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Physiological basis for enduring vestibular symptoms

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SUMMARY Four examples of patients who sustained a vestibular insult and did not fully recover over a prolonged period are described. The reasons for this failure of compensation are discussed in relation to the experimental literature, particularly that concerning the importance of extra-vestibular inputs upon the vestibular system.

Vertigo and dizziness are among the most frequent complaints of patients presenting to the neurologist. In the majority the symptoms are relatively short-lived. In a few this is not the case. This latter group often become increasingly disabled and consult numerous physicians who, because of the paucity of neurological signs, frequently conclude that the patient is primarily suffering from a psychiatric condition. Whilst this decision is sometimes justified, it is not always so.

Over the past two decades the mechanisms of recovery from acute vestibular dysfunction have been clarified. In this paper we review some aspects of this compensation and draw attention to the ways in which it may be prevented by alteration of visual and somataesthetic sensory input and central nervous system disease. We further emphasise how neuro-otological testing can often demonstrate abnormalities in patients who are apparently without objective signs of neurological dysfunction. Four case histories are presented as illustrative examples of some of the reasons for failure of recovery from vestibular dysfunction.

Case reports

Case 1, BM, A99033

This woman was seen at the age of 40 years (1978) with a two year history of incapacitating vertigo. She experienced sensations of floating, detachment and vertigo and could not move about without accentuating her symptoms. Walking produced a sensation of the ground being unsteady and she avoided places crowded with moving people as they induced an unpleasant sensation. On occasions she took to a wheelchair for prolonged periods. During this time she also experienced drop attacks episodes of hemianopic visual field loss and hemisensory disturbance. In 1964, 1966 and 1975 she had seen neurologists because of episodes of dizziness of uncertain cause. Unlike the current symptoms, these past episodes of dizziness had resolved. There was a past history of migraine and she had one leg amputated because of severe peripheral vascular disease associated with hyperlipidaemia. She was a heavy smoker and used an oral contraceptive. In addition she had received treatment for severe depression over many years including a prolonged inpatient stay. Examination revealed few neurological signs. There was a variable 1st° horizontal nystagmus to the left and slight incoordination of the left hand. Her gait was mildly ataxic but the assessment was complicated by the amputation. Caloric tests showed a directional preponderance of the induced nystagmus to the left, there was a clockwise deviation of the visual vertical and horizontal, and on eye closure there was a 3rd° nystagmus to the left. CT scans performed on two occasions demonstrated an infarct in the left cerebellar hemisphere (fig). Although there was some symptomatic

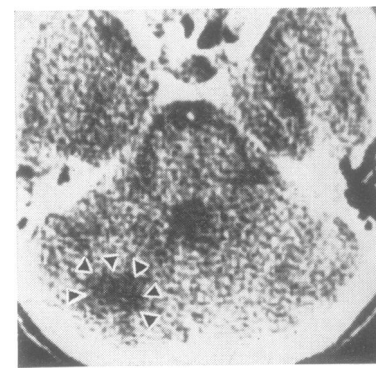

Figure *Case 1, BM, CT scan demonstrating infarction within the left cerebellar hemisphere (arrowed).*

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response to vestibular exercises and Cinnarizine (Stugeron-Janssen) the patient has been readmitted several times since 1978 with dizziness and depressive symptomatology. Short-term improvement has occurred each time with antidepressant treatment. *In summary* this patient with persistent dizziness had clinical evidence of ischaemia within the vertebro-basilar territory and radiological proof of cerebellar infarction. She had evidence of both atherosclerosis and migraine.

Case 2, MM, A89752
In 1974 at the age of 28 years, this man suffered a severe attack of migraine during which he was blind for some hours and became extremely vertiginous, unsteady and nauseated. Following the attack he noted diplopia with the false image slightly above and to the right of the other. In addition he felt constantly unsteady and the ground did not seem firm. When he walked he experienced oscillopsia which improved on riding a horse or in a car. He felt extremely uneasy in traffic or when people rushed past him and he was unable to walk between the shelves in a supermarket. Occasionally he was nauseated. Frequently he found difficulty in going to work because of these symptoms. He was referred to a number of ophthalmic surgeons and physicians who felt he was elaborating his symptoms. When seen in 1976 he had a patch of sensory loss over the right side of the face related to an old war injury and mild sensory loss over the left foot. He veered to the left when walking with his eyes closed and he fell when asked to stand with his eyes closed. There was a variable diplopia on looking up and to the right which could not be resolved into a single peripheral nerve or extra-ocular muscle dysfunction. On eye closure there was a 2nd° nystagmus to the right. The caloric responses were depressed. Rotational testing showed a directional preponderance to the left and optokinetic responses were deranged with directional preponderance to the right. CT scan suggested the presence of left cerebellar infarction. The patient improved after intensive vestibular exercises although from time to time he has had further symptoms. *In summary* the enduring dizziness this young man experienced was due to a severe attack of migraine causing ischaemic lesions within the vertebro-basilar territory.

Case 3, MG, A62841
In 1964 this 47-year-old patient suddenly developed severe rotational vertigo, nausea and imbalance and was admitted to hospital where she remained for three months. No definitive diagnosis was made. Although there was partial recovery she still experienced episodes of vertigo interspersed with long periods of vague imbalance. During the bouts of vertigo objects rotated left to right and this was often precipitated by head movement. She was frightened to walk around and always felt worse in a crowded place, in traffic or when walking between the shelves in a supermarket. When travelling in a car she felt that the road lines were coming up towards her. Her vision always seemed slightly blurred, a symptom made worse by movement. Over the succeeding years she was unable to obtain relief despite many medical opinions and psychiatric care. Neurological examination in 1978 revealed tonic pupils which did not react to light and reacted only slowly to accommodation. Lower limb reflexes were absent but all sensory modalities were preserved. She veered to the left when walking with the eyes closed and the Romberg test was positive. A CT scan was normal. Nerve conduction studies showed absent H reflexes. Pharmacological testing documented that she had a tonic pupil. Caloric tests revealed a mild left canal paresis and right directional preponderance. There was clockwise deviation by 4° of both visual vertical and horizontal. On electro-nystagmography there was bilateral 1st° nystagmus (R < L) with eye closure and there was a directional preponderance of optokinetic nystagmus to the right. These latter findings varied from time to time. *In summary* this was a patient with the Holmes-Adie syndrome who failed to compensate for a left peripheral vestibular lesion.

Case 4, GS, B02530
In 1978, this 47-year-old woman was referred with vertigo, vomiting and imbalance which developed suddenly during the convalescent phase of an attack of gastro-enteritis. Initially there was a sense of severe rotation but later a constant sensation of vague dizziness exacerbated by head movement. Six years before she experienced similar symptoms but these resolved over two weeks. She had been blind in both eyes for 18 years owing to chronic uveitis. On examination there was mild right sided pyramidal weakness and left sided cerebellar incoordination. Past pointing was present towards the right and she veered to the right on walking. There was no nystagmus. Caloric responses were prolonged with a directional preponderance to the right. Electro-nystagmography revealed that there was a tonic deviation of the eyes to the left. CT scan showed cerebral atrophy. Her symptoms persisted over many months although there was some improvement following vestibular exercises. *In summary* this patient who is blind developed a complex lesion of the vestibular apparatus, pyramidal tract and cerebellum following an attack of gastro-enteritis. She made a partial recovery.

Discussion

The feature common to these four case histories is that there has been a persistence of dizziness for years following an acute vestibular lesion. All patients have been severely disabled and largely confined to the house. Although three had experienced subsequent episodes of rotational vertigo, the major symptoms have been less dramatic and included floating or rocking sensations and dizziness provoked by specific circumstances such as when walking between shelves in a supermarket. These symptoms, often dismissed by clinicians as non-organic in origin, have a sound physiological basis. In each patient the bizarre nature of the symptoms and the virtual absence of physical signs led to referral for psychiatric treatment; however, neuro-otological investigations confirmed the presence of

Table 1 *Neuro-otological abnormalities*

	Nystagmus	*Postural disturbance (eye closure)*	*Visual vertical and horizontal*	*Caloric responses (with fixation)*	*OKN*	*Rotation*
BM	1st° left becoming 3rd° in dark	Difficult to interpret (amputee)	Clockwise deviation	DP to left	Normal	
MM	2nd° right eye closure	Veered left		Depressed	DP right	DP left
MG	1st° right > left eye closure	Veered left	Clockwise deviation	Mild left canal paresis DP to right	DP right	
GS	Nil. Tonic deviation eyes left in dark	Veered right Pastpointing to right		Enhanced and prolonged DP to right		

DP = directional preponderance. OKN = optokinetic nystagmus.

vestibular dysfunction (table). It was perhaps not surprising that after many years of dizziness these patients became depressed and hypochondriacal. Similarly it seems natural that if any of the patients had a pre-existing neurotic trait, then they should cope less well with enduring dizziness.

To understand the symptoms these patients experienced presupposes a basic knowledge of the physiological changes which occur with damage to the vestibular apparatus. After a unilateral lesion the input to ipsilateral vestibular nuclei is diminished in response to linear and angular acceleration. In the resting state there is an imbalance of tonus or vestibular bias which is at variance with visual and proprioceptive input, and the patient experiences dizziness which may be a subjective feeling of rotation or imbalance to the side opposite the lesion. There is an objective postural deviation to the side of the lesion mediated by activation of intact vestibulospinal reflexes. Nystagmus to the side opposite the lesion is produced by imbalance of tone of the vestibulo-ocular reflexes and the patient may experience blurred vision if the nystagmus is of second or third degree.

Vestibular bias is not the only disturbance caused by a vestibular lesion—there is also a disturbance of the precision of the vestibulo-ocular reflex. The physiological role of the vestibulo-ocular reflex is to mediate the compensatory eye movements which occur with head movement, in order to maintain fixation on a stationary target, for example when walking, running or riding in a car. It is also the basis of the doll's head eye movements. The vestibulo-ocular reflex lends itself to physiological study since head and eye movements may be accurately quantified. Its function is measured in terms of gain (eye velocity/head velocity) and phase (an index of the synchronicity of head and eye movement). In normal subjects in the light gain is unity and the phase difference is 180°. Where the vestibulo-ocular reflex has been deranged, for example by an acute vestibular lesion, the head movement will produce apparent movement of stationary objects, termed movement dependent oscillopsia, a feeling of instability, dizziness, and in extreme cases nausea or vomiting.

Usually the clinical features of an acute peripheral vestibular lesion disappear over a period of weeks. Examination of patients six months after unilateral vestibular nerve section or labyrinthine destruction reveals no abnormality of eye movement or equilibrium, although nystagmus to the side opposite the lesion occurs with removal of fixation.[1] The mechanism for this compensation has not been fully determined. However, it is apparent that there is a re-adjustment of the vestibular bias and restoration of the precision of the vestibulo-ocular reflex utilising extra-vestibular sensory information, particularly visual and proprioceptive cues.

Ito[2] proposed that the cerebellum plays a crucial role in modulating the vestibular system by monitoring its performance against visual input. The vestibulo-ocular reflex is a three neuron reflex comprising the primary vestibular afferent, an inter-neuron from the vestibular nuclear complex to the oculomotor nuclei and an effector neuron to the extra-ocular muscles. There is no closed loop feedback yet some control is necessary since during a lifetime the vestibular apparatus may be subject to trauma, toxic drugs, alcohol, vascular disease and other insults. It is proposed that there is an open loop control and that the cerebellum compares vestibular input and other sensory information, particularly visual, so that modulation of the vestibulo-ocular reflex may occur, with precise eye movements made with each head deviation. This form of modulation is also known as parametric adaptive control. Anatomically the cerebellum is ideally situated to do this. Apart from the collaterals of the first and second order vestibular fibres[3] the floccular Purkinje cells receive visual information via climbing fibres from the dorsal cap of the inferior olive as well as mossy fibres.[4]

The remarkable plasticity of the vestibulo-ocular reflex has been demonstrated in man and cats with chronic wearing of reversing prisms.[5 6] Under these circumstances the vestibulo-ocular reflex is inappropriate since with a head movement the resultant eye movement is in the opposite direction necessary to maintain gaze on a stationary target. However, as

time passes compensatory changes occur. There is a gradual reduction in gain towards zero followed by a change in phase and a return of gain towards unity so that after a period of about one month the vestibulo-ocular reflex becomes partially reversed. This plasticity is dependent as far as gain is concerned upon the cerebellum since adaptive gain control is abolished in cats after extensive vestibulo-cerebellectomy.[7] More recently it was shown that such gain control (measured in the dark) was abolished in the cat by lesions of the dorsal cap of the inferior olive[8] and it was suggested that this may reflect a decrease in the inhibitory effect of Purkinje cells on neurons in the vestibular nucleus.

Changes in the spontaneous discharge from neurons of the vestibular nuclei following unilateral labyrinthine destruction have been recorded in cats by micro-electrodes.[9 10] Initially there is an imbalance of the vestibular tonus since spontaneous activity on the ipsilateral side is abolished. Gradually the spontaneous activity returns to the ipsilateral vestibular nuclei which also respond now to contralateral semi-circular canal stimulation. This recovery of activity parallels the time course of the relief of clinical symptoms and signs.[11] The genesis of the renewed ipsilateral spontaneous vestibular discharge remains unresolved. McCabe *et al*[10] produced additional surgical lesions including cerebellectomy, midbrain section, spinal cord section and oblique and vertical midline brain stem section. None of these lesions prevented the resumption of spontaneous activity in the vestibular nuclei. However, they found that the cerebellum has a pronounced damping effect on the discharge of the contralateral vestibular nuclei in the acute phase (the ipsilateral nuclei being silent) and in this way acts as a "first line of defence" in preventing the full effect of the labyrinthine lesion. Similarly Haddad *et al*[12] found that vestibulo-cerebellectomy did not prevent long-term compensation of nystagmus in cats, although it was delayed. Interestingly in the rat, chemical lesions of the inferior olive prevented the acquisition and retention of the compensation for postural and oculomotor abnormalities produced by hemilabyrinthectomy[13 14] suggesting that the integrity of the climbing fibre pathway from the inferior olive to the cerebellum was essential for recovery.

Thus while it does appear that the cerebellum plays an important part in the short-term adaptation of the vestibulo-ocular reflex, it may not be essential for long-term adaptation although this is certainly slowed by cerebellar lesions confined to the floccular nodular lobe. Some of the long-term adaptation of vestibular bias may occur at the vestibular nuclear level itself.

There is no doubt that a lack of alternative sensory input will grossly impair the restoration to normal of vestibular tonus and vestibulo-ocular reflex precision. Vision is clearly important since compensation is delayed in cats confined to darkness following labyrinthectomy.[15 16] Similarly spinal afferent systems are also involved including sensory input from the muscle spindles and joint receptors, a fact shown by the prevention of recovery in normally seeing baboons subjected to vestibular neurotomy and encased in restraining splints.[17] The powerful effect of vision on vestibulo-ocular reflex suppression is readily demonstrated by observation of the nystagmus induced by caloric irrigation of the ears, since the response is normally instantaneously suppressed in the presence of optic fixation. There is good evidence that this visual-vestibular interaction occurs at the vestibular nuclei as in the monkey it has been shown that vestibular neurons discharge in response to purely visual (optokinetic) stimulation.[18]

From the foregoing review of the experimental and theoretical literature, enduring and disabling vestibular symptoms would be expected in the following situations: (1) peripheral labyrinthine lesion in a patient with inadequate supplementary sensory input, (2) peripheral labyrinthine lesion in a patient with a disorder involving the cerebellum or its connections such that the integration of supplementary sensory information is not possible or impaired, (3) lesions of the vestibular nuclear complex producing a permanent bias of vestibular tonus.

These three mechanisms are, of course, not mutually exclusive and in view of the fact that the vestibular nuclei and the vestibulo-cerebellum are closely situated anatomically, and that the labyrinth, brain stem and cerebellum are supplied by the vertebro-basilar arterial system, a combination of lesions is commonly encountered.

Returning to the four cases presented, it is now possible to offer explanations for the persistent vestibular symptoms. In case 1 there was clinical evidence for ischaemia in the vertebro-basilar territory and a CT brain scan demonstrated cerebellar infarction. Similarly in case 2 a young man suffered an ischaemic insult to the brain stem which was migrainous in origin and a CT scan also suggested cerebellar infarction. Case 3 was unique in that the patient failed to compensate for an isolated vestibular lesion. However, she had the pupillary abnormalities of the Holmes-Adie syndrome which were associated with loss of the Ia afferent fibres from the muscle spindles. These fibres are recognised as an important source of proprioceptive information ascending to the vestibulo-cerebellum. The final patient, case 4, had a complex lesion of the vestibular apparatus, pyramidal tract and cerebellum following

an attack of gastroenteritis. In addition she was blind so that even if the vestibular nuclei and cerebellum were intact, compensation by the integration of alternative sensory information would be impaired. All these patients, therefore, had a sound physiological basis for failing to compensate for a vestibular insult since they had either lost a major extra vestibular sensory input, or sustained damage to the cerebellum or the vestibular nuclei or both, preventing the utilisation of this information to compensate for a deranged vestibular bias and vestibulo-ocular reflex.

In conclusion, in this paper we have reviewed the literature concerning the mechanisms of recuperation from vestibular lesions and discussed the reasons for failure of compensation using illustrative cases. The problem of enduring dizziness is common and encountered widely in many medical disciplines. The principles outlined here are relevant to the syndrome of "space phobia" as several of the patients described in the two papers by Marks[19 20] had evidence of organic brain pathology. Although there is still little to offer these patients in terms of specific therapy, many are relieved if the clinician can provide an explanation and reassure the patient that there are other people with similar unpleasant sensations which are not imaginary.

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