Clinical signs of visual-vestibular interaction

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SUMMARY Visual suppression of vestibulo-ocular reflexes (induced vestibular nystagmus) differs between normal subjects and patients with various neurological disorders. Abnormalities of VOR suppression were associated consistently with abnormalities of the visual and/or vestibular oculomotor reflexes and in particular with abnormal smooth pursuit eye movements in the direction of abnormal suppression. Absent VOR suppression in a gaze position of, and in the same direction as, a spontaneous nystagmus was found exclusively in patients with spontaneous nystagmus of central nervous system origin. Conversely, ability to suppress in these circumstances was found only in patients with spontaneous nystagmus of peripheral labyrinthine origin. Suppression of VOR was abnormal ipsilaterally in patients with unilateral cerebral hemisphere lesions and abnormal in both the horizontal and vertical planes in patients with basal ganglia lesions. Failure of VOR suppression in the absence of spontaneous nystagmus indicates a supratentorial lesion.

The function of normal pursuit, optokinetic, and vestibulo-ocular reflexes is to stabilise retinal images by generating eye movements which compensate accurately for movements of the head and for movements of the visual scene. Natural head movements activate both visual and vestibular reflexes and result in various types of visual-vestibular interaction. If, for example, a subject views a stationary target and at the same time moves his head, the pursuit reflex and the vestibulo-ocular reflex (VOR) together move the eyes in the direction opposite to the head movement, the familiar "doll's head reflex." If, on the other hand, a subject tries to track a moving target using his head as well as his eyes, the pursuit reflex will move the eyes in the same direction as the target and the head, but the VOR will tend to move the eyes in the opposite direction. In this condition the success of tracking (and presumably the success of retinal image stabilisation) will depend on the ability of the pursuit reflex to overcome the inappropriate VOR (Gresty and Leech, 1977). This ability is referred to as "visual suppression of the VOR" which is the same as visual suppression of induced vestibular nystagmus.

Results of certain clinical studies have suggested that inability to suppress visually an induced vestibular nystagmus (Ledoux and Demanez, 1970; Alpert, 1974; Takemori, 1977; Zee, 1977; Dichgans *et al.*, 1978) or a spontaneous nystagmus (Hood, 1968) is a sign of central nervous disease. Others have maintained that similar significance can be attached to a derangement of the pursuit reflexes (Baloh *et al.*, 1977). The aims of this study have been to verify the value of a simple bedside test of VOR suppression, to extend the diagnostic ability of the test to the differentiation of peripheral labyrinthine, posterior fossa and supratentorial lesions, and to relate abnormalities of suppression to abnormalities of pursuit.

Methods

Vestibulo-ocular reflex (VOR) suppression was tested clinically by two methods. One was that described by Dichgans *et al.* (1978) in which the patient views the finger of his extended arm while he turns smoothly at the waist from side to side with arm, trunk, and head en bloc. The other was an adaptation of the method described by Barnes and Sommerville (1978) employing a helmet-mounted target. In our adaptation the patient turned his head smoothly from side to side or up and down while viewing a small target mounted

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Fig. 1 Normal subject demonstrating a clinical method of testing horizontal VOR suppression. The subject fixes her attention on the coloured top of a small plastic bottle fixed to the end of a wooden spatula, while smoothly and regularly oscillating her head from side to side. The examiners look for the presence of nystagmus beating in the direction of head movement.

at the distal end of a wooden spatula, held firmly with the teeth (Fig. 1). With each method the examiner looked at the patient's eyes for the appearance of vestibular nystagmus, which beats in the direction of head movement. With practice it proved possible to make a graded judgment of the velocity or frequency of head movement at which nystagmus first appeared, and the intensity of the nystagmus.

Supplementary laboratory studies were also carried out in which eye displacement was measured by DC electro-oculography. (For simplicity throughout the text, direction of VOR suppression refers to the direction of head and target movement, which is the same as the direction of the fast phases or beats of any induced vestibular nystagmus.) Horizontal VOR suppression was examined by sinusoidally oscillating a rotating chair from which the seated patient viewed a small light fixed directly in front of him, rotating with the chair. Recordings of vertical VOR suppression were made only in those patients with clinically evident vertical eye movement abnormalities. In such cases we used a chair which could be oscillated in the sagittal plane about a horizontal axis passing through the semi-circular canals. Again, the seated patient viewed a small light fixed directly in front of him and moving with the chair. Horizontal VORs were measured using one or more of the following stimuli: (a) impulsive rotation in darkness, (b) sinusoidal oscillation in darkness, (c) bithermal caloric tests. Pursuit reflexes were measured during tracking of a small light spot moving with a triangular waveform on the screen of a 600 mm oscilloscope. Vertical pursuit and VORs were measured only in those patients with clinically evident vertical eye movement abnormalities. Vertical VORs were measured by sinusoidal

oscillation of the head in darkness. Vertical pursuit was measured during tracking of the oscilloscope spot moving in the vertical plane.

As most of the patients studied had right-left asymmetries or gaze-modulated abnormalities of conjugate eye movement, we found it difficult to apply the methods of frequency analysis used successfully by Benson and Barnes (1978). They have shown that the pursuit reflex as well as VOR suppression each have both frequency and velocity response characteristics. We chose instead to analyse head and eye movements in terms of their velocities. In order to minimise the effects of frequency dependent changes in pursuit and VOR suppression, head movements were always restricted to less than 1.0 Hz and whenever possible to less than 0.75 Hz.

Results

NORMAL SUBJECTS

On clinical examination of horizontal and upward VOR suppression, a few small beats of nystagmus appeared at rapid rates of head shaking. With a further increase in rate, the examiners found it difficult to make clear observations. This is not unexpected considering that the performance limits of the examiner's pursuit reflex are likely to be similar to the performance limits of a normal subject's VOR suppression. Downward VOR suppression was noticeably inferior, down beating vestibular nystagmus appearing at moderate rates of downward head movement.

The pattern of VOR suppression was similar in the eight normal subjects examined, although there were significant quantitative differences. Figure 2 shows the raw records of the subject with the least effective VOR suppression. There are no eye movements until head velocity reaches

Fig. 2 Above: raw records of VOR suppression in a normal subject—top trace is head displacement, bottom trace is eye displacement. The appearance of vestibular nystagmus is shown to depend on the velocity of head movement. Below: plots of leftward head velocity versus rightward, slow-phase eye velocity for two normal subjects. $\circ$ — $\circ$ is the plot of the subject whose raw record is illustrated above and whose VOR suppression was the least effective of the normal subjects tested; $\bullet$ — $\bullet$ is the plot of the subject with the most effective VOR suppression; $\blacksquare$ — $\blacksquare$ is the plot of leftward head velocity versus rightward eye velocity in a patient with a right sided peripheral labyrinthine lesion and whose raw record is shown in Fig. 3.

30°s^{-1} ; vestibular nystagmus then appears with increasing slow phase velocity so that by 100°s^{-1} eye velocity approaches head velocity. These results are presented in the plot of Fig. 2 ($\circ$ — $\circ$) which also shows the data of the subject with the most effective suppression ($\bullet$ — $\bullet$). The plots of the other normal subjects lay between these two extremes and their slopes were approximately parallel. For each subject the maximum velocity of accurate pursuit was approximately the same as the head velocity at which VOR suppression first failed. Normal vertical pursuit and VOR suppression were not measured systematically although in general the results conformed to the findings of Benson and Guedry (1971). The limits of upward VOR suppression and pursuit were the same as of horizontal suppression and pursuit; downward suppression and pursuit were significantly less effective.

PERIPHERAL LABYRINTHINE LESIONS

Four patients with partly compensated or uncompensated peripheral vestibular lesions were examined.

All had a first or second degree spontaneous nystagmus which was enhanced significantly in darkness. On clinical testing of VOR suppression, the spontaneous nystagmus was unchanged at low rates of head movement but was enhanced at moderate rates of movement in the direction of the spontaneous nystagmus beats. Figure 3 shows a raw record of VOR suppression from a 38 year old man with an acute right sided vestibular neuronitis. In light he had a 2°s^{-1} , second degree, left beating spontaneous nystagmus. The figure shows that the spontaneous nystagmus is not significantly modulated by head movements at 45°s^{-1} , indicating that VOR suppression is intact at that velocity. Rightward VOR suppression eventually failed at 80°s^{-1} whereas leftward VOR suppression failed at 50°s^{-1} , as plotted in Fig. 2 ($\blacksquare$ — $\blacksquare$). Leftward pursuit reflexes were mildly abnormal (Fig. 4) but vertical eye movements were normal. The horizontal VORs were asymmetrical—with the head moving to the left, rightward eye movement velocity exceeded head velocity; with the head moving to the right, leftward eye movement velocity was less than head velocity.

Fig. 3 Raw records of VOR suppression in five patients with lesions at different sites in the nervous system and who are described in detail in the text. Eye displacement shown in the top traces and head displacement in the bottom traces. Time and amplitude scales indicated on the left side of the diagram apply to all records, except to the record of the patient with cerebellar degeneration, whose own time scale is given.

Fig. 4 Raw records of pursuit in the same five patients whose VOR suppression is shown in Fig. 3. Eye displacement is shown in the top trace, target displacement in the bottom trace. Time scales are 2 s, amplitude scales 20°.

POSTERIOR FOSSA LESIONS

Twenty-one patients with various focal and diffuse brainstem and cerebellar disorders were examined (stroke, multiple sclerosis, cerebellar degeneration, intrinsic and extrinsic tumour). All had horizontal nystagmus, the slow-phase velocity of which was enhanced in darkness in three and suppressed or unchanged in 18. Other eye movement abnormalities included vertical nystagmus, rebound nystagmus, and VOR hyperexcitability. Horizontal VOR suppression was markedly impaired or absent so that vestibular nystagmus appeared at the lowest rates of head shaking. In the patients with cerebellopontine angle tumours suppression was consistently worse towards the side of the lesion than towards the other side. Vertical VOR suppression was also impaired or absent in the patients who had spontaneous first degree vertical nystagmus. Pursuit through the primary position was absent or impaired, commensurate with the impairment of VOR suppression.

These abnormal patterns are illustrated in the records of two patients in Fig. 3. A 34 year old man with a cerebellar degeneration had bilateral first degree, gaze-evoked nystagmus, bilateral rebound nystagmus, first degree, up beating and down beating nystagmus, but no primary position nystagmus and no VOR hyperexcitability. During attempted VOR suppression with the eyes in the

primary position, brisk vestibular nystagmus occurred in each direction, the slow phase velocity of which approximated head velocity. Vertical VOR suppression was similarly impaired, with brisk vestibular nystagmus on upward and downward head movements. Horizontal (Fig. 4) and vertical pursuit through the primary, nystagmus-free position, was absent.

In a 31 year old woman with idiopathic, acquired, periodic alternating nystagmus, the recording was made during one of the regular 100 second cycles of second degree right beating nystagmus. The spontaneous nystagmus was sinusoidally enhanced and inhibited during attempted VOR suppression, the increment and decrement in nystagmus slow-phase velocity being approximately the same as the head velocity. This indicated that horizontal VOR suppression was bilaterally impaired or absent, the induced vestibular nystagmus adding to or subtracting from the spontaneous nystagmus. Horizontal pursuit through the primary position (calculated as the increment or decrement in nystagmus slow-phase velocity during pursuit through the primary position) was also impaired bilaterally (Fig. 4). Vertical eye movements were normal.

UNILATERAL CEREBRAL HEMISPHERE LESIONS

There were seven patients in this group. Four had had unilateral hemispherectomies, two others had recent cerebral infarcts, and one a stroke-like illness in childhood. All showed other hemisphere signs such as hemiparesis or dysphasia; only one did not have a homonymous hemianopia. Vestibulo-ocular reflex suppression and pursuit reflexes were impaired towards the side of the lesion but were normal towards the opposite side. Figure 3 shows poor rightward VOR suppression in a 17 year old girl with a right hemispherectomy who had a left hemiparesis, absolute left homonymous hemianopia, and a cortical pattern of sensory loss on the left. Pursuit reflexes were impaired to the right (Fig. 4) but vertical eye movements and horizontal VORs were normal.

BASAL GANGLIA LESIONS

Three patients with Parkinson's disease, three with progressive supranuclear palsy, and two with Huntington's chorea had mild bilateral horizontal and vertical impairment of VOR suppression and pursuit. A child with a bilateral thalamic glioma had absent horizontal and vertical pursuit and VOR suppression.

CONGENITAL NYSTAGMUS

Six patients with nystagmus since early life were

examined. All had a nystagmus-free position of gaze (null position) in which vision was good and a nystagmus which showed a jerk wave form in at least one gaze position. When VOR suppression was tested clinically with the eyes held in a gaze position of spontaneous nystagmus the nystagmus was enhanced during head movement in the direction of the nystagmic beats. The measured increment in slow-phase velocity was approximately the same as the head velocity indicating that the VOR suppression was absent in that direction. Horizontal VOR suppression was also impaired when tested with the eyes in the null position. Figure 3 shows VOR suppression in a 36 year old man with congenital nystagmus, with the eyes held in the null position which happened to be the same as the primary position. Although horizontal VOR suppression was bilaterally impaired, eye velocity was less than head velocity, indicating that VOR suppression was not totally absent. Horizontal pursuit through the null position was impaired bilaterally (Fig. 4). Vertical eye movements, including VOR suppression, were normal.

Discussion

Our results confirm that VOR suppression is abnormal in patients with lesions at several different levels of the nervous system (Ledoux and Demanez, 1970; Alpert, 1974; Takemori, 1977; Zee 1977) and that abnormal VOR suppression is consistently associated with abnormal pursuit reflexes (Dichgans *et al.*, 1978). All our patients with abnormal suppression had abnormal pursuit in the same direction; no patient with abnormal pursuit and normal vestibulo-ocular reflexes had normal VOR suppression in the direction of the abnormal pursuit. Generally the maximum velocity of pursuit eye movements through a position of gaze (in these experiments usually the primary position) was the same as the minimum head velocity at which suppression failed. Although these results do confirm suggestions that the pursuit reflex suppresses vestibulo-ocular reflex eye movements in the opposite direction (Benson and Barnes, 1978), they give little indication of the anatomical pathways mediating VOR suppression in man. Single cell neurophysiological recordings and lesion experiments in animals indicate that the cerebellum, particularly the flocculus, is important for VOR suppression and pursuit (Takemori and Cohen, 1974; Ito *et al.*, 1977; Lisberger and Fuchs, 1978). Although several of our patients had clinically definite or pathologically verified lesions involving the cerebellum, the majority did not.

The results from patients with peripheral lab-

yrinthine lesions indicate that enhanced or imbalanced activity of the VOR can also impair VOR suppression. The plot of leftward suppression in the patient with the right sided peripheral labyrinthine lesion (Figure 2 ■—■) has a slope similar to the normal plots but is presumably negatively biased by the asymmetrical VOR. It is this VOR asymmetry rather than an impairment of visual oculomotor reflexes themselves which accounts for the slight impairment of pursuit and VOR suppression in this patient.

Although VOR asymmetry and hyperexcitability were also found in some patients with posterior fossa lesions, their VOR suppression was distinctly different from the suppression of the patients with peripheral labyrinthine lesions. When VOR suppression was tested in a gaze position with spontaneous nystagmus, the patients with peripheral labyrinthine lesions showed little or no modulation of the spontaneous nystagmus slow phase velocity until the head velocity approached the normal upper limits of VOR suppression. Suppression first failed in the direction of the spontaneous nystagmus. On the other hand, when patients with posterior fossa lesions were tested in this way there was impaired or absent suppression even at the lowest velocities of head movement in the direction of the spontaneous nystagmus. In most cases both horizontal and vertical VOR suppression were impaired even in nystagmus free positions of gaze. In patients with congenital nystagmus who had normal VORs, VOR suppression was impaired in both horizontal directions when tested in a nystagmus free or null position. Vertical eye movements were, however, normal.

From these observations certain clinical and physiological deductions can be made about visual suppression of spontaneous nystagmus and of induced vestibular nystagmus. In patients with nystagmus of central nervous system origin there is impaired or absent visual suppression of both the spontaneous nystagmus and of an induced vestibular nystagmus in the same direction. This suggests that there are some common neural mechanisms for the visual suppression of different inappropriate eye movements. Clinical testing of VOR suppression can be used to help differentiate a nystagmus of central origin from a nystagmus caused by a peripheral labyrinthine lesion. When tested in a position of gaze with spontaneous nystagmus, ability to suppress vestibular nystagmus in the same direction indicates that the spontaneous nystagmus is of peripheral labyrinthine origin. Inability to do so indicates that it is of central origin.

Ipsilateral impairment of VOR suppression in

the patients with unilateral cerebral hemisphere lesions explains the ipsilateral directional preponderance of caloric and rotational nystagmus, which shows only in the presence of visual fixation (Carmichael *et al.*, 1961). Clinical testing of VOR suppression can be useful in patients with suspected cerebral hemisphere lesions.

The pattern of VOR suppression in patients with basal ganglia lesions resembled the pattern in patients with posterior fossa lesions. They were, however, distinguished by spontaneous nystagmus which was present in all the patients with posterior fossa lesions, but in none with basal ganglia lesions. Failure of VOR suppression in the absence of spontaneous nystagmus indicates a supratentorial lesion.

The results verify that most diagnostic deductions about VOR suppression can be made from simple clinical observation, without laboratory quantification of head and eye movements. With practice the clinician can estimate nystagmus intensity (frequency and amplitude) relative to head velocity. For him the principal advantage of electro-oculography is that a permanent objective recording is obtained.

Conclusions

Impaired visual suppression of an induced vestibular nystagmus—that is, the vestibulo-ocular reflex—is a diagnostically useful clinical sign that can be elicited and interpreted at the bedside. It can help to distinguish spontaneous nystagmus of peripheral labyrinthine origin from nystagmus due to central causes. In the absence of spontaneous nystagmus it can be a sign of unilateral or bilateral supratentorial lesions. It appears that there are some common neural mechanisms for the visual suppression of different inappropriate eye movements and that these are closely related to the pursuit reflex.

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