

# Vestibular neuritis spares the inferior division of the vestibular nerve

M. Fetter and J. Dichgans

Department of Neurology, Eberhard-Karls University, Tübingen, Germany

Correspondence to: M. Fetter, Department of Neurology, Hoppe-Seyler Straße 3, 72076 Tübingen, Germany

## Summary

Acute unilateral vestibulopathy, or vestibular neuritis, is the second most common cause of vertigo. To quantify the involvement of the different semicircular canal (SCC) afferents in this disease, we studied the three-dimensional (3D) properties of the vestibuloocular reflex (VOR) in 16 patients 3–10 days after onset of symptoms. Using 3D magnetic search coil eye movement recordings, we measured the speed and axis of eye rotation during spontaneous nystagmus and during rotation in the planes of the different SCCs. In all patients, spontaneous nystagmus axes clustered between the direction expected with involvement of just one

horizontal SCC and the direction expected with combined involvement of the horizontal and anterior SCC on one side. Likewise, dynamic asymmetries were found only during rotations about axes which stimulated the ipsilesional horizontal or ipsilesional anterior SCCs. No asymmetry was found when the ipsilesional posterior SCC was stimulated. Thus, both measurements suggest that vestibular neuritis is a partial and not a complete unilateral vestibular lesion and that this partial lesion affects the superior division of the vestibular nerve which includes the afferents from the horizontal and anterior SCCs.

**Keywords:** unilateral vestibulopathy; vestibuloocular reflex; three-dimensional eye movements; magnetic search coil; human

**Abbreviations:** HOR = horizontal plane; LARP = left anterior–right posterior semicircular canal plane; RALP = right anterior–left posterior semicircular canal plane; SCC = semicircular canal; 3D = three-dimensional; VOR = vestibuloocular reflex

## Introduction

Acute unilateral peripheral vestibulopathy, also known as vestibular neuritis, is the second most common cause of vertigo (Ruttin, 1909; Nylén, 1924; Hallpike, 1949; Dix and Hallpike, 1952). Although in most cases the aetiology is never proven, it is believed that vestibular neuritis is usually due to viral infection (Schuknecht and Kitamura, 1981). The chief symptom is acute-onset, severe, prolonged rotational vertigo, associated with nausea, postural imbalance and spontaneous nystagmus.

The aim of this study is to determine, non-invasively, which branches of the vestibular nerve are affected in vestibular neuritis, using 3D analysis of the VOR. This reflex helps stabilize the retinal image by rotating the eyes to compensate for movements of the head. Its sensory input comes via the vestibular nerves from the SCCs, which detect angular acceleration of the head. There are three pairs of canals, working in a push–pull arrangement in three roughly orthogonal planes in the head. Owing to methodological

limitations, most studies of the VOR have looked at only the horizontal canals. To study the VOR in all three rotational degrees of freedom one must be able to stimulate the subject in three dimensions and to record the resulting eye movements in three dimensions. Using a computer-driven rotating chair and the magnetic search coil technique of eye movement recording, we were able to evaluate the 3D properties of the VOR in patients with acute unilateral vestibular neuritis.

In vestibular neuritis, the inputs from one or more canals are blocked. The resulting loss of accelerometer function on one side of the head results in dynamic asymmetries; e.g. the slow phase eye velocity response to ipsilateral head rotation is weaker than the response to contralateral rotation. Moreover, a vestibular lesion may lower or abolish the tonic discharge, or resting activity, in the vestibular nerve on one side, and the imbalance between the tonic inputs on the two sides leads to spontaneous nystagmus.

The idea behind the present study was that the axis of the

**Table 1** Summary of patient data

Subject	Age (years)	Sex	Side	Canal paresis (%)	Day
1	45	M	L	100	11
2	73	M	L	100	10
3	69	M	L	100	10
4	62	M	L	88	10
5	67	M	L	100	6
6	45	M	R	100	15
7	35	F	R	40	5
8	37	M	R	100	10
9	49	M	R	100	10
10	51	F	R	71	4
11	33	F	L	100	3
12	58	M	L	100	4
13	42	F	R	n.a.	11
14	56	F	R	100	5
15	25	F	R	100	5
16	61	M	L	n.a.	4

L = left-sided lesions; R = right-sided lesions; canal paresis = difference between the combined right-sided and left-sided responses (maximum slow phase velocity) to bithermal caloric stimulation divided by the sum of the responses; Day = day of recording after onset of symptoms; n.a. = not available.

3D eye velocity vector during the slow phase of spontaneous or rotary vestibular nystagmus gives information about which SCCs are driving the eye movement. It is known that electrical stimulation of single canal nerves induces eye movements roughly in the plane of the canal (Suzuki and Cohen, 1964). If we assume that the different canals combine at least roughly linearly to drive the eyes, this implies that a lesion of a single canal should induce spontaneous nystagmus with slow phases in the off-direction of that canal. If multiple canals are lesioned, the slow phases should be in a direction that is a weighted vector sum of the axes of the involved canals. Therefore we recorded 3D eye velocity vectors in patients with acute vestibular neuritis during both spontaneous nystagmus and whole-body rotation in the planes of different canal pairs, and we compared the axes of these vectors with those expected with involvement of different combinations of SCCs.

## Methods

Sixteen patients (10 male, six female, mean age  $50.5 \pm 13.6$  years; eight with right-sided lesions and eight with left-sided) and 10 control subjects (mean age  $44.0 \pm 12.3$  years; without oculomotor or vestibular abnormalities) were tested with eyes open in complete darkness in a motor-driven 3D rotating chair. Patients were recruited during an 18-month period. All fulfilled the criteria for a diagnosis of vestibular neuritis, with acute-onset rotational vertigo lasting  $>24$  h. None of the patients had hearing loss, tinnitus, or a sensation of fullness of the ear, or any previous history of inner ear disease, and all were otherwise healthy. Table 1 gives the general data on the patients. Most patients had complete

unilateral vestibular lesions (100% canal paresis on bithermal calorics, with 44° and ice water). All subjects gave informed consent to participate in the study, after being informed about the rationale of the study and the methods, involving wearing a contact ring for ~5 min on the anaesthetized left eye. The study received approval of the local ethical committee.

## Coordinate frames

To describe the 3D velocity vectors of the eye and head, we used a right-handed, head-fixed 3D Cartesian coordinate system. When the head was in its reference position, upright and facing straight ahead, the *x*-axis, also known as the torsional rotation axis, of the coordinate system pointed forward in the horizontal plane (HOR); the *y*-, or vertical rotation, axis pointed left along the interaural line; and the *z*-, or horizontal rotation, axis pointed up, orthogonal to the HOR. In this coordinate system, the positive rotation directions in the three dimensions are clockwise, down and left, as seen from the subject's viewpoint.

The head was fixed in a helmet in a comfortable upright position. In this position the angle between Reid's stereotaxic HOR of the head (defined by the outer acoustic meatus and the lower orbital rim) and the earth-HOR was measured and ranged from 8° to 11° nose up. Coordinate transformations during data analysis put the eye velocity vectors during spontaneous nystagmus in stereotaxic coordinates for easier comparison with the anatomical data of Blanks *et al.* (1975).

## Vestibular stimuli and eye movement recording

The magnetic search coil technique (Robinson, 1963; Colleijn *et al.*, 1985; Ferman *et al.*, 1987) was used to measure 3D-angular positions of the left eye. The subject sat within a lightproof, 1.9-m diameter fibreglass bulb, firmly secured by belts, form-fitting vacuum cushions, bitebar and a helmet with an inflatable lining. The subject's head was at the centre of rotation of the chair. Three pairs of field coils, 1.4 m in diameter, were mounted in a cube-like configuration on the outer surface of the bulb. Three-dimensional position of the left eye was recorded at 100 Hz using a dual search coil: a silicone rubber ring containing two effectively orthogonal search coils that adheres to the sclera by suction (Ferman *et al.*, 1987).

Eye coils were calibrated in all three dimensions (horizontal, vertical, torsional) with a micrometre gimbal system, a small device that allowed precise positioning of the eye coil in all dimensions. Confirmatory calibrations in the horizontal and vertical dimensions were also carried out with the coil on the subject's eye before and after testing, by having the subject look to targets at known positions. During data recording, signals from the search coil were sent to a preamplifier and were then conveyed by slip rings to a decoding unit that computed and stored the 3D positions of the eye on hard disk. During off-line analysis, eye position

**Table 2** Expected normalized coordinates of spontaneous nystagmus direction for lesions of single or combined canals based on the stereotaxic coordinates of the canals (Blanks *et al.*, 1975)

Lesioned canal	E(T)	E(V)	E(H)	Lesioned canal	E(T)	E(V)	E(H)
lh	-0.365	0.158	-0.905	rh	0.365	0.158	0.905
la	-0.757	-0.561	0.320	ra	0.757	-0.561	-0.320
lp	-0.652	0.753	-0.017	rp	0.652	0.753	0.017
lh+la	-0.845	-0.304	-0.441	rh+ra	0.845	-0.304	0.441
lh+lp	-0.617	0.553	-0.560	rh+rp	0.617	0.553	0.560
la+lp	-0.969	0.132	0.208	ra+rp	0.969	0.132	-0.208
la+lp+lh	-0.931	0.184	-0.316	ra+rp+rh	0.931	0.184	0.316

E(T) = torsional eye velocity; E(V) = vertical eye velocity; E(H) = horizontal eye velocity; lh = left horizontal canal; la = left anterior canal; lp = left posterior canal; rh = right horizontal canal; ra = right anterior canal; rp = right posterior canal.

and angular velocity of the nystagmus slow phases were computed as described by Tweed *et al.* (1990).

In the first part of the experiment, spontaneous nystagmus was recorded in darkness for 1 min and the average slow phase eye velocity vector of spontaneous nystagmus was calculated. This vector was then expressed in stereotaxic head coordinates to see whether the nystagmus direction would align with the direction of a given healthy canal or the combined direction of healthy canals in the case of the lesion of more than one canal. These directions were calculated based on three assumptions. First, we assumed a simple vectorial addition of the actions of the six canals. Then, knowing the average stereotaxic orientation of the canals (Blanks *et al.*, 1975) and the fact that electrical stimulation of a single canal nerve in animals evokes eye movements roughly in the plane of that canal, we calculated the vector sum of the remaining canals when one or more canals on one side are missing. We calculated the expected vector of eye rotation for lesions of single afferents of one of the three canals on one side (i.e. left horizontal, left anterior and left posterior canals) or any combination of canals of one side. Finally, the calculated vectors were normalized (Table 2).

In the second part of the experiment, subjects were rotated sinusoidally at 0.3 Hz with an amplitude of  $\pm 20^\circ$  and a maximum speed of  $\sim 37.5^\circ \text{ s}^{-1}$  about fixed axes. At the beginning of the experiment, a visual target in the straight ahead position (a red light projected onto the inner surface of the bulb) was illuminated and subjects were instructed to try to maintain fixation on its remembered location, fixed in space, during the subsequent rotation in darkness. The rotation axes used in this study were body-vertical (for HOR rotation, stimulating mainly the horizontal canals) with the rotation axis earth-vertical, and in the idealized planes of the vertical canal. The latter stimulation axes were approximately orthogonal to the planes of the two vertical canal pairs, with the stimulation axis earth-horizontal and the head turned either  $45^\circ$  to the right [for pitch-roll rotation in the left anterior-right posterior semicircular canal plane (LARP), stimulating mainly the left anterior and right posterior canals] or  $45^\circ$  to the left [for right anterior-left posterior semicircular

canal plane (RALP) rotation, stimulating mainly the right anterior and left posterior canals].

For each subject, peak slow phase eye velocities for each direction were averaged over 20 s of consecutive sinusoidal stimulation. The control database of 10 subjects was used to determine the upper limits of normal asymmetries of vestibular responses for stimulation in the two directions for each canal pair. For this purpose we calculated the average maximum speeds (the length of the eye velocity vector) for the positive and negative directions ( $P$  and  $N$  in the equation below) about a rotation axis and defined the response asymmetry for that axis according to the formula:

$$|(P-N)/(P+N)| \quad (1)$$

In patients, positive and negative directions were first corrected for the amount of spontaneous nystagmus.

## Results

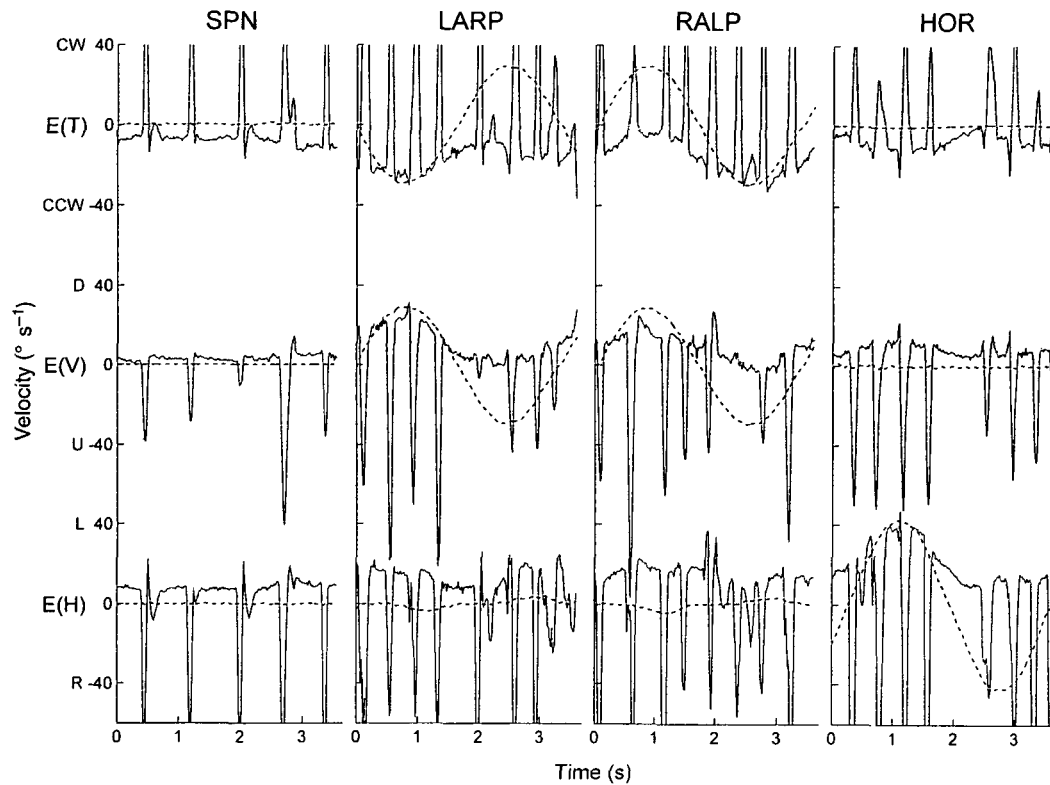
### Normal subjects

Normal subjects had no spontaneous nystagmus. Averaged across all normal subjects, VOR gain was about  $-0.4$  for the roll component, and about  $-0.7$  for yaw and pitch. In yaw, the average speed and standard deviation for excitation of the right horizontal SCC amounted to  $28.1 \pm 8.1^\circ \text{ s}^{-1}$  versus  $27.1 \pm 9.0^\circ \text{ s}^{-1}$  for excitation of the left horizontal SCC. In LARP, these values were for excitation of the right posterior SCC  $23.2 \pm 3.1^\circ \text{ s}^{-1}$  and of the left anterior SCC  $23.6 \pm 4.1^\circ \text{ s}^{-1}$ . Similar values were found for stimulation in RALP with  $22.2 \pm 4.9^\circ \text{ s}^{-1}$  for excitation of the right anterior and  $21.8 \pm 5.0^\circ \text{ s}^{-1}$  for excitation of the left posterior SCC. The average responses of the normal subjects were nearly symmetrical in all directions, with identical average asymmetry scores for all stimulation planes of  $0.05 \pm 0.05$ . According to the usual procedures we defined the upper limit of normal asymmetry as the average plus two SDs. Thus an asymmetry of  $>15\%$  was regarded as pathological.

### Patient data

#### Spontaneous nystagmus

Patients showed spontaneous nystagmus with horizontal-torsional components beating toward the good ear and a



**Fig. 1** Original data of a patient with a left-sided lesion (Number 11) 3 days after the onset of symptoms. Eye (continuous lines) and head (dashed lines) velocity data are plotted against time. Head velocity has been multiplied by  $-1$ .  $E(T)$ ,  $E(V)$  and  $E(H)$  are torsional, vertical and horizontal eye velocity; SPN = spontaneous nystagmus (no head movements); LARP, RALP and HOR indicate sinusoidal stimulation in the left anterior-right posterior canal plane, in the right anterior-left posterior plane, and in the horizontal plane. The left column shows considerable spontaneous nystagmus with the slow phases to the left, down and counterclockwise. As expected with a left-sided lesion, the horizontal VOR response was weaker for rotation toward the left and in the vertical canal planes for rotation toward the excitatory direction of the left anterior canal.

small upbeat component. Figure 1 shows individual responses of Patient 11 with a left-sided lesion 3 days after the onset of symptoms, which was the earliest measurement possible. Eye and head (dashed lines) velocity data are plotted against time, with torsional velocity in the first row, vertical in the second, and horizontal in the third. Columns indicate experimental conditions: the first shows spontaneous nystagmus, the second, third and fourth show responses to stimulation in the LARP, RALP and HOR planes. For comparison, head velocity traces are superimposed and multiplied by  $-1$  to reveal how well eye motion compensates for head motion. Figure 1 shows considerable spontaneous nystagmus, with slow phases left, down and counterclockwise. The VOR responses, as expected with a left-sided lesion, are weaker for rotation toward the left and, in the vertical canal planes, for rotation toward the excitatory direction of the left anterior canal.

Table 3 gives the three components of the average slow phase eye velocity vector of spontaneous nystagmus and the speed (i.e. the vector magnitude) for all subjects. The average speed for all patients was  $10.48 \pm 5.24^\circ \text{ s}^{-1}$ , ranging from  $3.94^\circ \text{ s}^{-1}$  to  $19.28^\circ \text{ s}^{-1}$ .

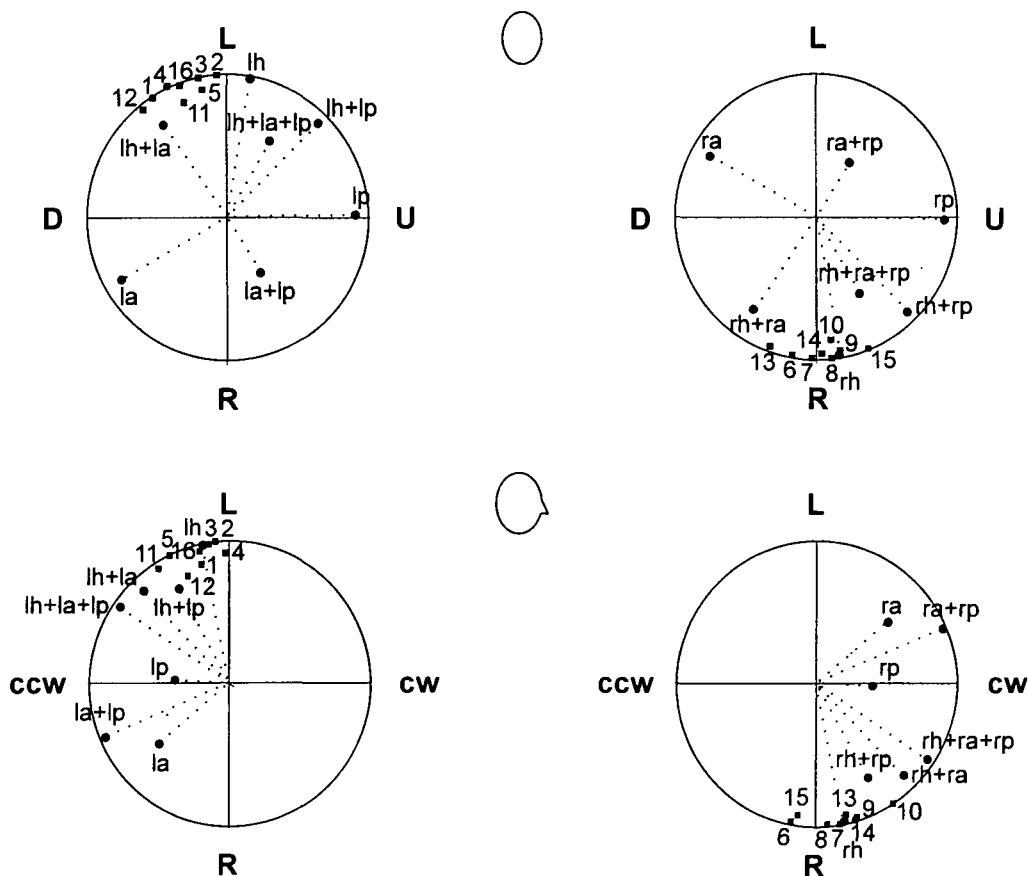
Figure 2 shows normalized average vectors of spontaneous nystagmus for all subjects, with left-sided lesions in the left column and right-sided lesions in the right column. To avoid clutter, only the tips of the vectors are shown (as filled squares). The upper row shows the projection of the vectors into the coronal plane as seen from behind, with the horizontal component on the ordinate and the vertical component on the abscissa; the lower row shows the projection into the sagittal plane seen from the right side, with the torsional component on the abscissa. Theoretical vectors, showing the eye velocities expected if one or more canals are missing, are also plotted, based on the data of Table 2 (filled circles connected to the origin with dotted lines).

In patients with left-sided lesions, the eye velocity vectors for spontaneous nystagmus clustered between the expected directions for a lesion of the left horizontal canal alone or a combined lesion of the left horizontal plus left anterior canals. Similarly, with right-sided lesions the spontaneous nystagmus directions clustered along the expected direction for the right horizontal canal or the right horizontal plus right anterior canals. In none of our patients did the spontaneous nystagmus direction indicate a combined lesion of the afferents of all

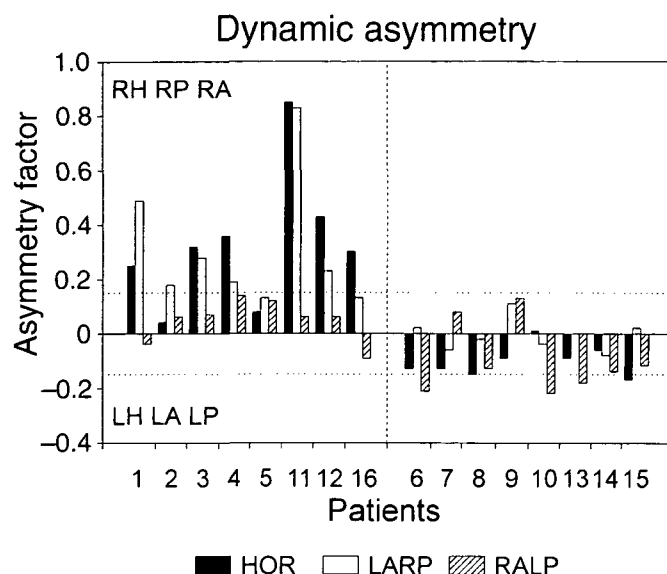
**Table 3** Spontaneous nystagmus velocity [ $^{\circ} s^{-1}$ ] on the first measurement day

Subject	Eye velocity			Vector magnitude	Normalized values		
	E(T)	E(V)	E(H)		E(T)	E(V)	E(H)
1	-2.30	5.98	9.66	11.59	-0.20	0.52	0.83
2	-0.39	0.29	4.05	4.07	-0.10	0.07	0.99
3	-0.85	1.07	5.31	5.49	-0.15	0.20	0.97
4	-0.13	1.74	3.78	4.17	-0.03	0.42	0.91
5	-4.46	1.77	9.23	10.40	-0.43	0.17	0.89
6	-0.72	0.65	-3.82	3.94	-0.18	0.16	-0.97
7	2.45	0.64	-16.38	16.89	0.15	0.04	-0.99
8	0.71	-1.04	-9.28	9.36	0.08	-0.11	-0.99
9	4.13	-2.40	-13.31	14.14	0.29	-0.17	-0.94
10	9.67	-1.92	-16.53	19.28	0.50	-0.11	-0.86
11	-7.96	4.67	12.48	15.52	-0.51	0.30	0.80
12	-2.42	4.69	5.99	7.99	-0.30	0.59	0.75
13	1.44	2.03	-5.65	6.17	0.23	0.33	-0.92
14	5.09	-1.86	-18.41	19.19	0.27	-0.04	-0.96
15	-1.17	3.30	-8.22	8.94	-0.13	0.37	-0.92
16	-1.50	2.37	6.57	7.14	-0.21	0.33	0.92

E(T) = torsional eye velocity; E(V) = vertical eye velocity; E(H) = horizontal eye velocity.



**Fig. 2** Two-dimensional projections of the normalized average vectors of spontaneous nystagmus. Data for left-sided lesions are shown in the left column and for right-sided lesions in the right column. To avoid clutter only the tips (filled squares) of the vectors are shown. Theoretical vectors (dotted lines with filled circles at the tip of the vector) depict eye axes expected if one or more canals are missing. The upper row shows a view from behind and the lower row a view from the right side. The vectors of the spontaneous nystagmus clustered between the expected directions for a lesion of the horizontal canal and a combined lesion of the horizontal plus ipsilesional anterior canal. In none of the patients did the spontaneous nystagmus direction indicate a combined lesion of the afferents of all canals on one side or a singular or combined lesion of the vertical canals. For abbreviations see footnote to Table 2.



**Fig. 3** Asymmetry values for the different stimulation planes for the patients with left-sided lesions (left half of the figure) and with right-sided lesions (right half). Dotted lines indicate the upper normal limit of 15%. Positive values indicate better responses when one of the right-sided canals was excited (as in patients with left-sided lesions). Most patients showed asymmetries with significantly smaller eye velocities for stimulation in HOR when the ipsilesional horizontal canal was excited and in the vertical canal planes when the ipsilesional anterior canal was excited.

canals on one side or a singular or combined lesion of just the vertical canals.

### Dynamic asymmetry

Dynamic asymmetries were quantified using Equation 1. Figure 3 shows the asymmetry values for the different stimulation planes. Patients with left-sided lesions are plotted in the left half of the figure, and those with right-sided lesions on the right. Dotted lines indicate the normal upper limit of 15% asymmetry, as determined from the normal data base. Positive values indicate larger responses when one of the right-sided canals were excited (as in patients with left-sided lesions).

Seven of the eight patients with left-sided lesions showed asymmetries, with significantly smaller eye velocities for stimulation in HOR when the left horizontal canal was excited (six patients) and for stimulation in LARP when the left anterior canal was excited (six patients). For stimulation in RALP, all patients with left-sided lesions except Numbers 1 and 16 showed a smaller response when the left posterior canal was excited, but the asymmetries were not significant. These data suggest that in patients with left-sided lesions the afferents from the posterior canal were spared. The small asymmetries in the RALP plane can be explained by the lesioned afferents from the left horizontal canal, since this canal, owing to its 3D orientation relative to the head,

normally contributes to the response when the left posterior canal is excited in RALP.

For right-sided lesions the pattern was less consistent. Only two of the eight patients showed significant asymmetry for rotations in HOR, both giving weaker responses when the right horizontal canal was excited. Three other patients had significant asymmetries in RALP, all giving weaker responses when the right anterior canal was excited. As with left-sided lesions, none of the patients with right-sided lesions showed a significant asymmetry when the ipsilesional posterior canal was excited. Thus, in the cases with significant dynamic asymmetries the analysis suggested a combined unilateral lesion of the afferents of the horizontal plus anterior canal or a lesion of just the anterior or horizontal canal on one side, while the afferents of the posterior canal seemed to be spared in all cases.

Sparing of the posterior canal afferents was confirmed in Patient 14, who had a right-sided lesion. Three weeks after the acute onset of vestibular neuritis, this patient developed the typical clinical signs of benign paroxysmal positional vertigo (brief episodes of rotational vertigo precipitated by rapid changes of head posture, e.g. rolling over in bed). When tested another 10 days later, she was still unresponsive to ice water calorics on the right side, indicating horizontal canal paresis. We recorded her nystagmus in complete darkness during and after Dix–Hallpike manoeuvres in LARP and RALP (Dix and Hallpike, 1952). Stimulation in LARP elicited, after a short latency of 2 s, a vigorous nystagmus with the slow phases counterclockwise, down, and rightward with maximum velocities of  $-36.85^\circ \text{ s}^{-1}$  for torsional eye velocity,  $69.90^\circ \text{ s}^{-1}$  for vertical eye velocity, and  $-6.73^\circ \text{ s}^{-1}$  for horizontal eye velocity, lasting  $\sim 25$  s. Stimulation in RALP did not elicit any positioning nystagmus. The eye velocity vector during maximal nystagmus was closely aligned with the axis of the right posterior SCC. Thus, it is almost certain that canalolithiasis of the right posterior canal caused the nystagmus. But to produce nystagmus, the afferents of this canal must have been intact to transmit the signal to the vestibular nuclei via the VOR to the oculomotor neurons.

### Discussion

This study uses non-invasive 3D VOR analysis to determine which SCC afferents are involved in acute vestibular neuritis. The analysis of spontaneous nystagmus direction and dynamic asymmetries for stimulation in the different SCC planes suggests that in our patients, the disease involved either the horizontal SCC alone, or, more often, the horizontal plus anterior SCC on one side.

### Static asymmetries after acute unilateral vestibular lesions

A sudden unilateral lesion of the peripheral vestibular system abolishes the tonic, or resting, activity in the vestibular nerve

on that side. The resulting imbalance between the two sides causes spontaneous nystagmus, since a difference between the firing rates of the two sides is the signal to the central vestibular system that the head is rotating. Consequently, the vestibulo-ocular reflex produces slow phase eye movements toward the side with the lower tonic firing rate, resulting in fast phases toward the good ear. Electrical stimulation of single SCC nerves in animals induces eye movements which are approximately in the plane of the canal (Suzuki and Cohen, 1964; Cohen *et al.*, 1966). Stimulation of more than one SCC produced eye movements roughly in a plane constructed by linear addition of the sensitivity vectors of the stimulated SCCs. This suggests vectorial addition of the sensory information originating from the six SCCs. Therefore, we hypothesized that the angular rotation axis of spontaneous nystagmus should reflect the vectorial addition of the remaining SCC afferents. In all our patients, the nystagmus directions clustered between the direction expected from a singular involvement of one horizontal SCC and the direction expected from a combined involvement of the horizontal plus anterior SCC on one side. None of our patients showed nystagmus directions that would suggest an involvement of the posterior SCC or a combined lesion of all canals on one side.

However, Böhmer *et al.* (1996) showed in a recent study of patients with partial vestibular neurectomy that, regardless of which part of the nerve was resected, the spontaneous nystagmus vector coincided closely with the vector of the horizontal SCC. Only the additional deafferentation of the ipsilateral posterior SCC in a patient who had undergone selective vestibular neurectomy of the superior vestibular nerve 16 years before (making the lesion a complete cochleo-vestibular neurectomy) introduced a vertical component into the nystagmus.

These unexpected findings were attributed by the authors to the differing properties of the VOR in the horizontal, vertical and torsional dimensions (Böhmer *et al.*, 1996), e.g. the torsional VOR has a lower gain than the horizontal or vertical (Berthoz *et al.*, 1981; Crawford and Vilis, 1991; Tweed *et al.*, 1994a) and the horizontal VOR has a longer time constant, i.e. it takes 15 s for a horizontal nystagmus induced by a step in head velocity to decay to 37% of its initial value, versus just 6 s for vertical and torsional (Tweed *et al.*, 1994b). Another factor may be that pitch and roll rotations, which are signalled by the vertical canals, usually cause rotation of the gravity vector, which would normally be sensed by the otoliths. Therefore pathological activity in the vertical SCC afferents would cause sensory conflict which might reduce the eye velocity generated. These factors may all enhance horizontal eye movement components (Raphan *et al.*, 1979) and may be the reason in the neurectomy cases that the eye rotation vector of spontaneous nystagmus was tilted toward the horizontal SCC vector. And finally, little is known about the direction of eye movements evoked by stimulation of the utricle and saccule. For example, each utricle encodes all linear acceleration directions in the

plane of the macula. It seems, however, that stimulation of the utricle mainly induces horizontal eye movements (Fernández and Goldberg, 1976). This may also increase the horizontal spontaneous nystagmus component, when the utricle is involved in the lesion.

Unlike these neurectomy findings, our data showed vertical nystagmus suggesting that the anterior canal was involved. This difference may have arisen because our patients suffered acute lesions to their previously normal vestibular systems. Thus, they had no long-term adaptation, unlike the neurectomy patients. Further, the neurectomy patients were sometimes measured several weeks after surgery, giving them time for postoperative adaptation.

### *Dynamic asymmetries after acute unilateral vestibular lesions*

The vestibular system is organized bilaterally, with the two sides inhibiting one another via the vestibular commissures. This arrangement allows each labyrinth to influence vestibular neurons on both sides of the brainstem (Shimazu and Precht, 1966; Markham *et al.*, 1977; Goldberg and Fernández, 1984). But despite this push-pull arrangement, loss of function in a canal will still produce weak VOR responses to head rotations in its on-direction. For example, if the left horizontal canal is lost, the right canal afferents can still signal leftward head rotation by reducing their activity. But as the speed of head rotation increases, these neurons will eventually reach inhibitory cut-off, i.e. their firing rates will hit zero, and so no further increase in speed can be signalled. This is Ewald's second law (Ewald, 1892). In monkeys, the average tonic firing rate of vestibular afferents is  $\sim 90$  spikes  $s^{-1}$  and the sensitivity is  $0.5$  spikes  $s^{-1} \text{ deg}^{-1} s^{-1}$  (Goldberg and Fernández, 1971), which means that a typical vestibular neuron is driven into inhibitory cutoff when rotation velocity exceeds  $\sim 180^\circ s^{-1}$  in its off-direction.

Why do we then observe asymmetric responses in our patients when maximum head velocity is only  $\sim 40^\circ s^{-1}$ ? One explanation may be that the tonic firing rates or sensitivities are lower in humans than in monkeys, as is suggested by the fact that spontaneous nystagmus in humans even after acute lesions rarely exceeds  $20\text{--}30^\circ s^{-1}$  (the maximum in our patient group was  $19^\circ s^{-1}$ ), while in monkeys after a unilateral labyrinthectomy it can reach  $54^\circ s^{-1}$  (Fetter and Zee, 1988).

Another explanation is that tonic firing on the intact side may be actively lowered by some adaptive mechanism in order to reduce spontaneous nystagmus (McCabe *et al.*, 1972). One piece of evidence is that even in unilaterally labyrinthectomized monkeys, spontaneous nystagmus is much slower than the  $180^\circ s^{-1}$  that would be expected if the intact side had a tonic firing rate of  $90$  spikes  $s^{-1}$  and the lesioned side were silent. This suggests that either the tonic firing on the lesioned side has been partially restored, or the tonic firing rate on the healthy side has been actively reduced. Several lines of evidence support the active reduction idea.

For example, Fetter and Zee (1988) showed that in some monkeys, spontaneous nystagmus velocity increased 6–10 days after a complete unilateral labyrinthectomy. This may reflect an increased imbalance due to a restoration of tonic activity in the vestibular nucleus on the intact side. Furthermore, in monkeys with acute unilateral lesions, ice water calorics on the intact side, which temporally silence the tonic activity on that side, stop the spontaneous nystagmus but do not reverse its direction as would be expected if there were any significant vestibular tone on the deafferented side (Fetter and Zee, 1988). Nystagmus begins to reverse in later stages of vestibular recovery, when tonic activity on the lesioned side has been restored. Likewise in all of our subjects with 100% unilateral canal paresis on calorics, ice water irrigation on the healthy side did not reverse the spontaneous nystagmus in the acute situation.

If tonic firing is low, inhibitory cut-off is reached at small head velocities, leading to dynamic asymmetries already at low head velocities, as seen in our subjects. On the other hand, higher head velocities would probably have shown even stronger asymmetries, and would likely be the only way to detect residual asymmetries in the later stages of recovery from the lesion. Future studies should therefore include high velocity head impulses to improve diagnostic sensitivity.

Why were our findings less consistent for right-sided than for left-sided lesions? One possible contributing factor is that we recorded only one eye, always the left, to minimize patient discomfort. Since the projections from any one canal to the right and left eyes are different, it would be useful to record from the right eye or binocularly.

Our finding that the posterior SCC afferents are spared in vestibular neuritis confirms a proposal by Büchele and Brandt (1988), who observed that some patients develop ipsilateral benign paroxysmal positioning nystagmus after a vestibular neuritis with persistent horizontal canal paresis on calorics, as in one of our patients. Since, in its classic form, benign paroxysmal positioning nystagmus is due to otolithic debris in the posterior SCC, it shows that the afferents from that canal are intact (Brandt and Steddin, 1993). While Büchele and Brandt (1988) concluded that vestibular neuritis might be predominantly or wholly a lesion of the afferents of one horizontal SCC, our data suggests that a combined lesion of the afferents of the anterior plus horizontal SCC on one side seems more likely in this disease.

The hypothesis of partial involvement of the vestibular nerve in vestibular neuritis is supported by the temporal bone pathology found by Schuknecht and Kitamura (1981) and also by the histopathology of a case of herpes zoster oticus (Proctor *et al.*, 1979). In the latter case the otoliths and the posterior SCC remained intact. The afferent bipolar ganglion cells of the vestibular nerve (Scarpa's ganglion) are arranged in two cell masses in a vertical column within the internal auditory canal, the superior group forming the superior division of the vestibular nerve and the inferior forming the inferior division (Lorente De N6, 1933; Sando *et al.*, 1972).

The superior division innervates the cristae of the anterior and horizontal canals, the macula of the utricle, and the anterosuperior part of the saccular macula. The inferior division innervates the crista of the posterior canal and the main portion of the macula of the sacculus. Thus inflammation confined to the superior division of the vestibular nerve could explain the above findings.

Alternatively, an explanation of these findings can be based on the vascular supply to the labyrinth (Lindsay and Hemenway, 1956). The anterior vestibular artery, a branch of the labyrinthine artery, supplies the utricle, the ampullae of the anterior and horizontal SCCs, and a small portion of the sacculus. The posterior vestibular artery, a branch from the common cochlear artery, supplies the inferior part of the sacculus and the ampulla of the posterior SCC. Thus an ischaemic event involving only the anterior vestibular artery would produce the same pattern of involvement as would lesions of the superior part of the vestibular nerve. Further, ischaemic degeneration of the utricular macula might release otolithic debris into the posterior canal, which could explain the high incidence of benign paroxysmal positioning nystagmus as a sequel to vestibular neuritis (Büchele and Brandt, 1988). Thus the pattern of SCC involvement found in this study is consistent with either a vascular or an infectious cause.

In conclusion, these data cannot distinguish whether the lesion is vascular or infectious, but they suggest that the superior division of the nerve is much more sensitive to insults than the inferior part. Regardless of the aetiology of the disease, our technique allows for non-invasive determination of which canals are involved in acute vestibular neuritis. This information may help in vestibular rehabilitation by revealing the exact planes of imbalance, so that patients can be specifically stimulated in the planes of those canals that need adaptation.

## Acknowledgements

We wish to thank Dr Douglas Tweed and Dr Thomas Haslwanter for helpful discussion and correction of the English. This research has been supported by the Deutsche Forschungsgemeinschaft: SFB 307-A2.

## References

- Berthoz A, Jones GM, Bégue AE. Differential visual adaptation of vertical canal-dependent vestibulo-ocular reflexes. *Exp Brain Res* 1981; 44: 19–26.
- Blanks RHI, Curthoys IS, Markham CH. Planar relationships of the semicircular canals in man. *Acta Otolaryngol (Stockh)* 1975; 80: 185–96.
- Böhmer A, Straumann D, Fetter M. Three-dimensional analysis of spontaneous nystagmus in peripheral vestibular lesions. *Ann Otol Rhinol Laryngol* 1996. In press.
- Brandt T, Steddin S. Current view of the mechanism of benign



- paroxysmal positioning vertigo: cupulolithiasis or canalolithiasis? [Review]. *J Vestib Res* 1993; 3: 373–82.
- Bücheler W, Brandt T. Vestibular neuritis—a horizontal semicircular canal paresis? [Review]. *Adv Otorhinolaryngol* 1988; 42: 157–61.
- Cohen B, Tokumasu K, Goto K. Semicircular canal nerve, eye and head movements: the effects of changes in initial eye and head position on the plane of the induced movement. *Arch Ophthalmol* 1966; 76: 523–31.
- Collewijn H, Van der Steen J, Ferman L, Jansen TC. Human ocular counterroll: assessment of static and dynamic properties from electromagnetic scleral coil recordings. *Exp Brain Res* 1985; 59: 185–96.
- Crawford JD, Vilis T. Axes of eye rotation and Listing's law during rotations of the head. *J Neurophysiol* 1991; 65: 407–23.
- Dix MR, Hallpike CS. The pathology, symptomatology and diagnosis of certain common disorders of the vestibular system. *Ann Otol Rhinol Lar* 1952; 6: 987–1016.
- Ewald R. Physiologische Untersuchungen ueber das Endorgan des Nervus Octavus. Wiesbaden: Bergmann, 1892.
- Ferman L, Collewijn H, Jansen TC, Van den Berg AV. Human gaze stability in the horizontal, vertical and torsional direction during voluntary head movements, evaluated with a three-dimensional scleral induction coil technique. *Vision Res* 1987; 27: 811–28.
- Fernández C, Goldberg JM. Physiology of peripheral neurons innervating otolith organs of the squirrel monkey. III. Response dynamics. *J Neurophysiol* 1976; 39: 996–1008.
- Fetter M, Zee DS. Recovery from unilateral labyrinthectomy in rhesus monkey. *J Neurophysiol* 1988; 59: 370–93.
- Goldberg JM, Fernández C. Physiology of peripheral neurons innervating semicircular canals of the squirrel monkey. I. Resting discharge and response to constant angular accelerations. *J Neurophysiol* 1971; 34: 635–60.
- Goldberg JM, Fernández C. The vestibular system. In: Brookhart JM, Mountcastle VB, editors. *Handbook of physiology*. Sect. 1, Vol. 3, Pt. 2. Bethesda (MD): American Physiological Society, 1984: 977–1022.
- Hallpike CS. The pathology and differential diagnosis of aural vertigo. *Proceedings of 4th International Congress on Otolaryngology*, Vol. 2. London: British Medical Association, 1949: 514.
- Lindsay JR, Hemenway WG. Postural vertigo due to unilateral sudden partial loss of vestibular function. *Ann Otol Rhinol Lar* 1956; 65: 692–706.
- Lorente De Nó R. Vestibulo-ocular reflex arc. *Arch Neurol Psychiatry* 1933; 30: 245–91.
- Markham CH, Yagi T, Curthoys IS. The contribution of the contralateral labyrinth to second order vestibular neuronal activity in the cat. *Brain Res* 1977; 138: 99–109.
- McCabe BF, Ryu JH, Sekitani T. Further experiments on vestibular compensation. *Laryngoscope* 1972; 82: 381–96.
- Nylén CO. Some cases of ocular nystagmus due to certain positions of the head. *Acta Otolaryngol (Stockh)* 1924; 6: 106–37.
- Proctor L, Perlman H, Lindsay J, Matz G. Acute vestibular paralysis in herpes zoster oticus. *Ann Otol Rhinol Laryngol* 1979; 88: 303–10.
- Raphan T, Matsuo V, Cohen B. Velocity storage in the vestibulo-ocular reflex arc (VOR). *Exp Brain Res* 1979; 35: 229–48.
- Robinson DA. A method of measuring eye movement using a scleral search coil in a magnetic field. *IEEE Trans Biomed Electronics* 1963; 10: 137–45.
- Ruttin B. Zur Differentialdiagnose der Labyrinth- und Hörnerkrankungen. *Zentbl Ohrenheilkunde* 1909; 57: 327–31.
- Sando I, Black FO, Hemenway WG. Spatial distribution of vestibular nerve in internal auditory canal. *Ann Otol Rhinol Laryngol* 1972; 81: 305–14.
- Schuknecht HF, Kitamura K. Vestibular neuritis. *Ann Otol Rhinol Laryngol* 1981; 90 Suppl 78: 1–19.
- Shimazu H, Precht W. Inhibition of central vestibular neurons from the contralateral labyrinth and its mediating pathway. *J Neurophysiol* 1966; 29: 467–92.
- Suzuki J, Cohen B. Head, eye, body and limb movements from semicircular canal nerves. *Experimental Neurology* 1964; 10: 393–405.
- Tweed D, Cadera W, Vilis T. Computing three-dimensional eye position quaternions and eye velocity from search coil signals. *Vision Res* 1990; 30: 97–110.
- Tweed D, Sievering D, Misslisch H, Fetter M, Zee D, Koenig E. Rotational kinematics of the human vestibuloocular reflex I. Gain matrices. *J Neurophysiol* 1994a; 72: 2467–79.
- Tweed D, Fetter M, Sievering D, Misslisch H, Koenig E. Rotational kinematics of the human vestibuloocular reflex. II. Velocity steps. *J Neurophysiol* 1994b; 72: 2480–9.

Received November 13, 1995. Accepted 29 December 1995