are secondary to the abnormal head posture.

The recent development of botulinum toxin[12,13] to treat such patients has allowed us to investigate this problem further by analysing vestibular function before and after the correction of the abnormal head posture.

Patients and methods

Eight patients with isolated spasmodic torticollis causing predominant horizontal rotation of the head were studied (table 1). Patients with this particular head posture were selected because the function of the horizontal semicircular

Table 1 *Patient characteristics*

Patient No.	*Sex*	*Age (yr)*	*Disease duration (yr)*	*Torticollis**		
				Pre-treatment	*3 weeks after botulinum toxin*	*10 weeks after botulinum toxin*
1	M	35	6	15°L	5°L	0°
2	M	40	12	35°L	25°L	25°L
3	M	42	5	50°L	35°L	25°L
4	F	31	8	60°L	35°L	15°L
5	F	53	22	40°L	10°L	15°L
6	M	56	20	30°L	20°L	20°L
7	F	47	8	50°R	30°R	15°R
8	F	59	3	70°L	0°	20°L

*The degree of deviation of the chin (in degrees), either to the right (R) or left (L), in the horizontal plane is shown before, and 3 and 10 weeks after injection of botulinum toxin.

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canals is routinely examined by caloric and rotational testing. Apart from the torticollis, no patient had other abnormalities on routine neurological and clinical oto-neuro-ophthalmological examination. There were four females and four males, with a mean age of 44 years (range 31–59). Mean disease duration was 9·5 years (range 3–22). Seven patients had rotation of the chin to the left and one to the right. Medications were continued as long as they had not been commenced within two months of the study.

All patients had the angle of head rotation and/or tilt measured with a protractor. Eye movements were recorded with bitemporal DC electronystagmography (ENG) on to paper with an ink-jet polygraph (Mingograph). The patient's head was restrained as straight as possible using binaural head clamps and an occipital head rest, whilst sitting on a motorised revolving chair. Chair (head) motion was transduced by a tachometer. Recordings were measured by hand.

The vestibular stimulus consisted of sinusoidal rotation in the dark at a frequency of 0·3 Hz and peak velocity of 50°/s. Slow phase velocity of nystagmus during sinusoidal rotation was measured and at least six slow phases in each direction were averaged to calculate the gain of the vestibulo-ocular reflex (VOR), defined as the ratio of peak eye velocity to peak head velocity. A qualitative observation of the phase of the VOR was made according to whether the reversal of the direction of the slow component preceded or followed the reversal of chair direction; this was then expressed as either a phase lead or lag respectively. In addition, a velocity step of +/− 40°/s in the dark was delivered, and the peak velocity and the time constant of the slow component of nystagmus were measured. Time constant was defined as the time taken by the initial peak eye velocity to drop by 63%.

All patients received botulinum toxin in a dosage of 500 mouse units to each of the two most active muscles selected

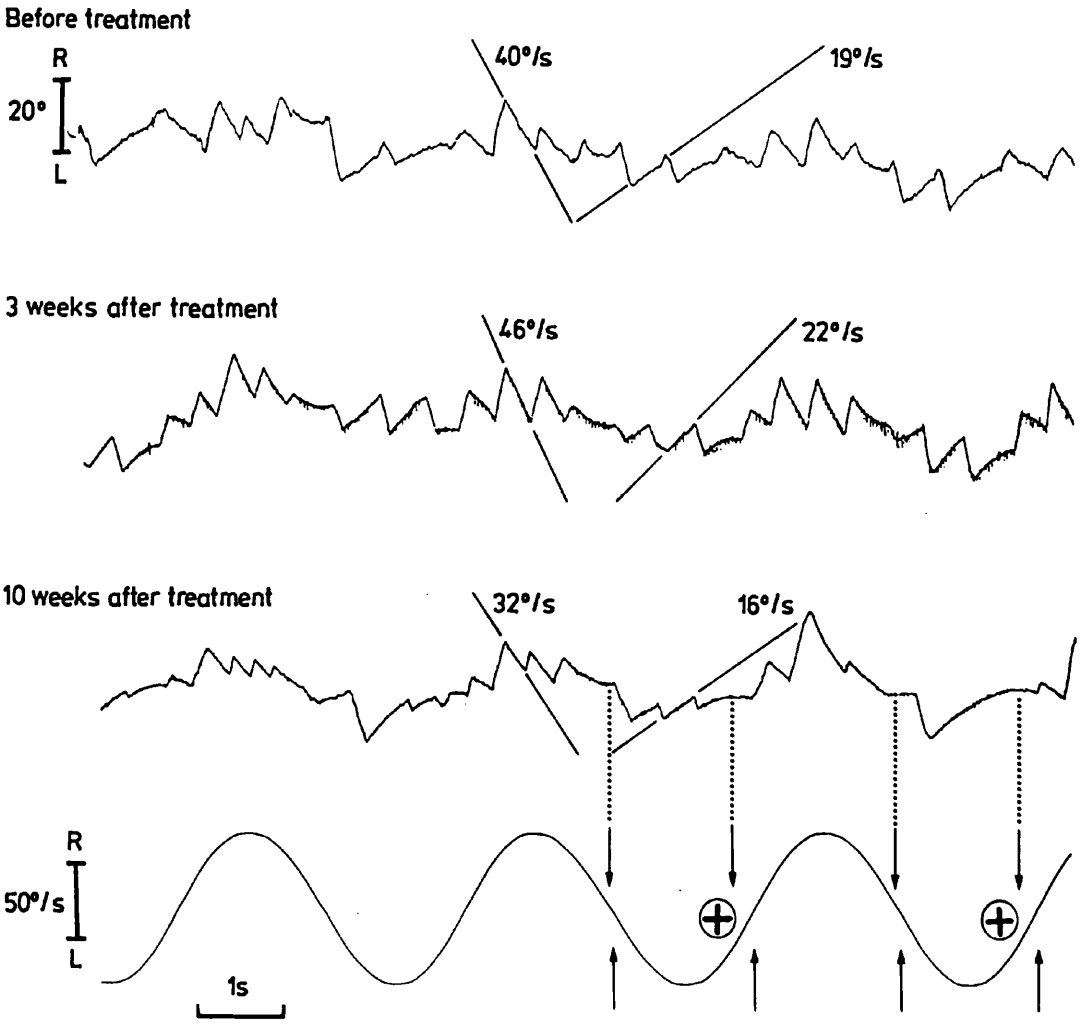

Fig 1 *Eye movements elicited by sinusoidal rotation in the dark in patient with torticollis (chin to the left) before, and 3 and 10 weeks after correction of head posture with botulinum toxin. Slow phase velocities to the left (that is, during nystagmus to the right), are greater than in the opposite direction in all instances. Bottom right: the upward arrows indicate the zero velocity points on the chair velocity trace (at the time of peak chair displacement), and the downward arrows indicate the points where the slow phase eye movements reverse direction. The + sign indicates a phase lead of the change in direction of the slow phase of the induced vestibular nystagmus with respect to peak chair displacement during leftward rotation.*

either clinically or on EMG using a technique described previously by us.[13] The patients were studied just prior to injection, and again at 3 weeks and approximately 10 weeks post-injection. Twenty normal subjects (age range 20–61 years) underwent sinusoidal rotation and 13 of these also underwent step rotation as above, for comparison.

Results

Figure 1 shows raw ENG records of patient 8 during sinusoidal rotation pre and post-treatment. This patient's head rotation was 70° to the left pre-treatment, and 0° and 20° to the left at 3 and 10 weeks respectively. On rotation of the chair to the right the slow phase velocity of the induced nystagmus persistently exceeded the velocity of the nystagmus induced by rotation to the left. There was no alteration in this asymmetry in the nystagmic response following treatment.

The results of sinusoidal rotation for all patients are summarised in table 2. For all patients with torticollis, the mean pre-treatment VOR gain (right and left combined) was 0·73 (SD 0·17), and the control value was 0·66 (SD 0·16); no patient lay outside 2 standard deviations from the mean of the normal subjects.

In order to assess the significance of the asymmetries found, the formula:

$$\frac{(\text{VOR gain to the right} - \text{VOR gain to the left})}{(\text{VOR gain to the right} + \text{VOR gain to the left})} \times 100$$

was applied to the pre-treatment data. This calculation is frequently applied in neuro-otological practice to quantify asymmetries of vestibular function.[14] Confidence limits were set at two standard deviations from the mean of the normal population. The control group had a mean value of 3·94% (SD 3·34). Five patients (cases 1, 2, 3, 6, 8) had an asymmetry of VOR gain with the more active nystagmus contralateral to the direction of the torticollis (chin), but this was within the confidence limits in patient 1. Three patients (4, 5, 7) had a more active response ipsilateral to the torticollis but in none of these was it significant. There was no clinical difference between these subgroups of patients. In all patients with a significant VOR gain asymmetry a phase lead for the slow phase of the vestibular nystagmus was found during chair rotation in the direction of the lower gain (see figure 1, bottom right), the net result being a prolongation of the duration of the nystagmus in the direction of the higher VOR gain.

Figure 2 summarises the change in head posture and figure 3 the asymmetry in VOR gain following botulinum toxin injection in all patients. For graphic purposes VOR symmetry is presented as the ratio between VOR gain ipsilateral divided by VOR gain contralateral to chin deviation, so that cases with VOR more active in the same-opposite direction of the torticollis are clearly identified. Arbitrarily, in the normal control group right VOR gain was divided by left VOR gain.

It can be seen that a considerable improvement of head posture was achieved in all patients but, despite this, the VOR asymmetry persisted essentially unchanged. A paired Student's t test confirmed that changes in head posture between pre and 3 weeks post treatment were statistically significant ($t = 4·89$; $p < 0·01$) whereas changes in VOR asymmetry were not ($t = 1·43$; $p > 0·05$). Patient 7 increased the degree of VOR asymmetry (more active ipsilateral to the torticollis) post-injection despite the improvement in head posture.

The results of the velocity step rotational test are shown in table 3. These were in general agreement with those of the sinusoidal test. The mean slow phase velocity (right and left combined) for control subjects was 32·04°/s (SD 8·01) and for the patients was 26·45°/s (SD 5·86). There was no statistical difference between these values ($t = 1·68$; $p > 0·05$). The mean time constant (tc) for control subjects was 13·35 (SD 4·45) and for patients 14·98 (SD 2·34); this difference was not significant ($t = 0·95$; $p > 0·05$). The formula used above to assess the significance of VOR asymmetry was applied to peak slow phase velocity of nystagmus.[14] The control group had a mean value of 2·00% (range—7·32 to 15·22). Six patients (cases 1, 2, 3, 4, 6, 8) had an asymmetry of the step rotational response with the more active nystagmus contralateral to the direction of the torticollis; in 3 of these (cases 3, 4, 8) the values lay outside the normal range. Two patients (cases 5, 7) had slightly more active nystagmus ipsilateral to the torticollis but in both of these it lay within the normal range. In three patients (cases 2, 3, 8) there was a considerable asymmetry of the time constant and in these cases it was shorter with rotation in the direction of the lower VOR gain and peak slow phase velocity of nystagmus. There was no significant change in the symmetry of peak velocity ($t = 0·47$; $p > 0·05$) and time constant ($t = 1·77$; $p > 0·05$) of

Table 2 *VOR gain (to right -R, or left -L) during sinusoidal rotation before, and 3 and 10 weeks after treatment with botulinum toxin*

Patient No.	Torticollis	Pre-treatment		3 weeks		10 weeks	
		R	L	R	L	R	L
1	L	0·97	0·73	0·27	0·23	0·40	0·30
2	L	1·04	0·55	1·28	0·69	0·80	0·54
3	L	0·51	0·39	0·54	0·36	0·36	0·26
4	L	0·75	0·85	0·76	1·06	0·62	0·80
5	L	1·00	1·05	0·83	0·94	0·68	0·80
6	L	0·82	0·59	0·82	0·53	0·55	0·34
7	R	0·59	0·53	0·78	0·66	0·86	0·76
8	L	1·01	0·61	1·08	0·68	0·68	0·56

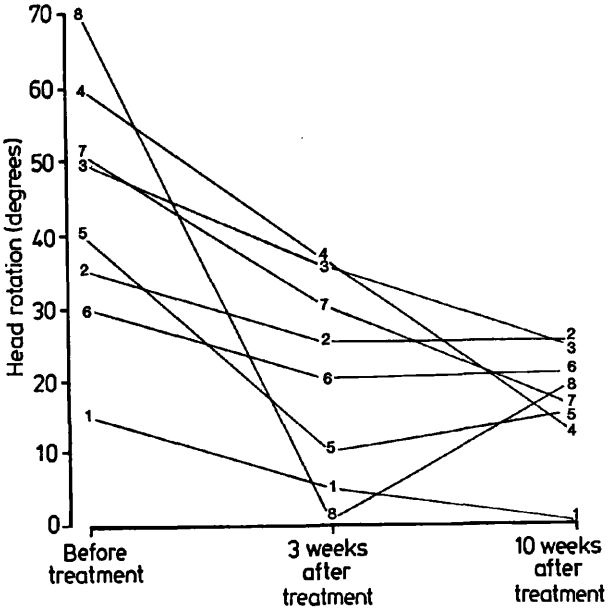

Fig 2 *Head position due to torticollis (horizontal rotation in degrees) before, and 3 and 10 weeks after botulinum toxin treatment. The numbers identify the individual patients as in table 1.*

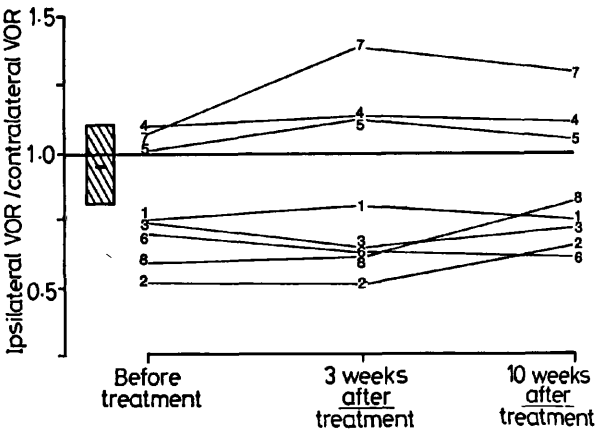

Fig 3 *Symmetry of the VOR during sinusoidal rotation before and 3 and 10 weeks after botulinum toxin, assessed as the ratio between VOR gain ipsilateral to the toricollis and VOR gain contralateral to the torticollis. Cases with a value < 1 have a VOR more active during rotation in the direction opposite to the chin deviation due to the torticollis. The hatched area represents mean (2 SD) of the normal controls after dividing VOR gain to the right by VOR gain to the left. The numbers identify the individual patients as in table 1.*

vestibular nystagmus before and after treatment.

Two further patients were studied during the collection of the above data. One a 34 year old man with pure retrocollis (20°) and the second a 49 year old woman with pure laterocollis (10°). In both normalisation of head position was achieved following botulinum toxin. In neither was there a significant asymmetry of either VOR gain or peak slow phase velocity of induced nystagmus.

Discussion

This study confirms previous reports of abnormal vestibular function in some patients with spasmodic torticollis.[10 11] Four out of the eight patients with predominantly rotational torticollis had a significant asymmetry of the VOR, with the more active nystagmus occurring in the direction opposite to that of chin deviation. There was good agreement between the various parameters measured during testing; a higher VOR gain in one direction during sinusoidal rotation usually was accompanied by a phase lead in the opposite direction. In addition, during the velocity step, there was a greater peak slow component velocity with a longer time constant contralateral to the torticollis. These results provide further quantitative support to our previous clinical review of patients with ST, of whom approximately 70% showed a directional preponderance of vestibular nystagmus (measured as duration of the response) in the direction opposite to the torticollis.[10] Since the direction of nystagmus is by convention in the direction of the quick component, the slow component of the VOR is therefore more

Table 3 *Peak velocity (PV) (°/s) and time constant (TC) (s) of nystagmus during velocity step rotation, before and 3 and 10 weeks after treatment with botulinum toxin*

		Pre-treatment				*3 Weeks*				*10 Weeks*			
		(PV)		*(TC)*		*(PV)*		*(TC)*		*(PV)*		*(TC)*	
Patient No.	*Torticollis*	*R*	*L*	*R*	*L*	*R*	*L*	*R*	*L*	*R*	*L*	*R*	*L*
1	L	33·5	27·5	13·5	12·5	53·5	40·5	14·5	14·0	23·0	16·5	9·8	8·0
2	L	37·5	30·0	20·0	10·5	49·5	39·0	18·0	10·5	45·0	40·0	16·0	10·0
3	L	23·0	16·5	16·5	11·0	45·5	37·5	18·0	12·5	28·0	20·0	20·0	22·5
4	L	29·5	21·5	13·5	10·0	38·0	55·0	17·0	20·0	27·0	38·5	9·5	14·5
5	L	33·0	35·0	20·0	18·0	42·0	37·0	17·5	22·0	32·0	34·0	23·5	23·0
6	L	31·0	25·0	17·5	15·0	35·5	30·5	16·5	12·0	17·0	12·5	19·0	12·5
7	R	23·0	21·5	17·0	16·7	63·5	59·0	12·0	65·0	36·0	32·0	17·5	23·0
8	L	28·0	18·0	20·5	7·5	25·0	22·0	15·0	11·5	20·5	7·5	30·0	27·0

active ipsilateral to the direction of the torticollis (defined by the deviation of the chin). As the slow component of the VOR is generated by the vestibular system, this indicates that in ST there may be a tonic bias of neural activity affecting cervical muscles and vestibulo-ocular balance in the same direction.

Following botulinum toxin injection, improvement in head posture was achieved in all patients. This benefit reached its maximum one week after injection and remained relatively stable until the patients were restudied 10 weeks later. Despite this sustained improvement in head posture, there was no change in the VOR asymmetry evident in either the sinusoidal or step rotational test, suggesting that the abnormal VOR is not secondary to the head posture per se. This conclusion is also supported by the following evidence, (1) in normal subjects, voluntary forced head rotation has no consistent effect on the symmetry of the VOR;[15] however, acute voluntary head rotation is not strictly analogous to chronic involuntary torticollis, (2) all patients were studied with their heads held in an almost neutral position, particularly after botulinum toxin treatment, which considerably facilitated adequate head positioning in the rotating chair, (3) recordings of the cervico-ocular reflex in ST patients suggests that an abnormal input from the neck proprioceptors onto the vestibular nuclei cannot be held responsible for the asymmetric VOR described.[16] We conclude that these asymmetric vestibular responses may be directly related to the underlying disorder producing the abnormal head posture in spasmodic torticollis.

There are at least two ways in which spasmodic torticollis and the vestibular system may relate to each other. First, it has been postulated that the torticollis may be due to hyperactive, disinhibited or perverted vestibulo-collic reflexes (VCR), which normally are responsible in animals for stabilising the head in space. Suggestive evidence for this conclusion was provided by Denny-Brown,[17] who described patients in whom the severity of their torticollis was significantly modulated when turning. However, a difficulty with this line of argument is that the influence of the vestibulo-collic reflex upon head posture diminishes as one ascends the phylogenetic scale. Indeed, the existence of the VCR in man has been questioned.[18] Although recent work indicates that vestibular signals do contribute to some extent to head stability in normal subjects,[19-21] it seems that hyperreactivity of the VCR in patients with torticollis does not occur;[22 23] whilst neck EMG activity during rotation at constant angular acceleration was shown to modulate in a proportion of patients, this was not of a magnitude sufficient to indicate a casual relationship between VCR and torticollis.[22] Similarly, an analysis of head movements evoked by random whole body oscillation has not provided evidence for a major effect of the VCR in these patients.[23] The fact that the mean VOR gain of our patients was essentially equivalent to that of the normal control group also argues against hyperexcitable vestibular responses. Accordingly, it could be suggested that modulation of the torticollis on turning, noted in some patients, may represent the response to a specific motor act rather than to the vestibular stimulus itself.

A second possibility is that the VOR abnormalities in spasmodic torticollis are a consequence of a more generalised disruption of the mechanisms controlling head posture and movement. Such a process would be expected to involve not only vestibular mechanisms, but also the processing of other sensori-motor signals relevant to head position, which might explain the commonly associated finding in spasmodic torticollis of exaggerated responses to somato-sensory cues.[17 24] This probably underlies the mechanism of the "antagonistic gesture" used by many patients to improve their head posture. Further support for a more diffuse disorder is the finding of abnormal brain stem reflexes, for example blink reflexes[25] in some patients with ST. These abnormalities may be explained by malfunction of reticular polysynaptic interneuronal pathways.[26] The intimate relationship between the reticular formation and the vestibular system is well known;[27 28] for example, most eye movement related neurons in the reticular formation are known to send descending branches which influence the cervical musculature coordinating head and eye motion[29] and, reciprocally, descending vestibular signals significantly influence reticulo-spinal pathways.[27] Of particular relevance are animal studies in which selected reticular nuclei have been lesioned to produce experimental torticollis and tonic eye deviation.[30-33] The most notable of these reticular nuclei is the interstitial nucleus of Cajal, which has bi-directional connections both with the vestibular nuclei and the basal ganglia. Unfortunately, detailed vestibular tests of animals with lesion-induced torticollis have not been reported, so that at present the relevance to human disease is not clear. Diseases affecting the basal ganglia in man are known to produce dystonia, and could do so via the projections to structures such as the interstitial nucleus of Cajal.

In conclusion, this study confirms the presence of vestibulo-ocular abnormalities in a considerable proportion of patients with idiopathic spasmodic torticollis. These abnormalities consist of a VOR asymmetry, with the more active slow component being ipsilateral to the direction of the torticollis. This abnormality dose not appear to be secondary to the abnormal head position, since correction of the latter with botulinum toxin does not alter the degree of asymmetry. Current data do not support the thesis

that a disinhibited vestibulo-collic reflex is responsible for torticollis, so we postulate a more widespread central derangement of the various mechanisms controlling head posture.

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The Vestibular System in Abnormal Head Postures and in Spasmodic Torticollis

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The relationship between spasmodic torticollis and the vestibular system has interested neurologists for many years. Any review of the subject should necessarily include a preliminary comment on the mechanisms normally responsible for the control of head position and the effects that derangement of these mechanisms can have on head posture. Impulses controlling the normal upright position of the head arise in the visual, vestibular, and proprioceptive systems. There is general agreement that the relative importance of the vestibular system declines along the phylogenetical scale and that, although vision is less effective in lower animals, it is able to generate righting reactions of the head in cats, dogs, monkeys, and presumably, in humans.

VESTIBULO-COLLIC REFLEX

In animals, stimulation of the labyrinths evokes a vestibulocollic reflex (VCR); this interacts with cervico-collic reflexes, elicited by stretch of the neck receptors, to stabilize head posture and gaze (1). In humans the existence of a VCR is less evident. However, during caloric tests a persistent deviation of the head in the direction of the slow phase of nystagmus can occur and it is possible that in normal subjects VCR responses are not apparent because they may be inhibited by the central nervous system (CNS). This would be in agreement with the fact that patients with extensive central lesions (e.g., advanced multiple sclerosis) sometimes have unusually large head deviations during irrigation.

Outerbridge and Jones (2) noted that, during angular rotation in the dark, movements of the head occurred which were synchronized with the ocular nystagmus. It is possible that these head movements help to achieve gaze stability. In contrast, Barnes and Rance (3) questioned the existence of a VCR, at least with high accelerations, and attributed the resulting head movements to the inertial properties of the head/trunk system. However, recent studies carried out upon labyrinthine defective patients show that they have abnormal head stabilization suggesting the existence of a functioning VCR in normal circumstances (4). In brief, head movements were elicited by sinusoidal rotation of a chair moving in an unpredictable manner in the horizontal plane in patients with absent vestibular function and in normal subjects while they attempted to keep optic fixation on an earth-fixed target. The evoked head displacements are compensatory to the trunk rotation, i.e., in the opposite direction of rotation, and are approximately in phase or lead the stimulus in the normal subjects. In the patients there is either a considerable phase lag or, occasionally, the head movements are largely unrelated to the stimulus. This suggests that in normal subjects an acceleration signal from the vestibular apparatus aids head stability and accounts for the phase lead usu-

ally present. Since similar phase lags to the ones found in the patients occur during head-eye coordinated following movements (5), the smooth pursuit system may be the generator of these compensatory head movements in the absence of vestibular function. The results of Diener et al. (6) on postural stability of normal subjects standing on a movable floor also indicate the existence of specialized mechanisms of head stability which they attribute to VCR activity.

ABNORMAL HEAD POSTURE OF NEURO-OTOLOGICAL ORIGIN

Lesions of the vestibular system can cause abnormal head posture, although this is exceptional in peripheral lesions (7,8). In his paper "On the Rotated or Cerebellar Posture of the Head," Brain (7) presented five cases with peripheral otological lesions in which the head (occiput) tilted and rotated towards the affected side. This attitude can be reproduced experimentally in animals by labyrinthectomy or VIII nerve section (9,10) and has also been described in patients with acoustic tumours (quoted in 7). Finally, in young children a form of paroxysmal torticollis sometimes accompanied by pallor, vomiting, ataxia, and "rocking movement of the eyes" has been considered equivalent to benign paroxysmal vertigo in childhood, although its neuro-otological origin has not been unequivocally established (11,12).

Damage to the brain stem can also produce abnormal head postures and Uemura and Cohen (10) produced severe head tilt in monkeys with lesions in the vestibular nuclei. In humans, extensive brain stem lesions induce head (occiput) deviation to the opposite side (7). Head tilt accompanied by skew deviation of the eyes in the same direction, i.e., lowermost eye to side of tilt, suggests an imbalance in the vestibular system and is probably the unopposed action of the contralateral impulses. The lowermost side of the head indicates the side of the lesion in most cases. However, care should be exercised in the interpretation of asymmetric head posture in the presence of a brain stem lesion since this could result not only from interruption of vestibular pathways but also from damage to supranuclear or nuclear pathways controlling voluntary neck movements or from the adoption by the patient of a head attitude to compensate for oculo-motor defects.

In hemispheric lesions, transient head rotation towards the same side accompanies the gaze palsy seen during the acute phase of stroke or is sometimes compensatory to a hemianopia. The vestibular system is not considered to play a part in this head deviation although it is known that hemispheric lesions can produce considerable asymmetry in the vestibulo-ocular system (13,14).

Finally, basal ganglia disease can severely interfere with mechanisms normally responsible for head posture. Martin (15) described cases of post-encephalitic parkinsonism and Wilson's disease in which the head slowly abandoned the normal upright position and fell flexed forward either spontaneously or on blindfolding the patients. On voluntary command or on restoring visual information, the normal posture was regained. This he took as evidence favoring the existence of a cortical mechanism regulating head position in humans.

VESTIBULAR INVOLVEMENT IN SPASMODIC TORTICOLLIS

In contrast to the defective postures described above, the head attitude seen in dystonic diseases, in particular spasmodic torticollis (ST), is due to a massive involuntary discharge of the postural muscles of the neck (16). The resulting asymmetric head posture and movements, whether rotational about the vertical axis or tilted with respect to gravity, have always directed attention towards a possible link with vestibular re-

flexes. Several cases have been reported in the literature in which ST developed in close association with unilateral lesions of the vestibular system or was modified by surgical procedures on the labyrinth (17–20). Vestibular mechanisms have also been invoked in relation to animal models of dystonia and idiopathic ST (21–24). In Denny-Brown's view (21,22), hemiplegic dystonia, which can affect the neck and produce lateral torticollis, represents a disinhibited state of postural reactions of tonic otolithic origin. On the other hand, he considered that torsion dystonia and related ST with rotatory displacement of the neck was due to distortion of phasic (canal) vestibular reflexes. The former can be modified by tilt with respect to gravity whereas rotation about the longitudinal axis of the body influences the latter. Impressive and coherent as they may be, these observations have not been submitted to quantitative analysis with adequate techniques of vestibular research and require further validation.

RELATIONSHIP BETWEEN ST AND THE VESTIBULAR SYSTEM

In considering the problem of the relationship between ST and the vestibular system we have addressed the following questions: (a.) Are there vestibular abnormalities in idiopathic cases of ST? and (b.) Can a primary vestibular lesion give rise to ST?

To this end, two groups of patients were studied: group I were patients with idiopathic, pure ST (25), and group II included three patients in whom ST developed after unilateral VIII nerve lesions.

Group I

Material and Methods

The clinical material reviewed comprised 35 patients (18 female patients and 17 male patients) without other neurological or vestibular symptoms. The mean age at the time of examination was 46 years (24–70 years) with a mean duration of ST of 4 years (10 weeks–19 years). The direction of the torticollis was specified by the chin position relative to the mid line, i.e., chin to the right is right torticollis.

Clinical neuro-otological evaluation included Romberg and gait tests and eye movement examination with particular reference to nystagmus in primary position or with gaze deviation, positional nystagmus, optokinetic nystagmus, and smooth pursuit. Caloric tests were performed in the presence and absence of visual fixation with the head held in the primary position. Direct current electro-nystagmography (ENG) was obtained. The recordings included traces on primary gaze and on 30° horizontal deviation in the presence of visual fixation and in darkness, optokinetic nystagmus (small or big drum), smooth pursuit, and impulsive rotation to a velocity of $40°sec^{-1}$ in the dark. Not all the patients had all the tests done.

Results

Body balance was largely preserved in ST; Romberg's test was negative in all 35 patients and gait was normal in 31.

A summary of the vestibulo-oculomotor findings and their relation to the side of the neck torsion is presented in Tables 1 and 2. The most frequent and consistent findings were found on rotational and caloric testing especially when fixation was removed. In approximately two-thirds of the cases a directional preponderance (DP) of vestibularly induced nystagmus in the direction opposite that of the torticollis was found.

An interesting correlation was found between the duration of illness and the DP. By dividing the duration of the induced nystagmus in the direction of the torticollis by that in the opposite direction, a DP index was calculated for each patient. In the presence of fixation, there was a positive log-

Table 1. *Frequency of abnormalities (%) in clinical vestibular testing (Group I)*[a]

	Spontaneous nystagmus (N = 35)	Positional nystagmus (N = 35)	OKN DP (N = 35)	SP (N = 15)	Caloric test (fixation) (N = 31)		Caloric test (darkness) (N = 9)	
					DP	CP	DP	CP
Ipsilateral	3	0	6	0	3	13	0	11
Contralateral	11	6	23	0	39	19	78	0
Bilateral	0	0	0	0	0	0	0	0
Normal	86	94	68	100	26	26	11	11

[a] (N) number of patients examined; (Ipsilateral–contralateral) abnormality in the same-opposite direction of torticollis (chin); (OKN) optokinetic nystagmus; (DP) directional preponderance of nystagmus; (CP) canal paresis; and (SP) smooth pursuit.

arithmic correlation between the duration of the illness and DP index ($r = 0.55$; $p < 0.01$). If only those patients who had rotational or caloric DP in the direction opposite to torticollis are considered (17 of the original 31 who had caloric tests done), a better inverse correlation between the duration of the torticollis and the DP is found ($r = 0.75$; $p < 0.01$). On the other hand, in the same group there was no correlation between the DP obtained on caloric testing in the dark or on rotational testing and the duration of the illness. These data indicate that, although the DP in the presence of fixation shows a progressive reduction with time, the DP in the dark remains unchanged.

The DP was not a trivial consequence of the head movement or posture since patients subjected to sinusoidal rotation in darkness with the head completely immobilized in the central position also showed asymmetric vestibulo-ocular reflex (Fig. 1). We have recently investigated the possibility that an abnormal proprioceptive input from the neck muscles is the cause of the nystagmic directional preponderance. This could be mediated by the cervico-ocular reflex, which is minimally active in normal subjects but markedly enhanced in certain pathological conditions (26,27). In a limited number of investigations on the cervico-ocular reflex in four patients with ST, either normal or slightly asymmetric responses were found but without significant increase in gain, indicating that the neck-eye loop is not responsible for the abnormal results of the vestibular tests (Fig. 2).

Group II

Material and Methods

The clinical material consisted of three patients who developed torticollis, indistinguishable from idiopathic ST, following unilateral VIII nerve lesions (Table 3). In addition to a routine neuro-otological evaluation as in group I, these patients had

Table 2. *Electro-nystagmography (ENG) abnormalities (%) in group I*

	Spontaneous nystagmus (N = 24)		OKN DP (N = 18)	SP (N = 13)	Rotat. DP (N = 13)
	Light	Dark			
Ipsilateral	0	12	5	0	23
Contralateral	0	46	39	15	76
Bilateral	4	17	0	0	0
Normal	96	25	55	85	0

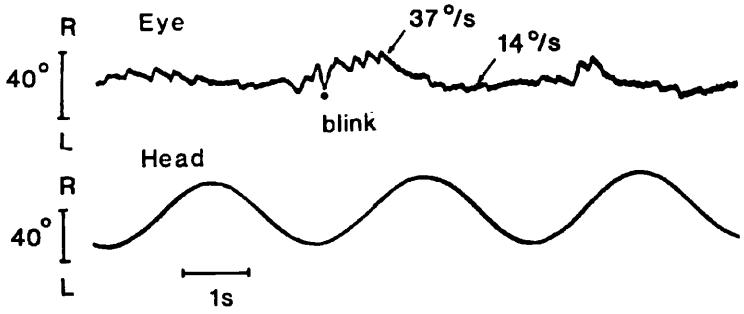

FIG. 1. Vestibulo-ocular reflex (VOR) in a patient with idiopathic ST with chin deviation to the left. The patient was oscillated in the dark with the head rigidly clamped to the rotating chair. Slow phase of the nystagmus elicited during rotation to the right is considerably faster than the one elicited during rotation to the left. ENG recording.

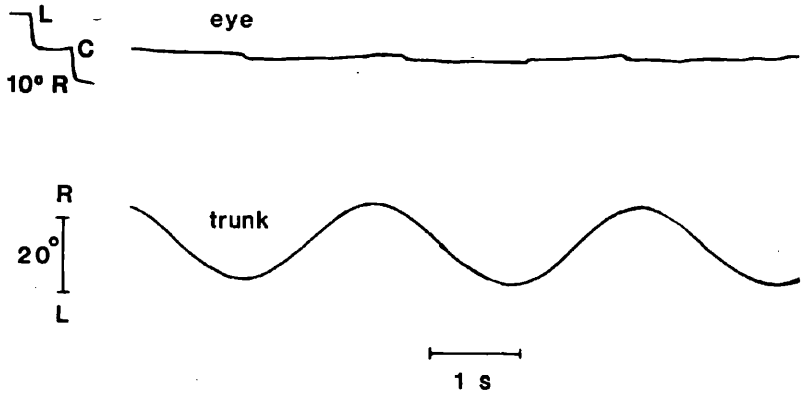

FIG. 2. Cervico-ocular reflex (COR) in the same patient shown in Fig. 1. Eye movements were recorded with the infrared reflection technique and the head was earth-fixed by means of a bite plate. Oscillation of the trunk in the dark evokes negligible eye movements.

surface electromyogram (EMG) recorded from the sternomastoid muscles during vestibular stimulation. The results were compared to control groups of six normal subjects and six patients with idiopathic ST. Quantitative EMG analysis was made with a Fourier analyzer (Solartron 1200) which displayed the power spectra and calculated the energy dissipated by the signal (power in band between 10 and 500 Hz). Quantifiable body tilt with respect to gravity (otolith stimulation) was obtained with a bi-axial gymbal where the patients sat tightly strapped with seat belts. The subjects were tilted in steps of 30° or 45° in the sagittal and coronal planes. Rotation (semicircular canal stimulation) consisted of periods of constant acceleration to right and left at 2

Table 3. *Clinical summary in group II*

	VIII nerve lesion		Torticollis		
	Side	Type	Side	Type	Other neurological features
Case 1	L	acoustic neuroma (removed)	R	tonic	L hemiparesis L VII palsy mild bilateral ataxia
Case 2	R	cerebello-pontine angle arterial loop	L	jerky	R trigeminal neuralgia treated with phenytoin and carbamazepine vertebro-basilar insufficiency
Case 3	R	vestibular nerve section because of suspected Meniere's disease	R	tonic	minimal R pyramidal signs facial tics in childhood

to $3°sec^{-2}$, up to a maximum velocity of $100° sec^{-1}$ in the dark with a revolving chair.

Results

An important clinical point shown in Table 2 is that there was no relationship between the side of the vestibular deficit and that of the torticollis. EMG was normalized in the resting condition (upright, no acceleration); the effects of vestibular stimulation were compared to this basal value. Consistent differences between the three groups tested were found during backwards tilt with the head free. In normal subjects the effect was negligible, but in the patients in group II a marked increase of EMG activity usually occurred. This was related to the degree of tilt and was maximal in the muscle most affected clinically (Fig. 3). In no case did a ST patient in the control group (idiopathic ST) present a comparable enhancement of the EMG in the more affected muscle. On the contrary, two idiopathic ST patients had significant reduction of muscle activity as they were tilted backwards. Eye opening or closure did not influence these responses. Other vestibular stimuli affected neck EMG in ways which did not allow a clear separation between the two groups of patients. These data are to be published soon (28a).

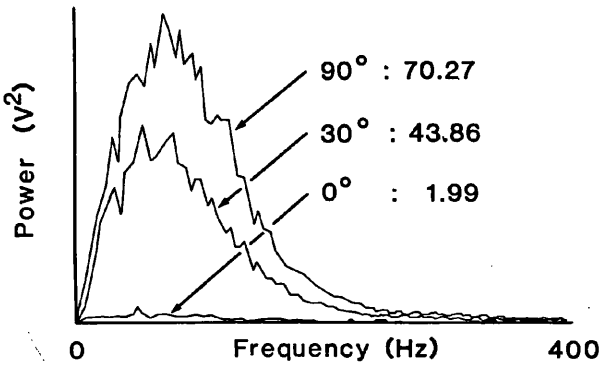

FIG. 3. Electromyogram (EMG) power spectra from the left sternomastoid in a patient with ST to the right, acoustic neuroma removed left side (patient 1, Group II). Recordings were taken at three different angles of backward tilt showing enhancement of EMG discharge as the patient was supinated.

DISCUSSION

The results of the vestibular tests in patients from group I show that neuro-otological abnormalities are common in idiopathic ST. The most consistent finding is the DP of vestibular nystagmus opposite to the direction of the torticollis. Since the DP is specified by the fast phase of the nystagmus, the vestibular-induced slow phase is greater in the opposite direction to the DP and thus in the same direction as the torticollis. The same trend was noted, although not emphasized, by Matthews et al. (28). Such a finding is consistent with the hypothesis that there is tonic imbalance of muscle activity both in the neck and the extra-ocular system which tends to deviate the head and the eyes in the same direction.

That this directional preponderance is not a trivial consequence of the head posture is supported by four observations. First, in normal subjects, forced rotation of the head does not result in a DP of the rotational response (27). Second, if the head is fixed during vestibular stimulation in a patient with torticollis, the DP persists. Third, if the DP were a consequence of the position of the head it might be expected to remain constant or even increase with time; in fact the reverse occurs in spite of the torticollis persisting. Fourth, the cervico-ocular reflex is not responsible for the vestibular bias found. For these reasons we think the DP of induced nystagmus is more fundamentally related to the torticollis.

The much higher incidence of DP or spontaneous nystagmus in the dark than in the light and the relative integrity of the more purely visuo-motor tests, such as smooth pursuit and optokinetic nystagmus, indicate that the vestibular system itself, rather than other ocular-motor sub-systems, is affected. At first sight, since three patients

developed ST following an eighth nerve insult (group II), it might be argued that the torticollis and DP stem from a vestibular end organ, nerve, or nuclear disturbance. Although this is a superficially attractive hypothesis, it is unlikely to be true since the direction of head deviation was not related to the side of the eighth nerve lesion in group II; two patients with nerve section on opposite sides had rotational torticollis towards the right.

It is more likely that the neuro-otological abnormalities are due to a central disturbance of posture which also affects the tonus balance of the vestibulo-ocular system. The vestibular system has complex connections within the brainstem, thalamus, and cortex where interaction with other sensory modalities can occur (29–31). It is possible that the abnormality in ST is a breakdown of these central connections and particularly their interaction with other sensory modalities controlling head and eye position. Such a breakdown would account for the observations that tactile, proprioceptive, and vestibular stimuli can induce striking modifications in some patients' torticollis (21,22,32).

The present investigations, however, indicate that the three patients in group II differ in their postural responses from cases of idiopathic ST and normal subjects. Backwards tilt with the head free in the normal controls did not modify the resting EMG, and in the idiopathic ST group, it did not change the activity significantly or reduce it. On the other hand, in the three patients in group II, neck EMG markedly increased during tilt, especially in the more affected sternomastoid. It is possible that these effects depend upon otolith macular activity. Magnus (9) described static vestibular reflexes in which maximal tonus in the decerebrate preparation occurred in the supine position and minimal tonus while prone. More recent studies (reviewed in 33) have indicated that it is in these positions that macular units reach their maximal and minimal firing frequencies, respectively. Since the utricular macula is approximately horizontal when the animal is in the normal standing position, this position is also the point of optimal sensitivity, i.e., maximal change of discharge frequency per angle of head deviation relative to gravity.

Normally, during backwards tilt the otolith should activate both sternomastoids in order to keep the head upright or aligned with the trunk. Clearly, if one VIII nerve is sectioned tilt backwards will produce a maximal imbalance of macular input to the CNS since one macula will greatly increase its activity while the other is silent. A patient with VIII nerve section and ST may be reasonably compensated in the upright position when the remaining utricle is in its optimal sensitivity position and is discharging at a moderate rate. The situation is different in the supine position. In these circumstances the utricular macula will be at its maximal firing frequency and minimal sensitivity. In the presence of deranged processing of head position information, such as seems to occur in ST, this could well lead to an increased neck EMG discharge. Thus, it is likely that the abnormal tilt-EMG reaction present in group II is due to the unique combination of two different factors: imbalance of peripheral macular signals, and perverted central processing of the information concerning head orientation.

In conclusion, neuro-otological tests in idiopathic cases of ST disclose frequent abnormalities especially in the form of a directional preponderance of vestibular nystagmus in the direction of the occiput. This finding is considered as evidence that in this disease there is a breakdown of the mechanisms responsible for signaling head posture. Three cases of "otogenic" ST presented here do not indicate that a vestibular disorder can be held directly responsible for producing a clinical picture of ST. However, there is some evidence that an VIII nerve lesion modifies and can perhaps aggravate ST by inducing further disruption in

the processing of sensory information about head position. It is likely from this latter finding that interventions on the vestibular system will not succeed in improving the clinical condition of patients with ST.

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OTOLITH STIMULATION EVOKES COMPENSATORY REFLEX EYE MOVEMENTS OF HIGH VELOCITY WHEN LINEAR MOTION OF THE HEAD IS COMBINED WITH CONCURRENT ANGULAR MOTION

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Previous investigations have failed to find significant compensatory eye movements in response to linear motion of the head. However, the fact that visual acuity is essentially preserved during natural head movements, which combine both linear and angular components, is evidence that there must be compensation for linear translation. Hence we examined the lateral eye movements produced by angular oscillation, in the dark, in yaw at 0.5 and 1.5 Hz, 80°/s peak, with the head both centred and positioned 30 cm eccentric from the axis of rotation in order to produce an additional linear acceleration acting tangentially. The combined stimuli produced high velocities of eye movement which were much greater than those produced by angular motion alone. The findings are evidence or a linear-compensatory reflex which is probably otolithic. The dependency of otolithic eye movements on concurrent stimulation of the semicircular canals is a possible explanation of positional nystagmus in neuro-otological disease in which it may be released by a pathological imbalance of canal function.

The preservation of visual acuity during head movements is accomplished by 'compensatory' movements of the eyes. For example, if the head is suddenly turned to the left, the eyes rotate in the orbit, automatically and synchronously, by a similar amount in the opposite direction, so that the head and eye movements cancel each other and the eyes remained fixated on the stationary environment. A powerful compensatory mechanism is the vestibular ocular reflex which is mediated by nervous pathways from the labyrinth of the inner ear to the extraocular muscles. There is extensive evidence [1] that the semicircular canals of the labyrinth, which are stimulated by angular acceleration, provide eye movements compensating for head rotations at high frequencies (0.5 to 5 Hz) and up to angular velocities in excess of 100°/s. In contrast, studies have failed to demonstrate eye movements deriving from the otolith organ of the labyrinth, which is sensitive to linear acceleration, which could adequately compensate for linear head movement [3, 4, 6, 8, 10, 11].

It may be that linear acceleration *alone* does not induce compensatory lateral eye movements for the reason that tilt of the head with respect to the gravity vector,

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which is a powerful stimulus to the otoliths, would provoke inappropriate eye movements. However, acuity is well preserved during normal head movement which combines both linear and angular components so that there must be some linear compensation. Accordingly, we investigated the possibility that compensatory eye movements derived from the otolith can only be detected during certain combinations of linear and angular displacements of the head. The experiment compared the velocities of eye movement produced by purely rotatory head movement with the velocities produced with the head rotating eccentrically from the axis in order to induce a significant tangential linear acceleration.

Subjects were seated upright in a chair mounted on a servo-controlled torque motor with the head, body and legs clamped with pressure pads. Combined lateral motion of both eyes, equivalent to a 'cyclopean' eye, was recorded using calibrated, direct coupled, electrooculography with a bandwidth up to 100 Hz. Angular acceleration of the head in 'yaw' (i.e. left–right rotation about a vertical axis) and the tangential linear component acting through the anatomical site of the labyrinths were recorded with precision accelerometers strapped tightly to the skull. The tachometer of the motor provided an angular velocity signal. The subject's attitude was either seated with head centered on the rotational axis of the motor or with head thrust forwards, eccentrically by approximately 30 cm (Fig. 1). The motion stimuli consisted of unfamiliar abrupt onset sinusoidal oscillation at 0.5 and 1.5 Hz. Actual head accelerations/velocities achieved varied between subjects and depended upon the relationship between body weight and the limited performance of the torque motor. Data were rejected if the distortion of the head acceleration waveforms (expressed as power) exceeded 5%. The range of variations are indicated in Table I. Geometry indicates that compensation for linear head displacement should only be required for near fixation points, so subjects were presented with a target in the form of a visual acuity test chart which was earth-fixed at eye level at a distance of 70 cm for both attitudes. Before each experimental run the subject fixated a central point on the chart, was then put into darkness and oscillation commenced. After 10–20 cycles the light was turned on and the subject fixated the target. During the dark periods the subject tried to maintain imaginary fixation on the target. Measurements were taken of mean and range of peak eye velocity for the first 10 cycles of response and of concurrent mean peak head accelerations and waveform distortion expressed as power. The results of 5 subjects are presented here (3 women and 2 men, age range to 20 to 40, with no history of visual or neuro-otological disease). Three were tested in the eccentric before the centred attitude.

Examples of raw data in Fig. 1 show that a higher peak amplitude of eye movement in the dark is attained with head eccentric than with head centred for comparable levels of angular acceleration. As with all subjects, the increase in amplitude was apparent on the first stimulus cycle and shows little amplitude variability (within $\pm 1°$). All subjects showed elevated peak velocities of eye movement in the eccentric attitude (Fig. 2 and Table I).

Estimates of the additional eye velocity attributable to the linear stimulation were made on the basis of the velocities achieved during head-centred oscillation with

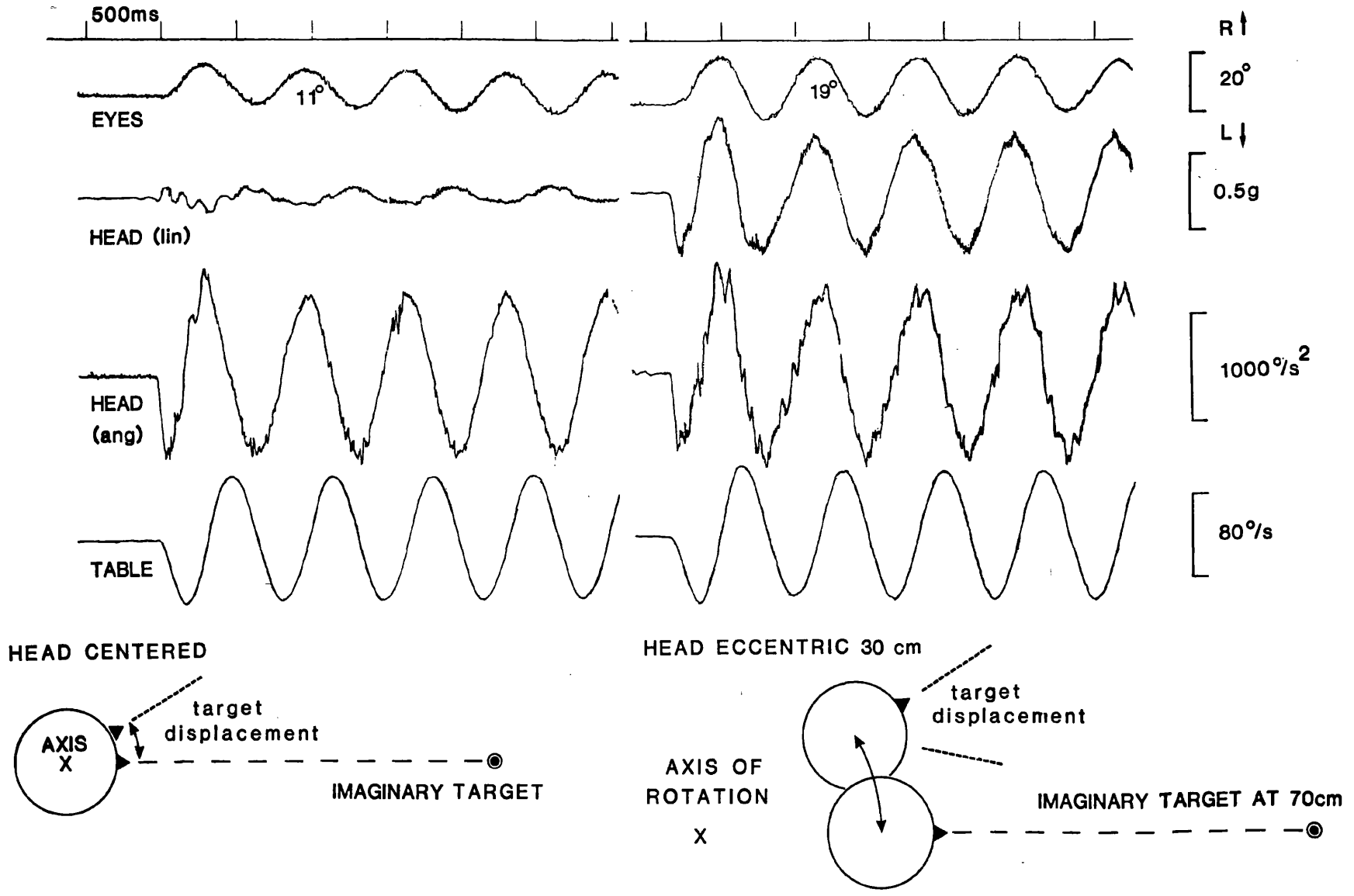

Fig. 1. Raw data records of lateral eye displacement, linear and angular head accelerations and motor tachometer signal relating to rotation in the lateral plane about a vertical axis, taken from a subject seated in the head-centred and head-eccentric positions as indicated in the diagrams below each set of data records. The diagrams indicate the geometrical relationships between target and subject for equal-angle rotation in the head-centred and head-eccentric attitudes. Note that the relative angular displacement of the target is greater in the head eccentric position. The oscillation was performed in the dark with the subject imagining an earth-fixed target at 70 cm distance.

TABLE I

MEAN PEAK VELOCITIES (RANGES IN BRACKETS) OF EYE AND HEAD MOVEMENTS OF 5 SUBJECTS DURING OSCILLATION IN YAW AT 0.5 AND 1.5 Hz WITH HEAD CENTRED AND HEAD ECCENTRIC PERFORMED IN THE LIGHT AND IN THE DARK WHILST IMAGINING A TARGET AT 70 cm DISTANCE

Oscillation frequency	0.5 Hz	1.5 Hz
Angular head velocity achieved (centred or eccentric)	60°/s (56–69)	72°/s (56–81)
Linear head velocity achieved when head was eccentric	31 cm/s (27–35)	42 cm/s (32–51)
Eye velocity/head centred		
in darkness	45°/s (27–60)	73°/s (69–75)
in light	60°/s (52–71)	76°/s (71–85)
Eye velocity/head eccentric		
in darkness	65°/s (60–70)	95°/s (85–104)
in light	92°/s (61–120)	108°/s (85–142)

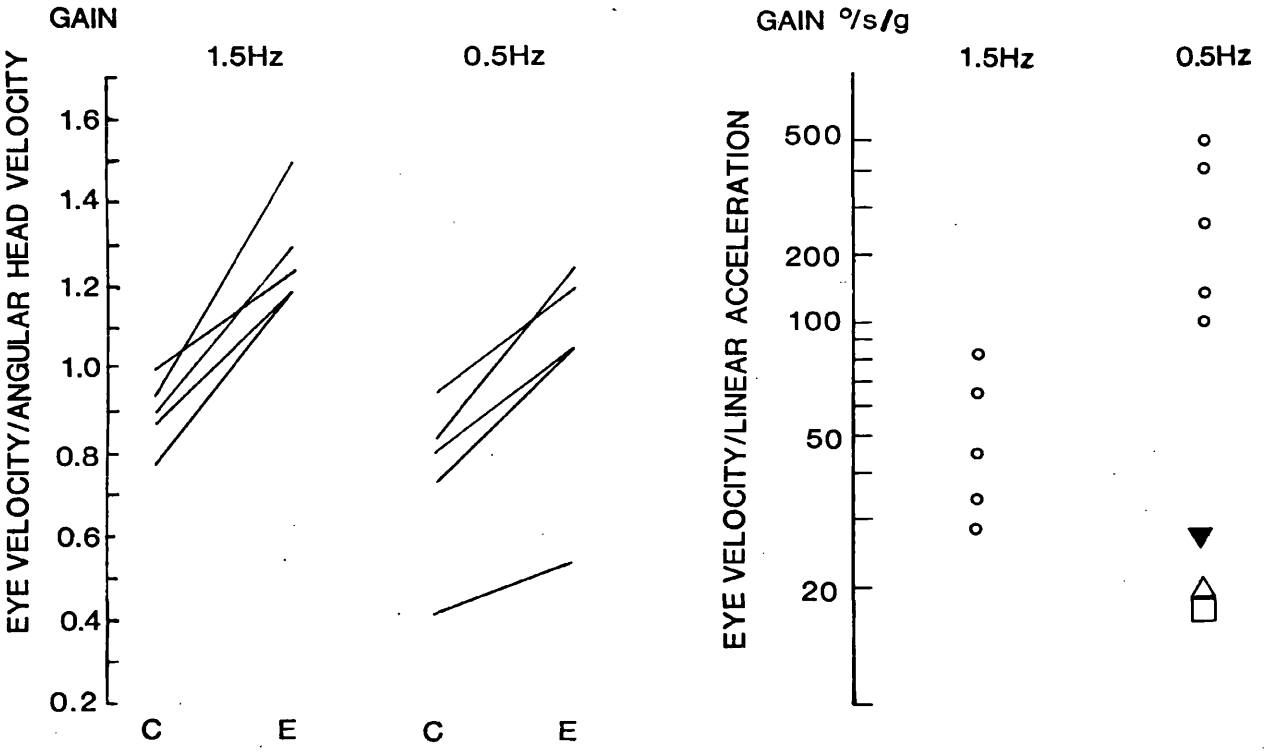

Fig. 2. On the left: gains of peak eye velocity/peak angular head velocity of 5 subjects. Each subject is represented by a line connecting the gain calculated in the head-centred attitude (C) with the gain in the eccentric attitude (E) for imaginary fixation on a target at 70 cm during oscillation at 0.5 and 1.5 Hz. On the right: gains of eye velocity/peak head acceleration, for 5 subjects (open circles) during oscillation in the head eccentric attitude, in the dark. The eye velocities used in computing the gains were estimates of the additional eye velocities attained during eccentric, in comparison with centred oscillation, which resulted from the additional linear stimulus. Previous highest gains were reported by Steer (9) (filled triangle), Correia and Guedry [6] (open triangle) and Niven et al. [8] (square) obtained at frequencies about 0.5–0.8 Hz.

allowance for the small linear component of motion in the head-centred attitude. The additional velocity averaged 22°/s peak at 1.5 Hz with a 0.4 *g* peak linear stimulus and 20°/s peak at 0.5 Hz with a 0.1 *g* peak stimulus. Certain individuals attained additional eye velocities with head eccentric of up to 40°/s in the dark. In comparison the highest eye velocities previously reported [8] were 9°/s (mean of 4 subjects) in response to a ± 0.58 *g* ($g = 9.81$ m/s^2) stimulus. Otolith-ocular reflex gains, which, by convention are computed as °/s per '*g*' are shown in Fig. 2. In the light, eye movement gains, calculated as eye displacement with respect to overall angular displacement of the head from the direction of the target, were within 5% of unity gain. However, the eye movements in the light could derive from smooth pursuit and from optokinetic as well as vestibular mechanisms.

The findings demonstrate that eye movements can be evoked by combining linear with angular oscillation which are significantly higher in velocity than those evoked by angular stimuli alone. The possible explanations of these eye movements are that they are otolithic in origin, or derive from 'voluntary, non-visual enhancement of the vestibular ocular reflex' [2], or from the fact that the canals can be stimulated by linear acceleration [9].

Non-visual enhancement of canal reflexes by imagining the relative target movement would particularly apply to predictable stimuli as employed in the present experiment. However, the enhancement we observed occurred on the first cycle of unexpected movement in the dark and is, hence, unlikely to be attributable to imagination. In addition, the ratios of angular eye velocity/angular head velocity we observed in the head eccentric position in the dark were much higher (see Fig. 2) than the maximum previously reported by Barr et al. [2], whose informed subjects were only capable of pushing gains up to unity for head-centred oscillation.

Despite elegant physiological demonstrations that the canals can be sensitive to linear acceleration, it is difficult to accept that this mode of stimulation can provoke significant eye movements because the strong linear stimulus produced by head tilt does not normally induce lateral eye movements.

We feel that the most likely explanation of the enhanced eye movement velocities observed in the head eccentric attitude is that they are attributable to an 'otolith-ocular reflex' which is 'switched in' by concurrent canal stimulation. The switching occurs because the concurrent canal stimulation indicates a natural mode of head movement which may demand both angular and linear compensatory eye movements. Other evidence that the otolith-ocular reflex works in conjunction with other oculomotor mechanisms rather than alone is the demonstration by Buizza et al. [5] that optokinetic nystagmus is modified by concurrent linear motion of the subject. Since it would seem that the otolith stimulation only evokes high velocity eye movements in combination with other ocular movements, it is possible that the otoliths can affect eye movements by modifying the gain of canal and other oculomotor reflexes.

The theory that otolith-ocular reflexes work in the presence of canal reflexes, provides a nice explanation for positional nystagmus and postional effects on eye movements found in neuro-otological disease [7]. In normal subjects, otolithic influences

on eye movements are released in the presence of asymmetrical canal signals produced naturally by rotation. Some patients may have an asymmetry of canal signals due to a pathological imbalance. As with normals, this releases otolithic influences which become manifest as positional nystagmus when the otoliths are stimulated by head tilting.

Our procedure promises to provide the basis for a dynamic test of otolith function. Further developments of the test will include comparison of responses to random and predictable stimulus waveforms and investigations of effects of target distance on response gain.

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Eye movement responses to combined linear and angular head movement

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Summary. Lateral eye movements evoked by linear head motion were evaluated in human subjects by subtracting the eye movement responses to head-centred angular oscillation in the dark, about a vertical axis, from the responses evoked by similar oscillation with the head displaced 30 cm eccentrically from the axis. The centred oscillation gave a purely angular stimulus whereas the eccentric oscillation gave an additional tangential linear acceleration acting laterally to the head. The stimuli used were relatively unpredictable, enveloped sinewaves at 0.02 to 1.2 Hz, 60°/s peak angular velocity, 0.004 to 0.24 g peak tangential acceleration, and subjects were either given no instructions or were told to imagine fixating on targets at 60 cm or 5 m distance. Eye movements of significantly higher velocity were evoked in the eccentric position, particularly at the higher frequencies and when subjects imagined near targets. The increase in velocity of eye movement was attributed to the linear stimulus and probably derives from stimulation of the otolith organs. The frequency response of the gain (°/s/g) of these movements gave an approximate slope of −1, indicating that the eye velocity bears a constant proportionality to linear head velocity. The findings are in accord with the theoretical prediction that eye movements compensating for linear head motion should only be required for viewing near targets. These otolithic influences on eye movements could either the mediated by a direct "otolith-ocular reflex" which is subservient to viewing conditions or, alternatively, the otolith signals may modify the activity of other oculomotor mechanisms.

Key words: Otoliths – Semi-circular canals – Vestibular ocular reflex – Imaginary target – Gravity

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Introduction

In human subjects, natural head movements consist of both linear and angular displacements. During these movements, the eyes remain reasonably well stabilised on features of the earth-fixed visual surround so that visual acuity is preserved. It is well established that pursuit, optokinetic reflexes and vestibular-ocular reflexes from the semi-circular canals of the labyrinth, which transduce skull rotation, all contribute to provide eye movements which are compensatory for head motion. In contrast, it is not clear whether stimulation of the otoliths, which are responsive to linear acceleration, can also evoke adequate compensatory eye movements.

Theoretical considerations indicate that the otoliths should only give rise to compensatory eye movements under certain conditions. In the first place, since gravity (g) stimulates the otoliths, there must be some indication of which aspects of the otolith signal come from head movement or from the effects of gravity, and compensatory movements should only be evoked in response to actual movement (discussed by Parker et al. 1985). For example, if the head is held tilted sideways g gives a strong lateral stimulus to the otolith but does not provoke a lateral compensatory eye movement which would be quite inappropriate since the head is stationary; in contrast a rapid lateral movement of the head, such as would occur during sparring, also involves a lateral stimulus to the otolith and might require a compensatory eye movement. The second consideration is that linear compensatory eye movements are only needed if the head is displaced with respect to a near target since the visual direction of distant objects is little affected by small linear head displacements.

Previous experimental investigations of otolith effects on eye movements (collated by Barnes 1979; Buizza et al. 1980) in which subjects were tested in

darkness, without instructions, have shown only weak eye movement responses to otolith stimulation. However, in a recent brief report (Gresty and Bronstein 1986), we related the finding that high velocity eye movements, attributable to linear stimulation, can be evoked using combined angular and linear motion and instructing subjects to imagine targets. The use of imaginary targets was an attempt to fulfill the visual requirements for linear compensatory eye movements as discussed earlier. Combined angular and linear motion was used because normal head turning usually involves some linear translation. These considerations would appear to have been neglected in previous studies. This need for an appropriate context for otolithic influences to become manifest is also highlighted by the observation of Buizza and colleagues that linear acceleration during presentation of optokinetic stimuli has striking effects on passive optokinetic slow phase velocity and linear motion perception.

The present study is an investigation of the dynamic characteristics of eye movements evoked by combined linear and angular head motion and their dependence upon the type of instruction issued to subjects.

Methods

Apparatus

Motion stimuli were provided by a "Barany chair" driven by a silent, velocity servo-controlled, torque motor oriented to provide angular motion in the horizontal (lateral) plane about a vertical axis. The chair was equipped with restraining pads for the legs, hips, chest and head so that the subject's body would closely follow the motion of the chair. Subjects were seated on the chair either with their head centred on the axis of rotation to provide predominately angular motion stimuli or with the head displaced forwards 30 cm in order to provide an additional tangential linear acceleration acting laterally through the plane of the utriculus (Fig. 1). The same upright orientation of the head was maintained in the centre and eccentric position with head clamps. Possible deviations from upright were indicated by gravity related offset signals from the linear accelerometer. In addition, the subjects' heads and necks were monitored for possible movements during the trials using an infra red sensitive video camera (Hitachi CCTV 40S) which was mounted in parallel alignment with the subjects' eyes and target and used invisible infra red light (Schott KG-3 5.5 mm filter on tungsten light) for illumination.

Chair motion was transduced by a tachometer. Angular head movement was transduced using a precision angular servo-accelerometer and tangential linear head motion was transduced using a precision piezoresistive linear accelerometer, both strapped to the skull with tape.

The movements of both eyes together as a "cyclopean" eye were recorded using direct coupled electro-oculography with a flat response to 90 Hz. At the beginning of the experiment an initial calibration was made using markers placed at 1 m from the subjects' eyes. Following each experimental condition (i.e. either head centred or head eccentric) a calibration was made by turning the chair through various angular displacements whilst the subject fixated the near and far visual targets. The eyes were then recalibrated on the markers to determine changes in the corneo-retinal potential. The potential did not change significantly through the experimental procedure and so the calibrations derived from chair motion were used as the basis of measurements.

Stimulus parameters

The stimulus parameters of head velocity and eccentricity and angular acceleration used were chosen from prior recordings of natural head movements (Gresty et al. 1986). The shape of the stimulus was chosen to be of short duration, so that subjects would not tire; to be sinusoidal for nice measurement characteristics and similar to the shape of natural head movements; to be relatively unpredictable; to give little transient response so that within the accuracy of our recordings the responses would reflect a pure sinusoidal stimulus and, finally, to give a smooth ride to help in fixing the head and body to the chair. The time course and power spectrum of the stimulus designed to satisfy these requirements is shown in Fig. 2 and consists of 2 cycles of a sinusoid preceeded and followed by a half cycle raised cosine and shaped by a trapezoidal window. The stimuli were constructed of sinusoids of 0.02, 0.1, 0.5 and 1.2 Hz with a peak velocity of 60°/s. With the head eccentric the linear tangential accelerations were respectively 0.004, 0.02, 0.1, and 0.24 g peak at these frequencies. The angular displacement of the visual direction of the target due to the head being eccentric was approximately one half of the angular displacement due to angular chair motion; thus at 0.5 Hz, the displacement of the target was 19° peak with head centred and 28° peak with head eccentric.

Experimental design

The experiment was designed to compare the eye movements evoked when the head was centred on the axis of rotation, in order to provide an angular stimulus to the canals, with those evoked when the head was in an eccentric attitude, which would give an additional linear tangential acceleration stimulus to the otolith organs. Any additional eye movement generated in the eccentric position could possibly be attributed to otolithic influences on eye movement. The combination of angular and linear stimuli was employed in order to reproduce natural head movements during which linear compensatory eye movements might be expected to occur. Because linear compensatory eye movements should only be expected for near targets the experiment was also designed to compare the effects of (imaginary) fixation on near and distant targets. In trials requiring subjects to imagine visual targets they were assisted by being shown real, 3-dimensional objects immediately before each stimulus presentation. The objects consisted of an 8 cm high toy monkey at 60 cm distance from the nasum for the near target and a 30 cm high toy teddy bear at 5 m distance from the nasum for the far target. The distance of the near target was chosen on the basis of the length of the human arm. Subjects were tested in darkness to exclude visually guided eye movements. So that the effect of target distance could be studied, subjects were given instructions to imagine targets in order to induce an appropriate mental set. The following experimental designs were employed:

i) No instructions were given to imagine visual targets. Six naive subjects were tested of whom three were tested in eccentric before centred attitude. In each attitude the 1.2, 0.5 and 0.1 Hz stimuli were each presented twice in overall random order. This was followed by one presentation of the 0.02 Hz stimulus which was reverse because our previous experience indicated that this

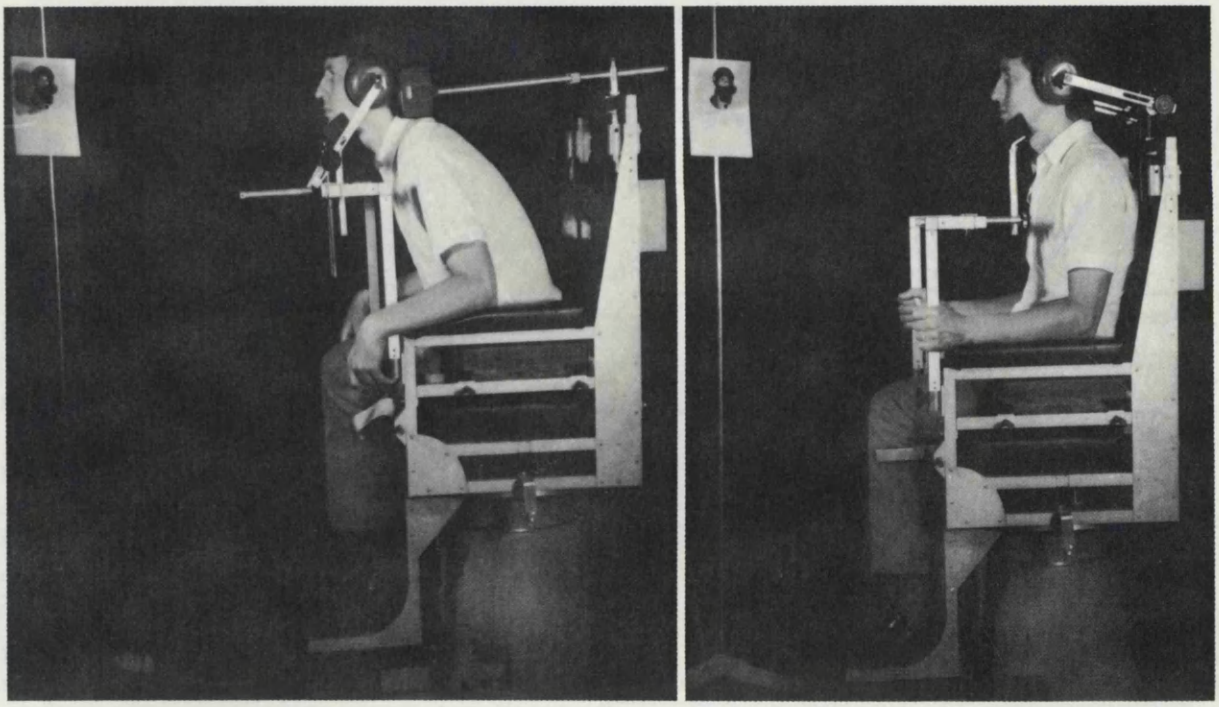

Fig. 1. Photographs of the experimental apparatus showing a subject seated, with head restrained, in the centred and eccentric attitudes. Lateral body clamps and eye and head movement transducers are removed to reveal the subject's posture. The target for visualization is to be found on the left margin of the pictures, directly in front of the subject

stimulus was soporific and adapting and could interfere with subsequent results. The direction of onset of each stimulus (rightwards or leftwards) alternated for each stimulus frequency.

ii) Instructions were given to imagine where the near target was in the darkness and to try to keep the eyes pointed in that direction during the stimulus. They were told that if they felt that the stimulus displacement was too great (0.1 and 0.02 Hz) they should imagine picking up new targets at the same distance. A further six naive subjects were used of whom three were tested in the head centred before the head eccentric attitude. The stimuli were presented as in design (i).

(iii) Stimuli were given only with the head in the eccentric attitude and instructions were given to imagine the near target at 60 cm and a far target at 5 m and to keep the eyes pointed in the target direction during the motion. Six subjects were used of whom three were tested firstly while imagining near targets. Only two randomly ordered presentations of each of the 1.2 and 0.5 Hz stimuli were employed since the results of experiments i and ii suggested that the low frequency stimuli were not suitable for testing linear compensatory eye movements.

The subjects comprised normal healthy adults with an age range of 20 to 55 years and of equal sex ratio. The subjects in experiments i and ii had not experienced this type of experiment previously. Two of the subjects in experiment iii had experienced experiment ii, otherwise the subjects were not exposed to the stimuli before the experimental runs.

Pursuit

In the presence of vision it is possible that smooth pursuit adds to angular compensatory eye movements to provide overall compensation for combined linear and angular head movement (Eckmiller 1982). In order to obtain some impesssion of whether pursuit could provide compensation for the linear motion component of our stimuli, pursuit was assessed in three subjects (from experiment iii). The subjects were seated with head fixed and presented with a red laser target projected onto a tangent screen at a distance of 3 meters. The target moved laterally with the stimulus waveform used to drive the turntable. The stimuli parameters were 0.05 Hz, 10° peak displacement and 1.2 Hz, 4° peak displacement. These were selected to be the same as the target displacement attributable to the linear motion component when the subjects were tested in the head eccentric attitude (see Fig. 2).

Measurements

Measurements were taken only during the central sinusoidal part of the stimulus pattern. For eye movements of each subject, angular velocity was measured by hand using a cursor to follow the tangent to the eye movement curve, and readings were taken of peak velocity for rightwards and leftwards movements for the two stimulus presentations. The resulting 4 values were averaged. The recordings of head acceleration were used to indicate whether there was undue head movement, and whether the head was properly positioned centrally or eccentrically.

Results

All subjects felt that the stimuli gave smooth rides, which would be of importance should they be used

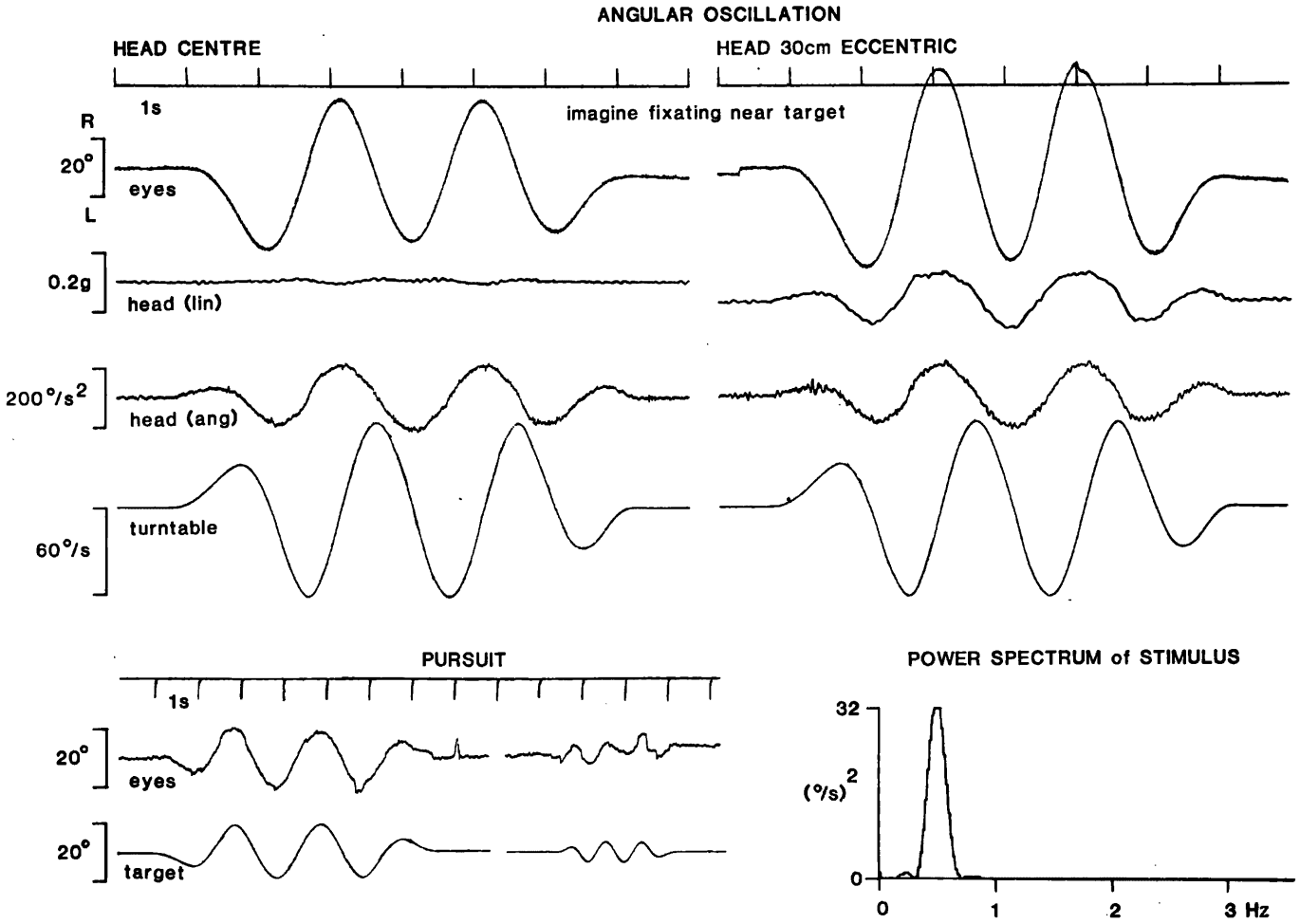

Fig. 2. The upper records are of the raw data of a subject in experiment (ii) showing the eye movement responses to a 0.05 Hz stimulus in the head centred and eccentric positions whilst imagining a target at 60 cm distant from the nasum. The lower right hand graph shows the frequency power spectrum of the stimulus. The lower right hand records illustrate a subject's pursuit in response to a visual target moving with the same waveform as the vestibular stimulus at 0.05 and 1.2 Hz with amplitudes equivalent to the angular target displacement which the linear component of the eccentric oscillation would induce

for clinical testing. The 1.2 Hz stimulus was considered quite unpredictable while the lower frequency stimuli felt predictable to some extent. The eye movement responses to the high frequency stimuli tended to be purely sinuosidal in shape with few saccadic intrusions.

Experiment (i): no instructions

The velocities of eye movement evoked with head eccentric were greater than those evoked with head centre at 0.5 and 1.2 Hz only ($p < 0.05$, paired observations t-tests). The individuals' data for this experiment, expressed as gain of peak eye velocity/peak angular head velocity, are presented in Fig. 3. For both head centred and eccentric a gain characteristic rising with increasing frequency was observed.

Experiment (ii): imagine a near target

The eye movement velocities achieved in the head eccentric position were much higher than those evoked with head centred for all subjects at stimulus frequencies of 1.2 ($p < 0.001$) and 0.5 Hz ($p < 0.01$). There was a trend towards higher gains in the eccentric attitude at the lower frequency stimuli but this did not reach significance at the 5% level. There also appears to be increased gain of eye movement with head centre at 0.5 and 1.2 Hz compared with the gains found with no instruction, although these are not easily comparable because the two experiments employed different subjects and individual variation in vestibular responses is high. Examples of raw data records obtained in this experiment are presented in Fig. 2 and individuals' data expressed as gain of peak angular eye velocity/head velocity are presented in Fig. 3. For both head centred and eccentric, gain

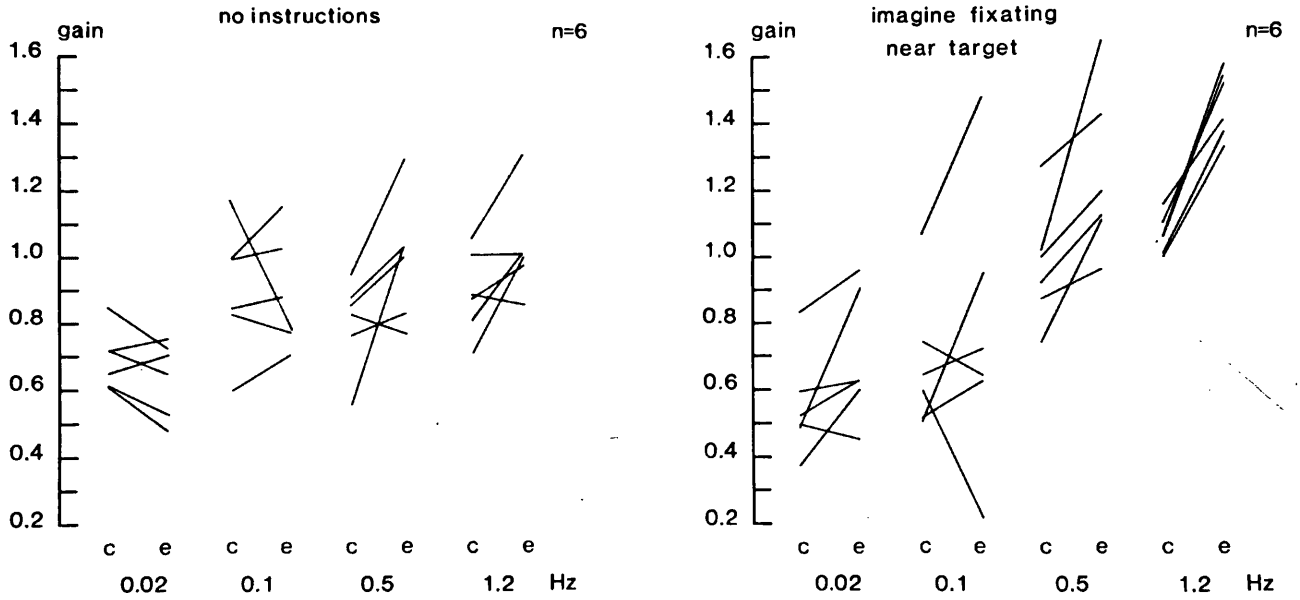

Fig. 3. Plots of each individual's averaged responses in experiments (i) and (ii) indicating the instructions issued. Each bar represents a subject and connects the gain obtained with centred "c" oscillation with the gain obtained with eccentric "e" oscillation. The gains are calculated as (peak eye velocity/peak angular turntable velocity)

rose with increasing frequency. The gain of the eye movement response to the linear component of motion was calculated by doubling the values found by subtracting the gain achieved with head centred from the gain found with the head eccentric (Fig. 4)[1]. The gain of the portion of the eye movements due to the linear motion, calculated as eye-velocity/tangential acceleration and using the means for all subjects, was inversely related to frequency (Fig. 5) with a slope of approximately −1. The actual additional eye velocities achieved with head eccentric ranged from of 21°/s at 1.2 Hz to 9°/s at 0.02 Hz (mean values).

Experiment (iii): imagining near/far targets

The eye velocities evoked by imagining a near target were significantly higher than those produced whilst imagining a far target ($p < 0.01$, both frequencies). Individuals' data, expressed as gain of peak angular eye velocity/head velocity are presented in Fig. 6. The gains attained with the far target were comparable with those found for head centre in experiment ii. The gains found with the near target were comparable with the gains in the eccentric position in experiment (ii).

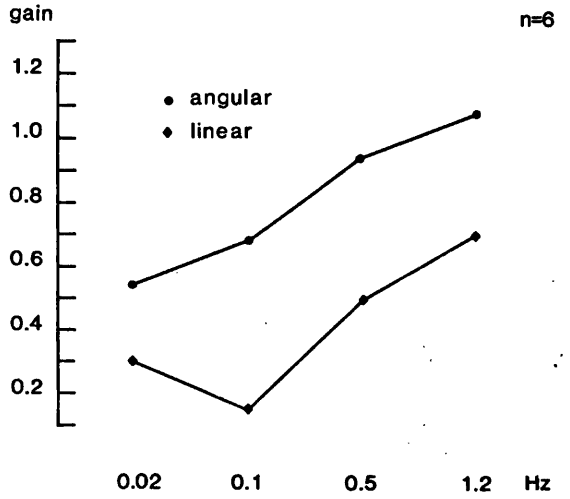

Fig. 4. Gains of the angular and linear component contributions to eye movement responses obtained in experiment ii (imagining near target, head eccentric). The gains are calculated as (eye movement velocity/velocity required for unity gain compensation on a real visual target) and are averaged over all subjects. The linear component was obtained by subtracting gains in the head centred position from those obtained with the head eccentric

Phase

For all experimental conditions a phase advance of eye velocity with respect to head velocity which ranged between 9 and 30° was found for the 0.02 Hz stimulus with no differences between head centre and eccentric. At other frequencies no systematic net phase shift was observed.

1 In the centred position the required gain for target stabilisation is 1. The eccentric position requires 50% more eye movement because of the linear head movement which is a gain of 1.5 if expressed as (eye velocity/angular head velocity). The extra 0.5 angular gain represents unity linear gain

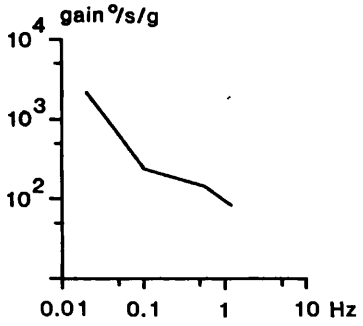

Fig. 5. Gains of the linear component of eye movement responses (obtained by subtraction) obtained in experiment ii (imagining near target head eccentric) calculated as (eye velocity/acceleration in g units) and averaged over all subjects. The slope of the characteristic approximates −1

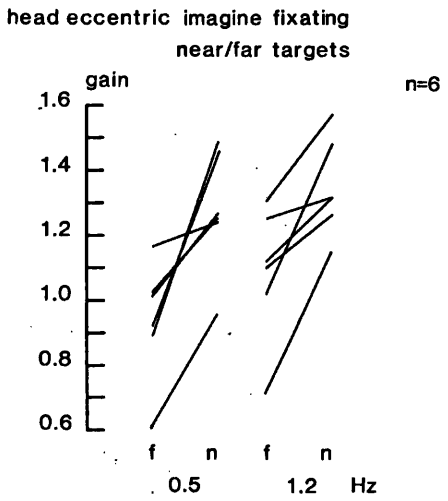

Fig. 6. Plots of each individual's averaged responses in experiment iii (head eccentric oscillation, imagining near and far targets) indicating the instructions issued. The gains are calculated as (peak eye velocity/peak angular turntable velocity). "f" and "n" indicate far and near targets respectively

Pursuit

Examples of responses to the pursuit stimuli are presented in Fig. 2. They show that smooth eye movements can be generated by pursuit which, when added to angular compensatory eye movements, can be of sufficient amplitude to provide compensation for the linear component of head motion for the stimulus parameters used in these experiments.

Discussion

The experimental results show that high frequency angular oscillation of the head combined with a linear acceleration acting laterally can evoke lateral eye movements of significantly higher velocity than those produced by angular oscillation alone. Although this effect is present without instructions it occurs more strongly with the mental set of imagining nearby targets. The importance of the mental set could be expected on the theoretical grounds that a linear compensatory eye movement should only occur for proximal targets.

There are several mechanisms to be considered which could give rise to the higher velocities of eye movement observed in the eccentric position; viz:

i) The interrelated factors of "Voluntary, non-visual enhancement of the VOR" (Barr et al. 1976), prediction of movement and arousal. It is well established that prediction of movement, the general state of arousal (affected by the mere presence or absence of instruction) and the use of instructions to imagine targets can elevate or depress canal reflex gains. However data from the literature (Barr et al. 1976) and our own results show that enhancement of the canal-VOR with head centre can only raise gains to levels of around unity or just above at high frequencies. This cannot explain the enhancement of gains to a mean of 1.4 which we observed with head eccentric at 1.2 Hz.

There is also the possibility that if a subject could predict the changing geometrical relationships in the head eccentric attitude then he may be able to enhance his canal-VOR by some central predictive mechanism. We attempted to remove the element of predictability in these experiments by using fresh naive subjects for each experiment and subjecting them to a novel stimulus which was unpredictable at high frequencies (the subjective experience of the 1.2 Hz stimulus is that one has little conscious awareness of what is happening or directive control of the eyes because the stimulus is so brief). The experimental design ensured that 50% of the naive subjects were exposed to the high frequency eccentric stimulus as their first experience and they showed the same enhancement as more experienced subjects. It is also of note that the more predictable low frequency stimuli did not give rise to greatly increased eye movement velocities in the head eccentric position. These observations suggest that the eye velocity enhancement at high frequencies is not mediated by prediction of the stimulus.

ii) Body attitude, particularly of the neck. There is no evidence that static posture of the spine-neck-head alters the gain of the canal-VOR in normal human subjects. In particular, recent experiments by Bronstein and Hood (1986) have shown that the canal-VOR gain is not systematically affected by extreme static torsion of the neck. Hence it is doubtful that the enhanced gains observed with head eccentric are attributable to the particular pattern of proprioceptive input from the neck.

iii) Otolith signals. At the high frequencies the responses are compensatory for the combined angular and linear motion. Therefore the drive signal for the linear compensatory eye movement must be linearly related to the head motion and work automatically at gain levels which are appropriate to real or imagined target distance. This drive signal most probable arises in the otolith organs of the labyrinth and has fairly immediate access to slow phase oculomotor mechanisms.

The signals which are recorded from the primary afferent fibres of otolith organs (in animals) show a response characteristic of gain (spikes/s/g) rising with frequency for irregular units and a more or less constant gain for regular units. Similarly, previous investigations (compiled by Barnes 1979) of eye movement responses to linear stimuli have tended to show a gain characteristic (°/s/g) which is flat or rises with frequency (peak acceleration held constant). In contrast, (accepting the low frequency values which show a trend) our experiments show a gain (°/s/g) which decreases with frequency (Fig. 5). This latter dynamic characteristic is what one would expect for compensatory eye movements because linear velocity decreases with frequency if a constant level of peak acceleration is maintained. (The higher actual velocities of eye movements seen with higher stimulus frequencies arise as a consequence of the much higher levels of linear acceleration attained.) The slope of -1 represents an integration of the regular signal seen in the primary afferent and indicates that the eye velocity signal is a constant proportion of the linear head velocity signal. This characteristic is also in accord with the frequency response of abducens motorneurone activity during lateral, sinusoidal linear acceleration as determined by Eckmiller in the monkey (1982). The value of the proportionality is presumably a function of the target distance and would be small for more distant targets and increase in value for nearer targets.

The eye movement responses to linear motion must be subject to a complex control process which involves consideration of target distance and changes in the direction of the g vector. This complexity suggests various ways in which the "otolith-oculomotor" signals may be processed. There is the possibility of a direct otolith-oculomotor pathway which is gated, amplified or attenuated by other oculomotor mechanisms so that it becomes fully effective when there is a requirement for visual stabilisation on nearby objects. Alternatively, the otolith signals may be fed to other mechanisms and used indirectly, for example, they may be used to bring about gain changes in canal reflexes or used as input to the mechanisms of smooth pursuit. We feel that it is unlikely that the otolith influences are mediated by the pursuit mechanism for two reasons. Firstly, the gain characteristic rising with frequency for the linear compensatory eye movements is comparable with that of canal reflexes and unlike that of smooth pursuit in the light. Secondly, the low frequency stimuli, which would be easier to pursue because they were more predictable and well within the dynamic range of smooth pursuit, gave low eye velocities. This is not what would be expected if pursuit was enhancing the VOR gain. As a consequence, if the otoliths influence eye movements indirectly, it is likely to be via their effect on the gain of canal reflexes.

In every day life situations it is difficult to assess whether compensation for linear head movement is preferentially derived from otolith signals or is due to smooth pursuit. The observations of Lisberger et al. (1981), together with our own data have demonstrated smooth pursuit eye movements of significant velocity in the frequency range of the stimuli used in these experiments and, under most everyday circumstances, may provide the predominant compensation required for visual stabilisation during linear head movement (Eckmiller 1982). However, smooth pursuit responds poorly to unpredictable target motion at frequencies above circa 1.5 Hz, partly because of the delay during visual processing. If otolith signals access the oculomotor system at a brainstem level the processing delay is much shorter, which suggests that otolithic influences may be of significance for high frequency, unpredictable head movements.

In the present experiment employing combined linear and angular head motion, the velocities of eye movements attributable to the linear component are much higher than those previously reported for linear stimuli alone. We do not know if linear motion alone is also able to produce high velocities of eye movements if subjects are given the appropriate instructions. Pure linear acceleratory stimuli can be equivocal in giving rise to sensations of movement and/or tilt with respect to gravity (Graybiel 1974; Guedry 1974). In addition, head movement is more accurately interpreted when there is combined angular and linear motion which is the case during everyday locomotion (Guedry 1974). For these reasons pure linear motion may not be suitable for investigating linear compensatory eye movements.

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Testing the vestibular-ocular reflexes: abnormalities of the otolith contribution in patients with neuro-otological disease

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SUMMARY Conventional vestibular rotation testing with the head centred on the axis stimulates the semicircular canals evoking compensatory eye movements. If the head is placed forwards of the axis in an eccentric position the otoliths are also stimulated by a tangential linear acceleration acting laterally to the skull. In normal subjects the additional otolithic stimulus evokes compensatory eye movements with a higher gain than with head centred, particularly for high frequency (> 0·1 Hz) stimuli. The responses with head centred and eccentric in various patients with known/suspected neuro-otological abnormalities have been compared. Patients with vestibular neurinectomies who have asymmetrical head centred responses showed greater asymmetry with head eccentric at higher stimulus frequencies. Some patients with cerebellar lesions showed abnormally enhanced or depressed and asymmetrical responses with head eccentric in comparison with head centred responses, which could be normal. The enhancing effects could be specific to low frequency stimuli. All patients who showed abnormal responses with head eccentric also had positional nystagmus provoked by the gravity acceleration vector when the head was tilted laterally. The direction of the positional nystagmus with respect to the gravity vector was not necessarily the same as the direction of the effect on eye movements of lateral acceleration during eccentric oscillation. Patients with benign paroxysmal vertigo or chronic linear vertigo in whom otolithic abnormalities are suspected were not found to have abnormal responses with head eccentric. We conclude that this method of testing may be useful in elucidating pathophysiology but is not a decisive clinical test for the presence of disordered otolith function.

The otolith organs of the labyrinth transduce linear accelerations of the skull. Their physiology remains obscure for several reasons. There is the initial technical difficulty of constructing linear acceleration devices suitable for delivering test stimuli. Further problems arise because, according to Relativity Theory, gravity and acceleration are identical which means that the otolith organ itself cannot distinguish between reorientations of the gravity vector caused by head tilt and imposed linear accelerations. The ambiguous, otolithic afferent signal must be interpreted with respect to accompanying canal, visual and proprioceptive input in order to make a correct assessment of head motion and tilt and thereby to initiate appropriate reflexes and actions. This means that appropriate investigations of otolith function must be concerned with the complex interactions of the various senses and sensory motor systems.[1]

In spite of these problems, there is a need for tests of normal and abnormal otolith function, for it is clear that certain patients with neuro-otological disease show abnormalities which are presumably otolithic. Examples of symptomatic abnormalities of otolith function are misjudgement of true earth vertical or false sensations of lateropulsion and tilt.[2] Accepted clinical signs suggestive of otolithic abnormalities are tilted body posture (particularly of the

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head),[3 4] positional nystagmus of the central type*[5 6] and comitant torsion and skew deviation of the eyes.[4 7 8]

One way of investigating otolith function in humans is to study "otolith-ocular compensatory" eye movements. During fixation on a stationary target, the head may be moved either actively or passively and the line of sight automatically remains more or less aligned with the target direction so that vision is preserved. The mechanisms responsible for this visual stabilisation are the "compensatory" or "dolls" eye movements. Compensatory eye movements derive (1) from the semicircular canals of the labyrinth which provide a vestibular ocular reflex (canal-VOR) which compensates for angular head displacements; (2) from the smooth pursuit reflex which effects tracking of apparent target motion; (3) from the optokinetic reflex which stabilises the eyes with respect to large areas of the visual world and (4) possibly, from stimulation of the otoliths which could produce eye movements compensating for linear displacements of the skull. Previous investigators have sought to evoke eye movements by stimulating the otoliths with low frequency (0·5 Hz and less) linear oscillation of the head, or by rotating the head about a tilted axis so that they are stimulated by the changing direction of the gravity vector.[9] This form of otolith stimulation does not appear to evoke eye movements of significant velocity (of the order of 7°/s maximum for 1*g* stimulus). In contrast, we have demonstrated that high velocity otolith-related eye movements can be evoked by combined linear and angular motion.[10 11] The technique is to subtract the eye movement caused by angular motion alone from the eye movement caused by the angular motion combined with a linear motion. The difference between the two is an amount of eye movement attributable to the linear component of motion, and thus probably due to otolith stimulation. It is possible that the combined linear and angular head movement, which is the common occurrence during natural head movement, provides a contextual combination of canal and otolith signals which can be appropriately interpreted (as discussed above).

*Note on "positional nystagmus": definitions and mechanisms.

Positional nystagmus is a nystagmus which is provoked or modulated in slow phase velocity by static tilt of the head with respect to the gravity vector and occurs with disease of the central nervous system, the vestibular end organ or nerve. In "ageotropic positional nystagmus" the nystagmus fast phase or "beats" are in the opposite direction to the earth; the slow phase is towards the earth. In "geotropic positional nystagmus", the nystagmus fast phase or "beats" are in the direction of the earth; the slow phase is away from the earth. If the head is tilted sideways to horizontal with one ear down, gravity effects a stimulus to the otoliths which is the same as an acceleration upwards in the direction of the upper ear. If the head were actually moving then one might expect a compensatory slow phase eye movement to be made in the downwards direction; for example, head accelerating upwards to the left ear, eyes compensate by moving rightwards producing ageotropic nystagmus. Normal subjects do not have a reflex eye movement when tilted for the brain correctly interprets that the head is tilted and not accelerating. Ageotropic nystagmus in patients may be evidence of the "release" of some form of compensatory eye movement. Geotropic nystagmus is in the wrong direction to be compensatory.

The purpose of the present study was to assess the applicability of the technique in evaluating vestibular-oculomotor disorders in a sample of patients with neuro-otological disease.

Methods

The experimental technique has been described extensively elsewhere.[10 11] In brief, the patient is seated upright, with head and body restraints, on a turntable which rotates about a vertical axis. The head may be centred on the axis to produce purely angular acceleratory stimuli which activate the semicircular canals and evoke lateral eye movements. Alternatively, the head may be offset eccentrically from the axis, in this case thrust 30 cm forwards (fig 1). Oscillation in the eccentric position produces the same angular stimulation and, in addition, involves a linear tangential acceleration vector which acts laterally on the skull to stimulate the otoliths. The motion stimuli used are relatively unpredictable "enveloped sinewaves" (fig 2) with constant peak angular velocity of 60°/s and centred on frequencies of 0·02, 0·1, 0·5 and 1·2 Hz. The linear acceleratory stimuli at these frequencies are 0·004, 0·02, 0·1 and 0·24 *g* respectively (*g* is the gravitational unit; $1\,g = 9{\cdot}81\ m/s^2$). Each stimulus is delivered twice, one commencing with rightwards rotation, the other with leftwards rotation. Overall stimulus presentation is randomised except for the lowest frequency stimulus which is presented last because it is soporific. Eye movements are recorded using direct-coupled electro-oculography. Testing is performed in darkness and the subject may be given no instructions other than encouragement to be alert or instructed to actively imagine fixating on earth fixed targets during the test runs. Instructions for imaginary fixation may considerably enhance vestibular responses; however, they are not used for patient testing be-

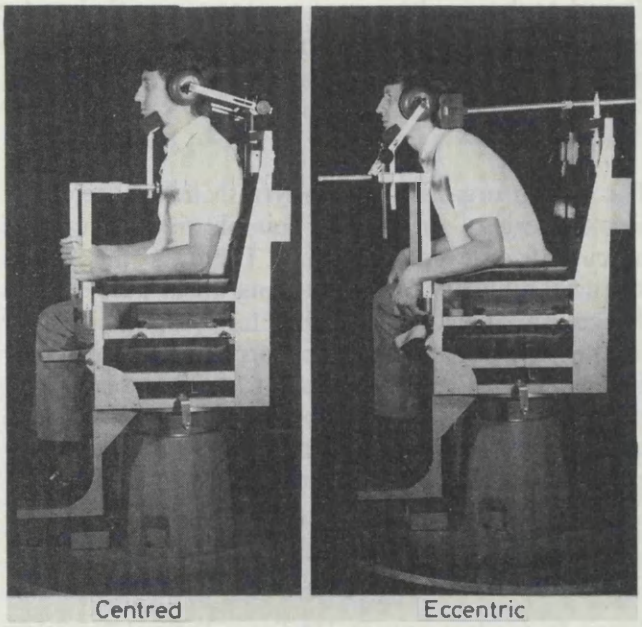

Fig 1 *Experimental apparatus showing a subject seated in the conventional head centred position for rotational testing and seated with head 30 cm eccentric.*

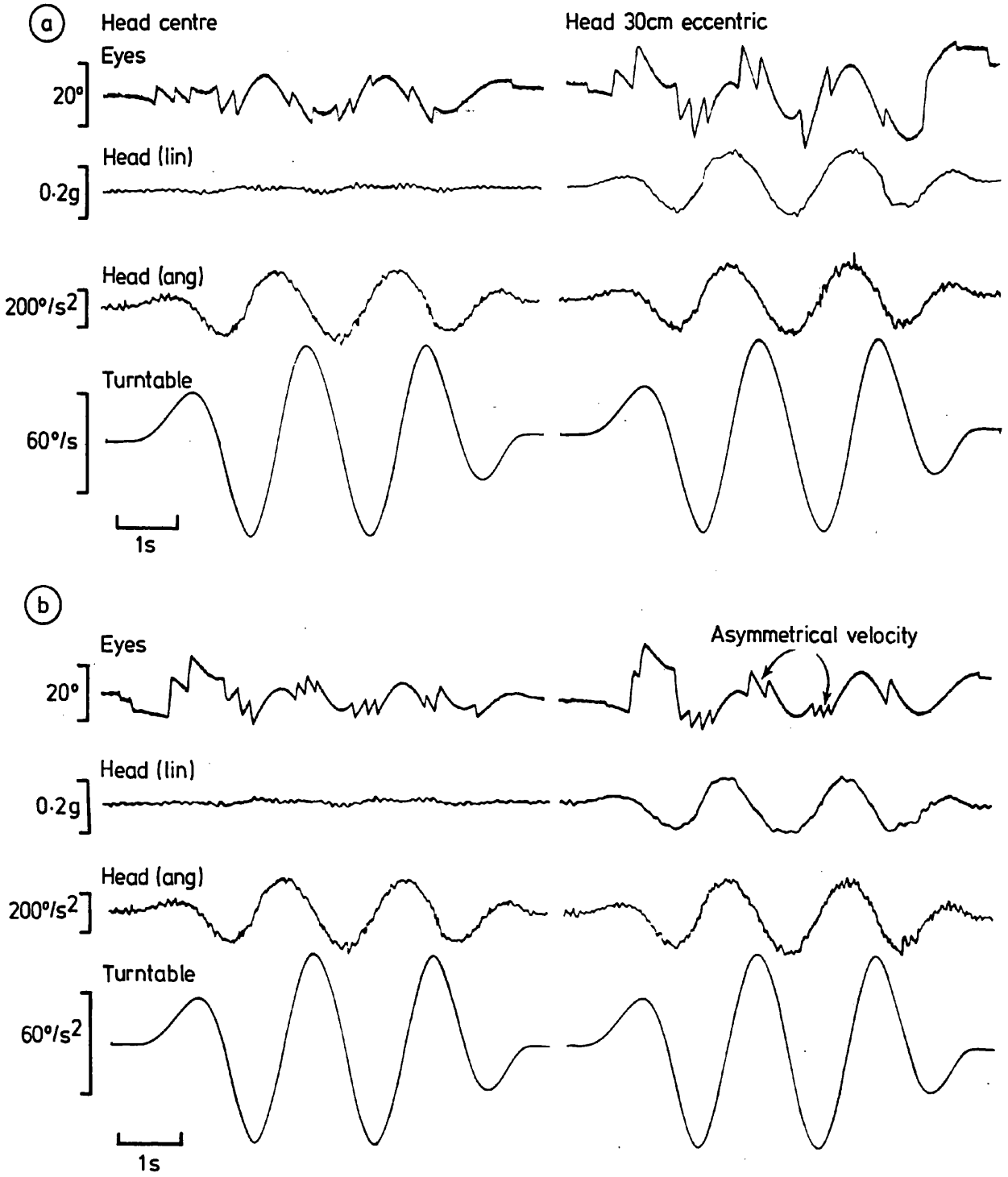

Fig 2(a) *Raw data records of a normal subject's responses to centred and eccentric oscillation at 0·5 Hz.* (b) *Raw data records of the responses of patient B11526. Head (lin): tangential linear acceleration acting laterally on the head. Head (ang) angular acceleration of the head.*

cause we have encountered difficulties of comprehension in some patients.

In order to characterise the data of the patients presented in this study, measurements were taken of peak rightwards and leftwards slow phase eye velocity attained during the central, undistorted parts of the stimulus waveform. Because it was found that patients may show considerable rightwards/leftwards asymmetry, the measurements were separately averaged for rightwards and leftwards movements and expressed as velocity ratios (ie mean peak eye velocity rightwards/peak turntable velocity leftwards). Normal subjects showed negligible asymmetries so rightwards

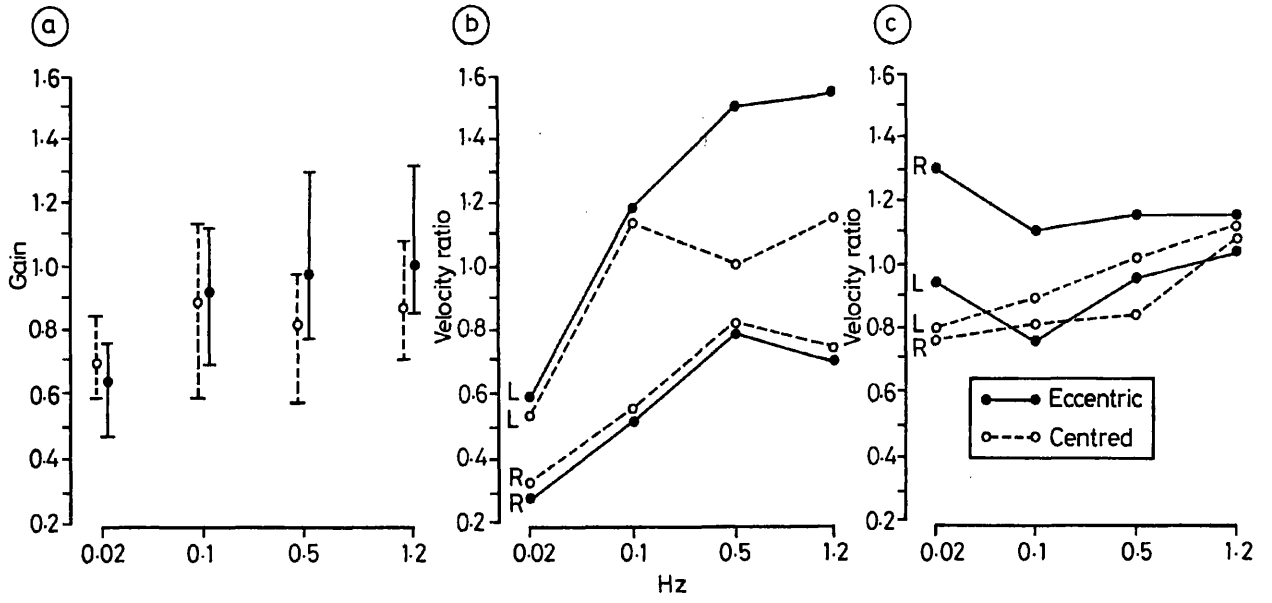

Fig 3(a) *Normal data of gain against frequency showing means and ranges. Rightwards and leftwards responses grouped together. In the present discussion, patients responses are only identified as abnormal if they lie outside the normal range.* (b) *Patient B45846. Velocity ratios of peak eye velocity rightwards and leftwards/peak turntable velocity leftwards and rightwards respectively.* (c) *Patient B11526. Velocity ratios of peak eye velocity rightwards and leftwards/peak turntable velocity leftwards and rightwards respectively. R = rightwards slow phase eye movements in response to leftwards rotation. L = leftwards slow phase eye movements in response to rightwards rotation.*

and leftwards movements were averaged together and expressed as gain (mean peak eye velocity/turntable velocity). Phase of response was measured as the relationship between the turning point of the slow phase eye movement with respect to zero turntable velocity. Phase measurements for 1·2 Hz condition may be up to 5° in error. Phase estimates are more reliable for lower stimulus frequencies.

Results

Normal data have been presented in detail elsewhere.[11] Normal subjects showed a significant increase in gain of slow phase eye movements in the eccentric position as compared with the head centred position at frequencies of 0·5 and 1·2 Hz. There was also a trend towards elevation of gain at 0·1 Hz. For both centred and eccentric attitudes, the peak velocity of slow phase eye movement was in phase with the peak velocity of the stimulus at 0·1 Hz and above. At 0·02 Hz the phase of the response was 20° to 30° in advance of the stimulus. An example of normal raw data records is presented in fig 2a. Gain data for the normal subjects is presented in fig 3a. We attribute the elevation of gain in the head eccentric attitude to an otolithic contribution to the vestibular ocular reflex. However, it is not clear how the otolith signal controls eye movements. One possibility is of a direct otolith-ocular reflex similar to canal reflexes. Alternatively the otolith signal may be used to adjust the gain control of canal reflexes.[11]

Certain patients have been selected to illustrate test results because they exhibited various combinations of enhanced/decreased responses with head eccentric and geotropic/ageotropic positional nystagmus. In addition, most had normal canal-vestibular-ocular reflexes on conventional, head centred rotation tests.
(1) *Absence of positional nystagmus. Failure to enhance the VOR with lateral acceleration.* Case example: B52832. Female aged 59 years who had suffered three episodes of vertigo over the previous two years. She was found to have bidirectional gaze paretic and rebound nystagmus in the lateral plane and almost absent smooth pursuit. Plantars were extensor. Magnetic resonance imaging showed appearances compatible with demyelination. Conventional rotational (with head centred) and caloric tests showed symmetrical hypoactive vestibular responses. There was a complete failure to evoke enhanced responses when tested with head eccentric.
(2) *Positional nystagmus beating ageotropically with enhancement of the VOR by lateral acceleration (eye movement provoked by gravity in the same direction as eye movement provoked by acceleration).* Case example: B45846. Female aged 45 years who was examined one year after the removal of a left sided acoustic neuroma. The significant vestibular findings were a total left sided canal paresis with spontaneous, right beating dark nystagmus which enhanced on positioning with the left ear down. On head centred oscil-

lation the slow phase eye movements evoked by head leftwards stimuli were at the low limit of normal range at all frequencies. Responses to rightwards stimuli were all of consistently higher gain and within normal limits. With head eccentric the responses to rightwards stimuli were elevated beyond the normal range, at high frequencies. Responses to leftwards stimuli were not different from the responses to head centred leftwards stimuli (fig 3b). Response phase data for leftwards (L) and rightwards (R) slow phase eye movements were as follows:

	1·2 Hz	0·5 Hz	0·1 Hz	0·02 Hz
Head centre	0°R, 11°L	2°R, 10°L	3°R, 8°L	16°R, 27°L
Head eccentric	0°R, 13°L	0°R, 15°L	0°R, 16°L	15°R, 36°L

Similar results were given by a second, similar patient following removal of an acoustic neuroma.

(3) *Positional nystagmus beating ageotropically with reduction of VOR by lateral acceleration* (the eye movement produced by gravity is in the opposite direction to the acceleration vector; the eye movement produced by lateral acceleration is in the same direction as the vector). We have not yet found a patient showing this pattern.

(4) *Positional nystagmus beating geotropically with reduction of the VOR by lateral acceleration in the head eccentric attitude* (the eye movements provoked by gravity and lateral acceleration are both in the same direction as the acceleration vector).

Case example: A38668. Female aged 64 years who, in 1968, was shown to have a cystic lesion extending from the level of C1 to the floor of the 4th ventricle which was successfully treated with radiotherapy. In summer 1985 there was a recurrence of symptoms. When examined in April 1986 she had diplopia due to a left convergent strabismus. Abduction was restricted bilaterally, but saccades in all directions were of near normal velocity. There was gaze paretic nystagmus in all directions, with bidirectional rebound nystagmus. Pursuit was absent and there was "slow build up" optokinetic nystagmus. Vestibular ocular reflexes were hypoactive. Ocular counterrolling was intact. There was positional nystagmus beating leftwards when lying horizontally with the left ear down and beating rightwards with the right ear down. Magnetic resonance imaging demonstrated a low density mass, probably an ependymoma, which lay to the left of the midline, extending from the upper cervical cord to the floor of the IVth ventricle and invading the low brainstem and posterior vermis of the cerebellum. The gains of the slow phase eye movements evoked by head oscillation in the eccentric position were uniformly reduced by 18% at 0·1 and 1·2 Hz and by 30% at 0·5 Hz. The slow phase eye movements provoked by the gravity acceleration vector in this patient were in the same direction as the slow phase eye movements provoked by the tangential acceleration vector during head eccentric oscillation.

(5) *Positional nystagmus beating geotropically with enhancement of the VOR by lateral acceleration* (the eye movement provoked by gravity is in the same direction as the acceleration vector while the eye movement provoked by lateral acceleration is in the opposite direction).

Case example: B11526. Male aged 50 years who, in 1980, developed headaches, neck pain, unsteadiness and rotatory vertigo with vomiting. A CT scan demonstrated a posterior fossa mass. Craniotomy revealed a tumour which was seen protruding between the two cerebellar hemispheres in the midline, which biopsy showed to be a low grade astrocytoma. The tumour and lining of the cystic cavity were removed. In July 1986 the patient was reviewed. He complained only of "height vertigo" and dizziness on neck extension. On examination, pursuit was mildly hypometric, there was right beating positional nystagmus evoked with the right ear down, and a left beating positional nystagmus evoked with the left ear down (fig 4). There was some weakness of the shoulder girdle. A highresolution CT scan at this time (fig 5) showed a large CSF density space between the cerebellar hemispheres with no evidence of recurrence of the tumour. Slow phase eye movement responded to oscillation with head centred were normal. With head eccentric the gain of the slow phase eye movements was significantly increased at low frequencies of stimuli for head leftwards stimulation (figs 2b, 3c). The slow phase eye movements provoked by the gravity acceleration vector in this patient were in the opposite direction to the slow phase eye movements provoked by the tangential acceleration vector during head eccentric oscillation. Response phase data for leftwards (L) and rightwards (R) slow phase eye movements were as follows:

	1·2 Hz	0·5 Hz	0·1 Hz	0·02 Hz
Head centre	6°R, 0°L	4°R, 0°L	5°R, 6°L	9°R, 9°L
Head eccentric	−4°R, 9°L	5°R, 5°L	5°R, 2°L	17°R, 6°L

In addition to the above, normal responses have been found in a variety of patients whom one might have expected, from their symptoms or signs, to have otolithic disorders. For example: (1) *"Benign paroxysmal vertigo"* attributed to degeneration of the otolith organ. Two patients with classical paroxysmal vertigo with torsional nystagmus provoked by positioning failed to show abnormal responses with head eccentric rotation.

(2) *Cerebellar-pontine angle lesion* from presumed ectatic basilar artery loop. A normal pattern of responses was found in this patient who had deafness and complete canal paresis on the left side. Perhaps of significance, this patient did not have positional or spontaneous nystagmus which may indicate that she compensated well for the loss of vestibular function.

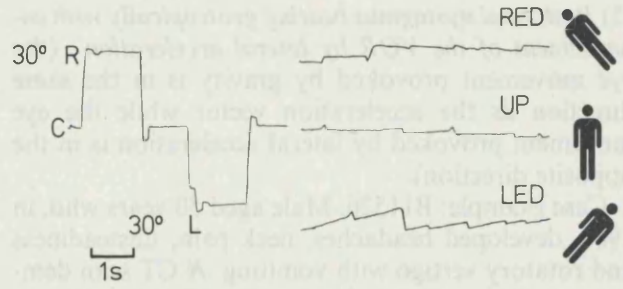

Fig 4 *Patient B11526. Positional dark nystagmus with lateral tilts of 45° left and right.*

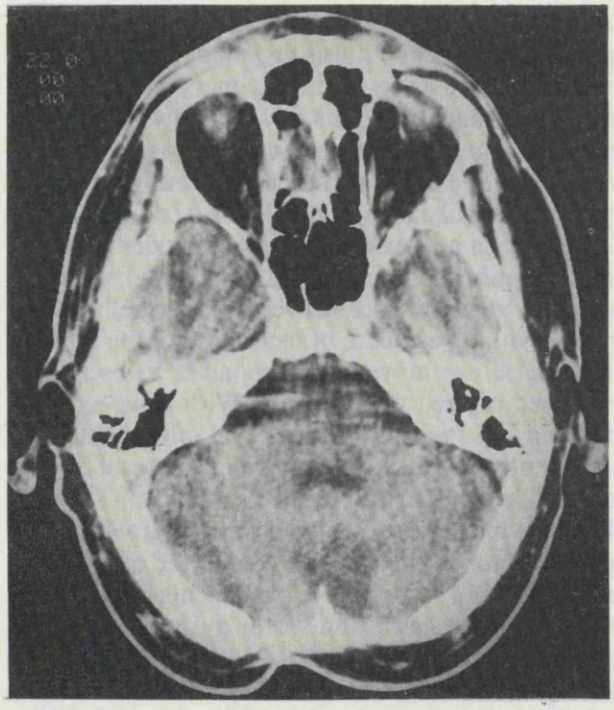

Fig 5 *Patient B11526. High resolution CT scan showing a large CSF density space between the cerebellar hemispheres.*

(3) *Chronic vertigo of unknown aetiology.* Normal responses were identified in a patient with a four year history of illusory sensations of linear motion of herself and the ground, "mal de debarquement". The linear nature of the illusory movement made one suspect a disorder of otolith function.

Discussion

The findings show that rotational vestibular testing performed with head eccentric oscillation can reveal abnormalities of eye movement responses in patients who are normal on conventional head centred rotational testing (for example, type v, patient B11526). Therefore, this method of investigating vestibular ocular reflexes has the potential of adding significantly to the understanding of a patient's neuro-otological status. However, to date, we have only detected abnormalities in the head eccentric responses in patients in whom there is also positional nystagmus. This suggests that the technique may be more of a research tool than a decisive clinical investigation for it constitutes an over-elaborate procedure in comparison with the simple task of identifying positional nystagmus!

The significant findings in our patients which relate to current concepts of otolith function are the enhanced gains (velocity ratios) associated specifically with high frequency stimuli (2, patient B45846) or low frequency stimuli (5, patient B11526).

(a) *High frequency abnormalities* In normals, high velocities of eye movement attributable to otolith stimulation occur particularly with high frequency stimuli. The patient who had had an acoustic neuroma removed showed higher gains for both centred and eccentric stimuli for movement in the direction of the intact side at the higher stimulus frequencies. Thus it is likely that her asymmetrical responses in the head eccentric position are attributable to otolithic effects which have become asymmetrical because of the nerve section, in a similar way to the canal reflexes. It is notable that in patients with acoustic neurinectomies, the eye movements evoked by movement to the lesioned side are similar for both head attitudes. This observation indicates that whereas their remaining canal could generate eye movements in both directions, the intact otolith on one side could only generate eye movements towards the contralateral side.

(b) *Low frequency abnormalities* The type 5 example of abnormal response (B11526) shows a unidirectionally enhanced velocity ratio at low stimulus frequencies. Responses provoked by low frequency stimuli may not be related to the otolith contribution to compensatory reflexes which our data suggest is mainly high frequency sensitive. Instead, they may reflect abnormalities of otolith function related to adaptation and eye velocity storage mechanisms,[12–15] both of which involve long time constants which one would associate with low frequency performance.

In types 3 and 5 the slow phase lateral eye movements evoked by the gravity acceleration vector are in the opposite direction to the enhancement of the slow phase eye movements produced by lateral acceleration during oscillation with head eccentric. In types 2 and 4 the eye movements evoked by gravity are in the same direction to those produced by lateral acceleration during oscillation with head eccentric. These observations underline two unresolved problems of otolith pathophysiology. Firstly, if we are to consider ageotropic nystagmus as a "released" compensatory phenomenon, what is the explanation of geotropic nystagmus which is in the opposite direction? Sec-

ondly, how can the response to phasic linear acceleration, even at low frequencies, be in the opposite direction to the static response as indicated by the direction of positional nystagmus?

One of our original intentions was to design a technique to investigate the otolith contribution to compensatory eye movements in patients with neuro-otological disease. In some, particularly those with feelings of "mal de debarquement", one suspects otolithic abnormalities because of the nature of their symptoms. However, not all such patients show abnormal responses on head eccentric testing although, clearly, the technique reveals some otolith-oculomotor abnormalities. These observations indicate that this method can provide valuable insights into vestibular-oculomotor pathophysiology, and will be worth extending to motion about other axes such as head pitch. However the negative findings also underline the fact that we have to rely too heavily on vestibular-ocular performance as an indicator of the integrity of balance.

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Experimental Brain Research

Short latency compensatory eye movement responses to transient linear head acceleration: a specific function of the otolith-ocular reflex

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Summary. Normal subjects were exposed to 0.26 g linear acceleration steps along the inter-aural axis whilst they fixated an earth stationary target at 110 cm distance. The stimulus evoked slow phase eye movements at a mean latency of 34 ms which attained the relative target velocity in 113 ms. In contrast, visual following with head fixed, of identical relative target motion, had significantly longer latencies and time to match target velocity. The short latency responses to linear acceleration were absent in an alabyrinthine subject. It is concluded that the otolith-ocular reflex is responsible for the short latency responses to linear head movement and functions to stabilise vision during sudden head movement before visually guided compensatory eye movements take effect.

Key words: Eye movement – Vestibular ocular reflex – Otoliths

Introduction

The stability of vision during head movements is preserved by compensatory eye movements which rotate the eyes in the opposite direction to head movement by an amount equal to relative target displacement. The most powerfull source of compensation for angular head movement is the vestibular canal-ocular reflex. It is presumed that the otolith organs contribute to compensation for linear head movement, however, previous investigations of otolith-ocular reflexes (OOR), which have been conducted in darkness to exclude interaction with visually guided movements, have shown responses, at frequencies between 0.5–1.0 Hz, with a gain of 17°/s/g, which is insufficient for visual stabilisation on targets closer than about 5 m (Barnes 1979; Buizza et al. 1980; Hain 1986) (gain is calculated by convention as angular eye velocity in degrees per second evoked per unit of gravitational acceleration; $g = 9.81\ m/s^2$). Accordingly, visually guided, slow phase eye movements (VGEMs) might predominate in compensation for linear motion (Eckmiller 1982). However, VGEMs movements have a long latency of 125 ms (Robinson 1965; pursuit of small target) whereas two factors suggest that OOR might have a unique role at an earlier stage of head movement. Firstly, an OOR, like canal reflexes (Lisberger 1984), should have a short latency. Secondly, because of the acceleration sensitivity of the responses, as shown in experiments in the dark, the OOR should give strong responses at the onset of movement. Therefore, in order to detect an effective OOR, we looked for short latency eye movements evoked by linear head acceleration. Since geometry dictates that compensation for linear relative motion is only required for viewing nearby targets an appropriate visual context was provided by presenting a visual target close to the subject.

Methods

Linear acceleration was provided by a car running on a precision levelled track and driven by two linear motors generating thrust against a reaction plate fixed along the centre of the track. The motors are powered by a 3-phase thyristor drive (Davy Linear Motors Ltd. Davy Corp. PLC.) which is controlled by velocity feedback from a tacho-generator driven by a friction wheel running on the track and together can accelerate a 75 kg subject at > 1 g. The car is capable of following the demand waveform with $< 0.5\%$ harmonic distortion (power). Subjects were seated sideways on the car with shoulders, hips and limbs restrained by pressure pads and screened from the motors by nickle-alloy "mu" metal. The head was fixed to the car and prevented from moving angularly by two conchoidal sacks of polystyrene balls which were compressed around the head between clamps. Horizontal eye movements were recorded with bi-temporal electro-oculography (DC-> 200 Hz) with leads secured to exclude microphonics.

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Linear head acceleration was recorded using a precision piezo-resistive accelerometer (Entran EGC-500 DSC-5, DC-> 200 Hz), mounted with surgical tape onto the forehead. Motion stimuli were velocity ramps to the subject's left or right which rose from 0.0 m/s to 1.11 m/s in 423 ms. Because of servo delay and starting friction the initial acceleration to the head was approximately 0.35 g peak reducing to approximately 0.25 g within 40 ms (see Fig. 1). At the velocity of 1.11 m/s the angular displacement of the subject with respect to the target was 12° and its relative angular velocity was 53°/s. The stimuli were presented, randomised in direction, within a Latin square design using 6 normal subjects (age range 24 to 61 years) and the following conditions: i) motion of the subject on the car in total darkness; ii) motion of the subject whilst fixating the centre of a target at a distance of 110 cm; iii) the target was mounted on the car and was fixated from a distance of 110 cm by the subject, who was seated, earth stationary, with his head fixed. In conditions ii and iii subjects were told to fixate the centre of the target and follow its motion. In the dark, subjects were only instructed to stay alert because pilot experiments had shown that encouraging mental imagery of target position had little effect on slow phase eye movement responses to linear motion in the dark.

The target used in the above experiments was a flat card subtending ± 20° horizontally and ± 15° vertically with a pattern of vertically oriented, black and white stripes (spatial frequency 0.5 cycles/°) having a circular centre point subtending 0.5° and which was viewed under normal room illumination. This was thought to be the optimal configuration for the possible development of the technique into a clinical test. However, in order to exclude the possibility that differences in the responses under the two conditions could result from different motion parallax cues with respect to the room background and/or relative target size, further investigations were made in two of the above subjects; a) using a similar target which subtended vertically and horizontally ± 100° of visual angle and, b) using a target consisting of a 0.5° black cross on a 1.0° luminous disk presented in otherwise total darkness. The larger target provided central and peripheral retinal stimulation without significant motion parallax. The smaller target provided largely central retinal stimulation without motion parallax.

In addition to the normal subjects a 67 year old patient with significantly reduced labyrinthine function, but otherwise neurologically normal, was studied in conditions ii and iii. He had a 20 years history of severe Menière's disease and underwent a right labyrinthectomy one year before being tested. His nystagmic responses to horizontal rotational velocity steps of ± 40°/s in the dark were bidirectionally reduced to about 10% of normal slow phase velocities and durations.

Measurements were made on a Solartron Schlumberger 1200 signal processor using a flat frequency bandwidth of 200 Hz and temporal resolution of 3 ms. Data collection included 150 ms before and 600 ms after the onset of car motion. Averages of between 4 and 8 data records from individual subjects were taken separately for rightwards and leftwards stimuli when artefacts were rejected. Between 7 and 14 records were averaged for experiments varying target size. Measurements were made on the averaged records of each subject of the latencies of slow phase compensatory eye movements evoked by the stimuli. To measure latency, cursors were drawn through the maximum and minimum peak levels in the eye movement trace during the 150 ms preceeding stimulus onset. A response was identified when the post stimulus trace exceeded the bounds of a cursor and maintained a consistent trajectory. Latency was measured with a resolution of ± 3 ms as the time from stimulus onset to the point at which the cursor was intersected. It is estimated that because of noise in the recordings, response latencies could appear to be longer than they were by up to 15 ms. In addition the time after stimulus onset required for eye velocity to match target velocity was measured. This was done by overlaying the eye displacement trace on an angular target displacement trace (the latter was constructed by digitally integrating and scaling car velocity on the signal processor as shown by the target trajectory in Fig. 1). These traces were seen to converge as the slow phase eye movement homed into the target trajectory and the velocities were judged to match when the traces became congruent.

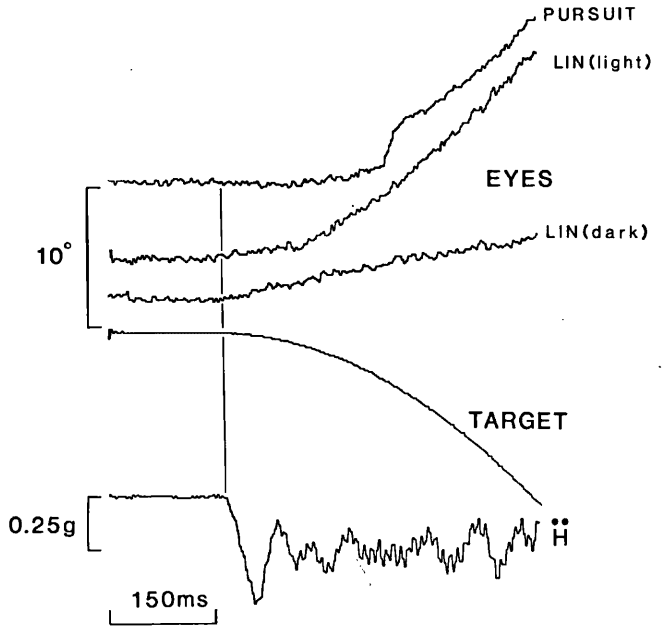

Fig. 1. Raw data records from a normal subject showing angular eye displacement responses under the three experimental conditions: i) the subject rides on the car in total darkness "lin(dark)"; the car begins at rest and then moves to the subject's left with a velocity ramp, ii) the subject rides on the car whilst viewing an earth stationary target at 110 cm in the light "lin(light)" and, iii) the subject is seated, earth stationary, and views the target riding on the car. The relative angular motion of the subject and target is the same in conditions ii and iii and is shown by the "TARGET" trace. $\ddot{H}$: linear acceleration of the subject's head measured along the inter-aural axis. The vertical line indicates stimulus onset from which eye movement response latencies are measured. A position corrective saccade is seen as a stepwise eye movement in the pursuit trace at 225 ms latency

Results

Examples of raw data records of the eye movement responses to head acceleration are given in Fig. 1, LIN(light) and LIN(dark) showing that a slow phase eye movement response, without saccades, commences within 50 ms of the stimulus onset. On average, the responses to head acceleration during target fixation had a mean latency from the onset of acceleration of 34 ms, range 14 to 54 ms (5 subjects, rightwards and leftwards directions combined; one subject was excluded because his response was initiated by an unsuppressed blink). Eye velocity matched target velocity after a mean of 113 ms,

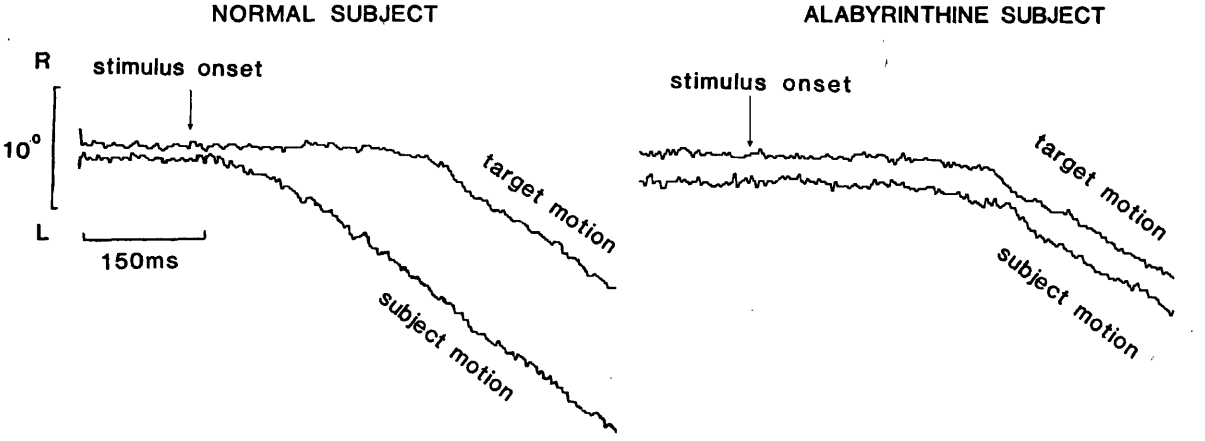

Fig. 2. Responses of a normal subject and of a labyrinthine defective patient to experimental conditions ii) subject motion and iii) target motion. The traces represent averages of 8 responses for each condition. Note that the normal response to subject motion, beginning shortly after stimulus onset, is absent in the alabyrinthine subject

range 52 to 246 ms (6 subjects). At this point in time, the mean relative angular velocity of the car and the velocity of the eyes were 15°/s, range 14 to 33°/s. In the dark, eye movement responses were variable in magnitude and ranged from absence of response to a peak slow phase eye velocity during the ramp stimulus of 94°/s. The mean latency of responses was 27 ms, range 15 to 60 ms (3 subjects combining rightwards and leftwards directions; the responses of 3 subjects were excluded because they were initiated by blinks).

For comparison, Fig. 1 also shows a raw data record of the eye movement response to motion of the target ("PURSUIT") which starts at a latency of 150 ms. On average, responses to motion of the target had a mean latency of 161 ms, range 101 to 197 ms (6 subjects). This was followed within 150 ms by a saccadic eye movement, also towards the target.

Following the saccade the eyes maintained a slow phase movement which matched target velocity, on average, after 264 ms, range 245 to 320 ms (6 subjects). The mean relative angular velocity of the target and of the eyes at this point were 36°/s, range 33 to 43°/s. The latency of responses and time taken for eye velocity to match target velocity for head acceleration with fixation were significantly shorter than those for target motion (Sign test: $p < 0.001$). There was no significant correlation between latency of eye movements in response to subject and to target motion.

Some subjects blinked at a latency of 27 to 50 ms in response to the first few head acceleration stimuli. The blinks merged with the subsequent slow phase eye movement and except for two subjects, habituated. Blinking is probably a startle response (Landis and Hung 1939; Fox 1978) to otolith stimulation (Halmagyi and Gresty 1983) and is part of a generalised activation of body musculature which has a threshold for evocation of the order of 0.3 g (Greenwood and Hopkins 1976).

Effect of target size. For the two subjects, slow phase responses to motion of the large target commenced with mean latencies of 160 and 148 ms with times to match target velocity of 282 and 330 ms. Slow phase responses to motion of the small, luminous target in darkness were at mean latencies of 167 and 173 ms with times to match target velocity of 420 and 320 ms. Mean response latencies when subjects moved linearly viewing the stationary small target in darkness were 48 and 46 ms with times to match target velocity of 138 and 112 ms. For comparison, the latencies of these subjects responses to head movement viewing the medium size target were 44 and 48 ms.

Figure 2 shows the averaged responses of a normal subject and of the alabyrinthine subject. In contrast to the normal subject, the patient with absent labyrinthine function had no short latency eye movements to head motion. His responses to both target and head movement were identical, commencing with a latency of 190–200 ms.

Discussion

The experiments have shown that linear head acceleration evokes a short latency compensatory eye movement. It is unlikely that this response is a visuomotor reflex because the latencies of eye movements to target motion in our subjects were five times longer than the latency of responses to head acceleration. The latencies we found for visually guided slow phase eye movements (VGEMs) in response to

target motion are in agreement to those accepted for human smooth pursuit (Robinson 1965). VGEMs at a short latency of 50 ms have recently been reported in the rhesus monkey (Miles et al. 1986), however, there is no evidence in the present experiments or, to our knowledge, in the literature, that human subjects are capable of such short latency VGEMs. In particular, we were unable to shorten visual following latencies by manipulating the target in size from that of a large optokinetic field (100°) to a central target (1°).

In contrast, responses to linear head movement were evoked at short latencies, less than 50 ms, regardless of target size or whether the subject was in darkness. The latency of the response to linear head motion compares favourably with the latency of compensatory responses to angular (Lisberger 1984) and combined angular and linear head motion (Virre et al. 1986) in the monkey. In addition, and perhaps of most importance, short latency responses were absent in the alabyrinthine subject. For these reasons the short latency response is almost certainly an otolith-ocular reflex (OOR). The importance of this finding is in showing that there is a robust OOR in response to purely linear motion which provides stabilisation of the visual axis before visually guided eye movements become effective. Thus, within the context of an earth fixed visual frame of reference, the OOR is evoked with consistency and appropriate scaling. Similarly, it has been shown that robust OOR responses can be evoked in man by periodic motion in context with concurrent canal signals (Gresty and Bronstein 1986) or optokinetic stimuli (Buizza et al. 1980) (see appendix for comparative values). It may be possible that the need for an appropriate sensory context for strong OOR responses to appear relates to the problem of distinguishing between gravitational and linear accelerat-ory stimuli which affect the otoliths equivalently but demand different oculomotor responses.

The OOR provides compensation during the early stages of linear head movement up to around 150 ms. From this time on, VGEMs combine with or replace the OOR in maintaining the eyes on target (Buizza et al. 1980; Eckmiller 1982). However, VGEMs alone do not become fully effective until around 250 to 300 ms whereas the OOR provides early eye acceleration which leads smoothly into target following without corrective saccades.

Since the eye movement provoked by linear head motion starts after the onset of movement it must have a higher initial acceleration than that of the stimulus in order that the eyes catch up with the target. This initial eye acceleration is possibly derived from the activity of the irregular otolith units in the primary afferents which respond to a partial derivative of acceleration, "jerk" (Fernandez and Goldberg 1976). Jerk sensitivity would allow a prediction of future demands on eye velocity. This view is consistent with previous observations on the dynamics of the OOR, showing a phase lead in the dark (Barnes 1979), which one would expect from the phase characteristic of irregular otolith units. Once on target, and before VGEMs commence (i.e. between 115 and 160 ms), eye acceleration is constant and could, therefore, be derived from the activity of regular otolith units which shows a constant proportionality to acceleration across frequencies.

Appendix

Comparative gain estimates of the OOR

The high frequency (ca. 0.8 Hz) gain of the OOR in the dark has previously been estimated as 17°/s/g in terms of eye velocity or 85°/s²/g in terms of eye acceleration (summarised in Barnes 1979). This represents a background level of sensitivity and does not take target distance into account. In the present experiments, eye acceleration could not be measured from the electro-oculographic records because the inherent noise in the signal would cause too much degradation of the data after double differentiation. However, the steady state eye acceleration after catching up with the target but before VGEMs become effective could be estimated from the acceleration of the stimulus velocity ramp, since eye and target displacement records were congruent, and was approximately 140°/s². In response to a head acceleration of 0.26 g this eye acceleration shows a gain of 540°/s²/g (at our target distance of 110 cm). This estimate compares well with the gain of 630°/s²/g for the response to the linear component of combined angular and linear head movement (Gresty et al. 1987) obtained from subjects imagining fixation on a target at 60 cm. These values are also the same order of magnitude as the estimate of 250°/s²/g for the sinusoidal modulation of optokinetic eye movements by linear head motion (calculated from Buizza et al. 1980).

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