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Unilateral vestibular deafferentation causes permanent impairment of the human vertical vestibulo-ocular reflex in the pitch plane

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Abstract Rapid, passive, unpredictable, low-amplitude (10–20°), high-acceleration (3000–4000°/s^2) head rotations were used to study the vertical vestibulo-ocular reflex in the pitch plane (pitch-vVOR) after unilateral vestibular deafferentation. The results from 23 human subjects who had undergone therapeutic unilateral vestibular deafferentation were compared with those from 19 normals. All subjects were tested while seated in the upright position. Group means and two-tailed 95% confidence intervals are reported for the pitch-vVOR gains in normal and unilateral vestibular deafferented subjects. In normal subjects, at a head velocity of 125°/s the pitch-vVOR gains were: upward 0.89 ± 0.06, downward 0.91 ± 0.04. At a head velocity of 200°/s, the pitch-vVOR gains were: upward 0.92 ± 0.06, downward 0.96 ± 0.04. There was no significant up-down asymmetry. In the 15 unilateral vestibular deafferented subjects who were studied more than 1 year after unilateral vestibular deafferentation, the pitch-vVOR was significantly impaired. At a head velocity of 125°/s the pitch-vVOR gains were: upward 0.67 ± 0.11, downward 0.63 ± 0.07. At a head velocity of 200°/s, the pitch-vVOR gains were: upward 0.67 ± 0.07, downward 0.58 ± 0.06. There was no significant up-down asymmetry. The pitch-vVOR gain in unilateral vestibular deafferented subjects was significantly lower ($P < 0.05$) than the pitch-vVOR gain in normal subjects at the same head velocities. These results show that total, permanent unilateral loss of vestibular function produces a permanent symmetrical 30% (approximately) decrease in pitch-vVOR gain. This pitch-vVOR deficit is still present more than 1 year after deafferentation despite retinal slip velocities greater than 30°/s in response to head accelerations in the physiological range, indicating that compensation of pitch-vVOR function following unilateral vestibular deafferention remains incomplete.

Key words Vertical vestibulo-ocular reflex
Semicircular canals
Unilateral vestibular deafferentation · Human

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Introduction

The human vestibulo-ocular reflex maintains retinal image stability during rotations of the head by generating smooth, compensatory rotations of the eyes. While passive, high-acceleration head rotations in the pitch plane are important during locomotion (Grossman et al. 1988, 1989), research on the vertical vestibulo-ocular reflex (vVOR) in the pitch plane has been dominated by reports using low-frequency, low-velocity sinusoidal stimulation in humans (Allum et al. 1988; Baloh et al. 1983, 1986; Baloh and Demer 1991; Demer 1992) as well as in animals (Correia et al. 1984; Darlot et al. 1981; Matsuo and Cohen 1984; Tomko et al. 1987, 1988). Furthermore few studies have measured the deficits in pitch-vVOR following unilateral loss of vestibular function: in humans following surgical unilateral vestibular deafferentation (uVD) (Halmagyi et al. 1992) or following acute spontaneous peripheral vestibular paralysis (Allum et al. 1988); in monkeys after uVD (Chae et al. 1990). We have previously reported that the human horizontal vestibulo-ocular reflex shows a substantial asymmetrical deficit after uVD in response to high-acceleration stimulation (Halmagyi et al. 1990).

Previous investigators have reported an asymmetric pitch-vVOR in normal subjects, with the upward vVOR having a lower gain and time constant than the downward vVOR when using low-acceleration passive onside stimulation in cats (Tomko et al. 1988), monkeys (Matsuo and Cohen 1984) and humans (Baloh et al. 1983, 1986). In contrast Baloh and Demer (1991) reported

symmetrical vVOR gain in humans during both upright and onside low-acceleration active head rotations.

In this study we have measured the pitch-vVOR in uVD subjects, who have only one set of functioning vertical semicircular canals. The pitch-vVOR was characterised by the oculomotor responses to rapid, passive, unpredictable, low-amplitude, high-acceleration head rotations in the pitch plane. The velocity and acceleration of these head rotations were within the range normally encountered during locomotion (Grossman et al. 1988, 1989; Leigh and Brandt 1993). The results show a significant permanent residual deficit in pitch-vVOR following uVD, with no systematic up-down asymmetry. Preliminary data have been previously reported (Halmagyi et al. 1992).

Materials and methods

The recording system

Angular displacement of the head and eye in yaw and pitch were recorded using the search-coil technique (Robinson 1963) with two search coils (Skalar, Delft): one coil was worn on the subject's left eye and the other on the subject's head. The head coil used to measure angular displacement of the head was fixed to the nosepiece of a lightweight spectacle frame worn by the subject. Signals were recorded from the head and eye search coils while the subject was seated in the centre of a 2-m^3 transmitter coil field (CNC Engineering, Seattle).

The four angular displacement signals were recorded at 1000-Hz sampling frequency with 16-bit resolution and a bandwidth of 0–100 Hz by a PDP-11/73 computer. Data acquisition programs were written in DAOS running under the TSX-plus operating system. Position and velocity data was displayed in real time on Amiga 1000 computers under the control of the PDP-11/73. The PDP-11/73 also controlled an array of light-emitting diodes (LEDs) to provide feedback to the operator during the test. A fixation spot was produced by a solid-state red laser rear-projected via mirror galvanometers onto a screen 1 m from the subject. For calibration, the galvanometers could be driven horizontally and vertically by the PDP-11/73.

Calibration of the system

The head and eye coils were calibrated before the test session on a 25-cm-diameter three-axis Plexiglass gimbal. Both coils were mounted on the gimbal to approximate their respective positions on the subject's left eye and on the the bridge of the subject's nose. Calibrations were performed in 5° steps over the range $\pm 30°$ in yaw and in pitch. The gain of the search-coil system was adjusted to match the analogue-to-digital converter range to the calibration range.

Subjects

We studied 19 normal subjects (21–55 years, mean 32.8 years) and 23 unilateral vestibular deafferented (uVD) subjects (18–73 years, mean 49.9 years). The normal subjects had no signs of vestibular disease. The 23 (12 left and 11 right) uVD subjects had undergone unilateral vestibular deafferentation either during surgical removal of an acoustic neuroma (11) or as treatment for Ménière's disease (8) or other types of intractable vertigo (4). One subject had bilateral vestibular deafferentation (VD) 8 years previously, during removal of bilateral acoustic neuromas, and therefore had no vestibular function. He was studied to ensure that the compensatory eye rotation in response to head impulses measured were of vestibular origin. The uVD subjects were studied from 1 month to 15 years (mean 2.3) after operation. Three uVD subjects were tested before and after surgery. Fifteen of the 23 uVD subjects were studied more than 1 year after deafferentation (mean 3.4 years); 8 uVD subjects were tested less than 6 months after deafferentation and 9 uVD subjects were tested more than 2 years after deafferentation. All the normal and uVD subjects gave informed consent and all protocols were approved by the Royal Prince Alfred Hospital Human Ethics Committee.

Experimental design

Each subject was seated in the centre of the magnetic coil fields. For initial alignment and calibration, the head was secured in a head holder with a chin rest. The height and position of the subject's left eye was adjusted to ensure that it was in the centre of the 2-m^3 coil field and 1 m from the screen on which the target was rear-projected. The head-coil offset was measured in this position and this became the zero reference position of the head. In vivo eye coil calibration was performed with the subject fixating on a 2-mm red laser target spot rear projected on the tangent screen. The target was moved through a range of $\pm 20°$ at 5° intervals in yaw or pitch. A linear regression analysis was carried out on-line to measure the gain and offset of the coil and the correlation coefficient of the calibrations. The calibrations were considered satisfactory if the on-line displays of the calibrations did not show any artifacts such as blinks or saccades and the correlation coefficient of the linear regression analysis was 0.99.

The computer created a software window of $\pm 1.5°$ in yaw and in pitch relative to the reference position of the head. A head "impulse" was a rapid, passive, unpredictable, low-amplitude (10–20°), high-acceleration head rotation (3000–4000°/s^2) in one of four directions: rightwards, leftwards, upwards or downwards. The start of the data acquisition was permitted only when the pitch and yaw head coil offsets were within the software window and the operator was prompted by the computer to deliver the impulse. This kept the head close to the reference head position before the head impulse. The operator stood behind the subject, held the subject's head and delivered a rapid, passive, unpredictable, angular head displacement of 10–20° in yaw or pitch while the subject fixated on the target. For each subject, at least 20 yaw (10 rightward and 10 leftward) and 20 pitch (10 upward and 10 downward) head impulses were recorded. After each trial, the computer checked head position and velocity and rejected the impulse if the maximum head position was greater than 30° or peak head velocity was less than 100°/s. The head impulse was unpredictable in timing as well as in direction to prevent the subject from making anticipatory eye movements. The peak head velocity ranged from 150–250°/s and the peak acceleration from 2000–4000°/s^2.

Data analysis

The data was analysed off-line using DAOS on a PDP-11/73 and Splus, a statistical analysis and display package (Becker et al. 1988) on a DECstation 5000/240 under Unix. To derive eye position with respect to head position, the computer program subtracted head position from gaze position (the eye-coil signal which represented the eye's orientation with respect to space), in both yaw and pitch. For purposes of comparison and display, eye position with respect to head position was inverted. Since these impulses were delivered by hand they were variable. Therefore, we defined criteria for selecting comparable stimuli across the subject population. The stimuli had to be monotonic head-velocity waveforms, with a peak head velocity greater than 100°/s and a peak head acceleration greater than 2000°/s^2 within 90 ms of onset. Data were excluded *only on the basis of these stimulus criteria and not on any response characteristics.*

We restricted our measurements to an interval of 100 ms, beginning 10 ms before the onset of head rotation to minimise the

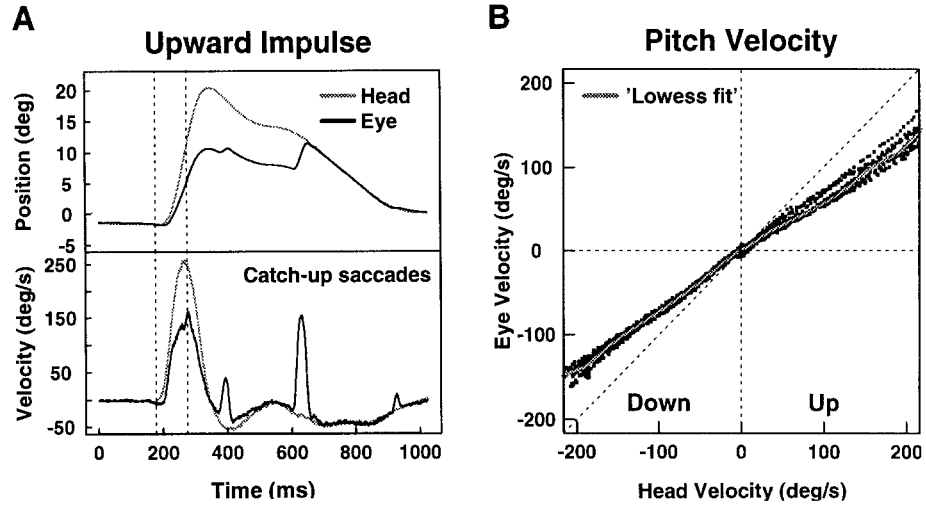
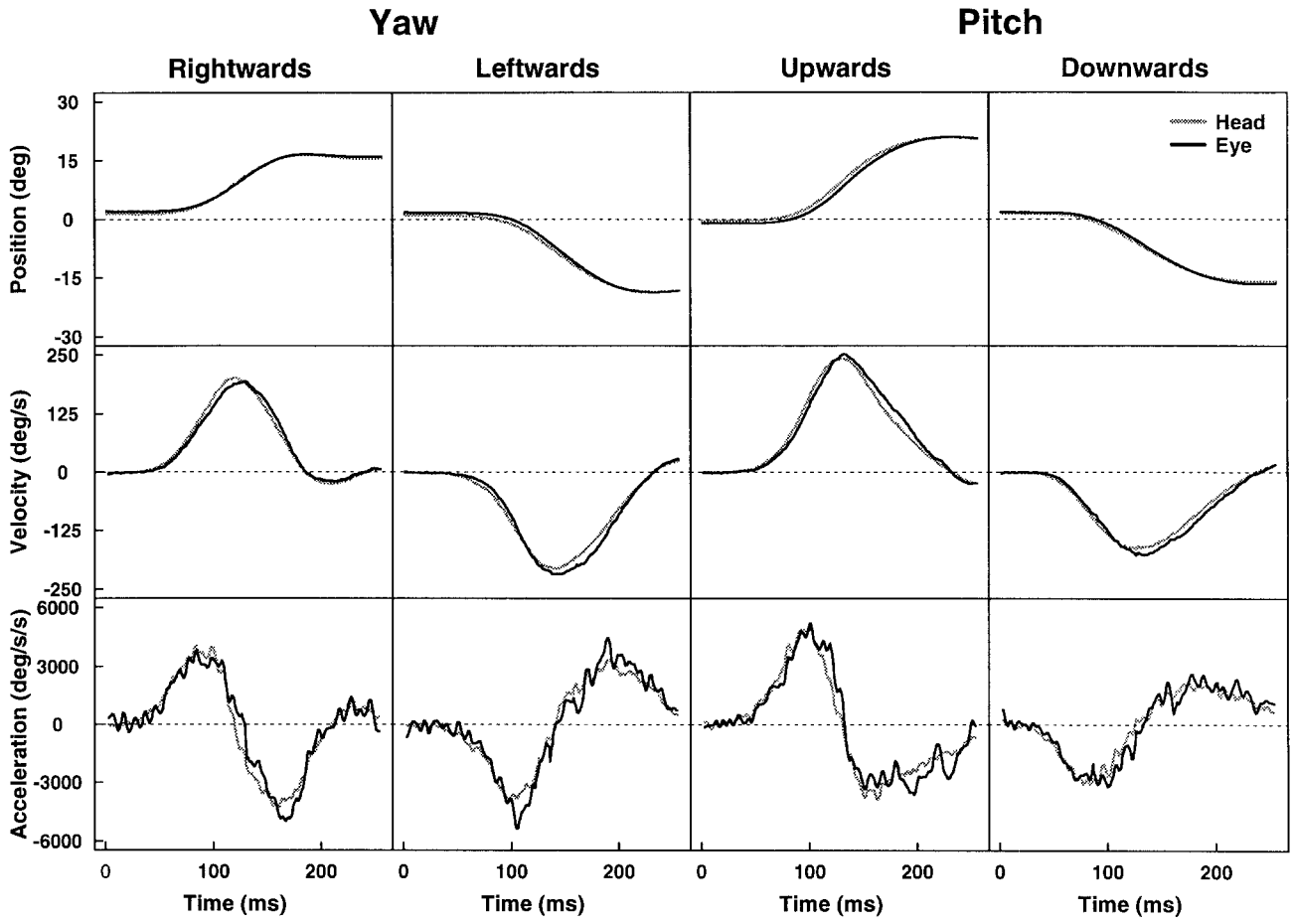


Fig. 1 **A** Position and velocity of an upward pitch head impulse 6 months after left vestibular neurectomy. The eye signals are inverted. The data between the *dotted lines* represents an interval of 100 ms, from 10 ms before onset of head impulse. This is the interval used in all subsequent data analysis. Note the two catch-up saccades which occur about 200 ms and 400 ms after the onset of the head impulse. **B** Eye velocity as a function of head velocity with the "lowess fit" (*grey*) for ten head impulses in each direction of the type shown in Fig. 1A



potential contribution of compensatory eye rotations from extravestibular sources such as cervico-ocular reflex and pursuit and optokinetic drives. Identification of the onset of each head impulse was achieved by using an in-house computer program in which the algorithm initially identified the peak head velocity in the direction the head impulse was delivered, then identified the point before the peak head velocity where the head velocity is 40°/s. From this point it checked to ensure that the head velocity before this point was between −10 and 40°/s for a period of 50 ms to detect any artefacts due to blinks. The point at which the head velocity was 0°/s was then taken to be the onset of the head impulse. To ensure that there were no undetected artefacts, the

Fig. 2 Compensatory eye rotation responses to single head impulses in four different directions: rightwards and leftwards in yaw, upwards and downwards in pitch, from a normal subject. The eye signals are inverted. The head and eye position, velocity and acceleration are displayed for each direction of the head impulse. Eye rotation responses closely mirror head rotations

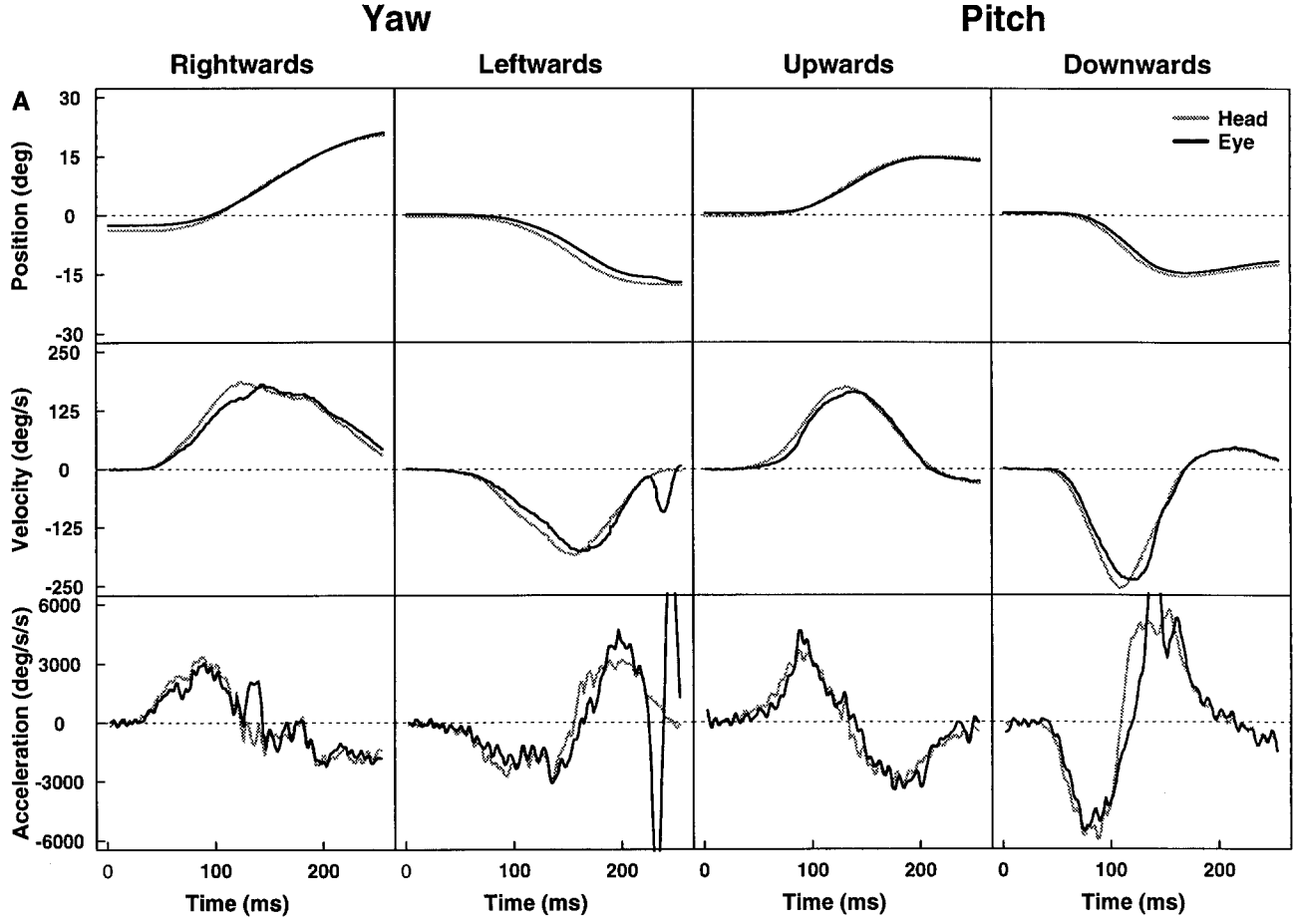
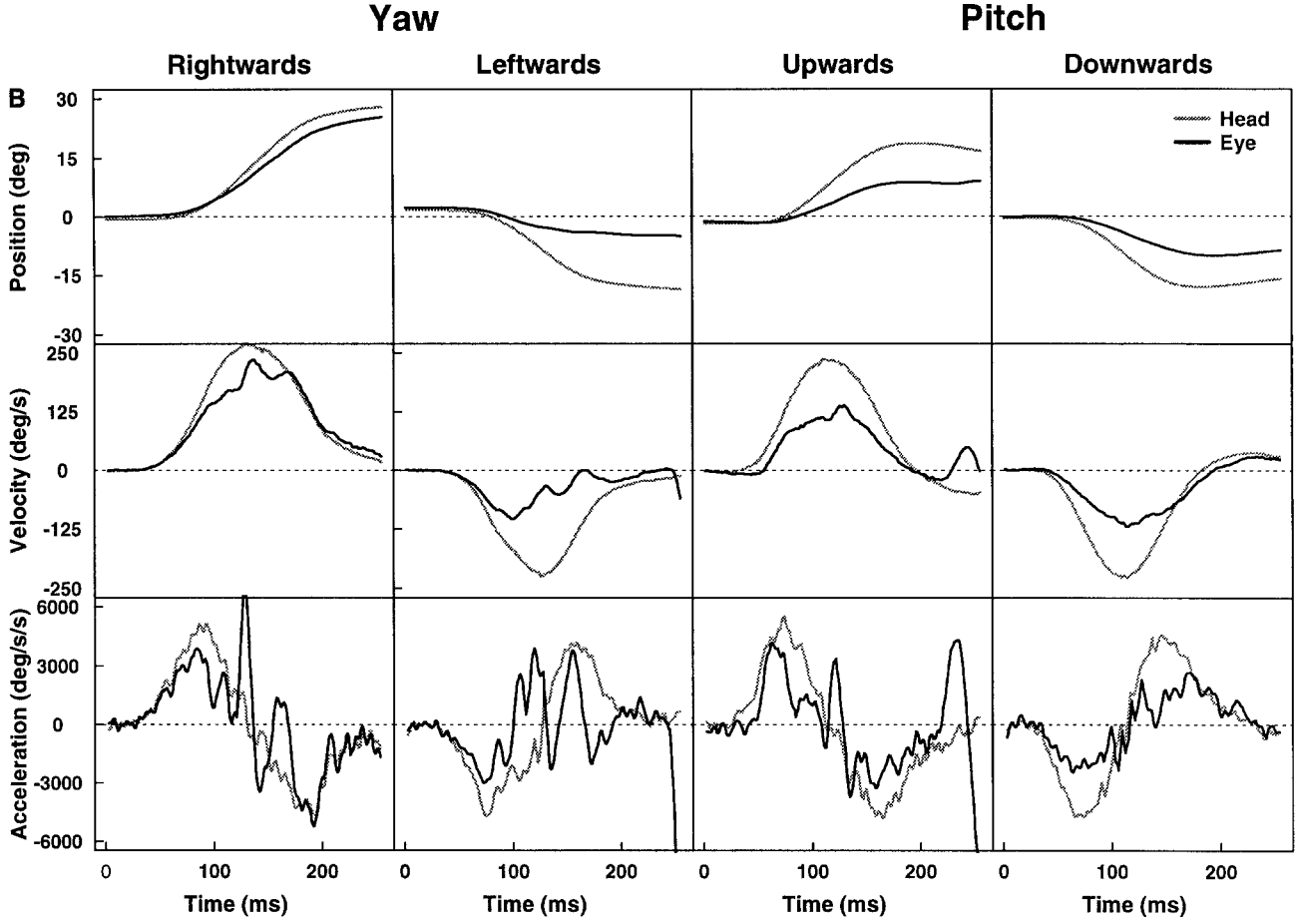


Fig. 3 **A** Compensatory eye rotation responses to single head impulses from a subject before vestibular deafferentation. The eye signals are inverted. Eye rotation responses closely mirror head rotations. **B** Compensatory eye rotation responses to single head impulses from a subject after left vestibular deafferentation. The eye signals are inverted. Compensatory eye rotations show deficits in each direction

position, velocity and acceleration plots of every head impulse and its corresponding eye response was visually inspected. An interval of 100 ms in each trial beginning 10 ms before the onset of the head impulse was then marked with dotted lines, as shown in Fig. 1A. Using this sampling window, we excluded the cervico-ocular reflex, which has a latency of more than 100 ms (Bronstein and Hood 1986), and pursuit, which has a latency of about 100 ms (Carl and Gellman 1987).

For each impulse, the data was plotted both as a time series: position, velocity and acceleration, and also as plots of eye velocity as a function of head velocity. Velocity was obtained by differentiation of position using a two-point central difference digital differentiation method with a bandwidth of 0–221 Hz (Bahill et al. 1982). The two-point central difference algorithm has no phase shift, so position, velocity, and acceleration records are temporally aligned. We did not desaccade the compensatory eye velocity data because there were no saccades in the first 100 ms of the data, as these saccades usually occur 150–200 ms after onset of a head impulse. In every subject, six impulses were chosen from each of the four directions by visual inspection to ensure that the head velocity profiles and the peak head velocities were comparable. The mean head and eye velocities were determined from these six matched head impulses from each subject. Because mean peak head velocity ranged from 150 to 300°/s, we chose 12 uVD subjects with comparable peak head velocities by visual inspection for the time-series graphs.Again we stress that stimulus *not* response characteristics were the basis for data selection. To calculate acceleration, mean head and eye velocities were digitally differentiated with the two-point central difference digital differentiation method. An Splus program calculated the group means and two-tailed 95% confidence intervals (CI) with n–1 degrees of freedom on the velocity and acceleration data.

In the plots of eye velocity as a function of head velocity, the mean eye velocity response as a function of head velocity was obtained by computing a polynomial fit to ten eye velocity responses in each direction using the lowess procedure in Splus (Fig. 1B). We refer to this polynomial fit as the "lowess fit". The lowess procedure uses a robust locally weighted regression algorithm for smoothing a scatterplot, (x_i, y_i), $i = 1, ...n$, in which the fitted value at x_k is the value of a polynomial fit to the data using weighted least squares, where the weight for (x_i, y_i) is large if x_i is close to x_k and small if it is not. This procedure guards against deviant points distorting the smoothed points (Cleveland 1979). The following parameters were used during the lowess procedure: fraction of data used for smoothing, 0.02; iterations, 3. Identical abscissa values were estimated independently. Because this procedure did not return eye velocity values at equally spaced head-velocity increments, a cubic spline procedure then interpolated through the data points to return eye velocity data at every 1°/s head velocity step. Eye and head velocity group means and 95% CI for every 1°/s head velocity step were calculated for normal and uVD subjects. For purposes of comparison between groups and to avoid computational artefacts such as noise, which might occur early in the response due to division by very small values, we used two arbitrary data points (the eye velocity at head velocity of 125°/s and 200°/s).



Statistical analysis

The statistical analysis used on the data was group means $\pm$ two-tailed 95% confidence intervals (CI) with $n-1$ degrees of freedom. The student's t-test for differences between two means of independent observations was used to compared the normal and uVD subjects. The t-test with dependent observations was used to test for: (1) asymmetry between upward and downward pitch-vVOR gain; (2) the difference between tests with and without visual fixation; (3) the difference in velocity between the head coil on the spectacle frame and a bite-bar during pitch head impulses. The significance level of $P=0.05$ was used in the data analysis (Winer et al. 1991).

Potential artefacts due to head and eye coil translations

As the stimulus was a combination of rotation and translation of the head and eye coils, we measured the effects of translation during rotation of the search coils. Two calibrated search coils were mounted on the gimbal, one on the axis of rotation, the other in a position approximating the position of the head coil in vivo. The first coil underwent pure rotation and the second coil underwent rotation with translation. Both the coils were rotated simultaneously through a range of $\pm 30°$ in 5° steps and the voltage outputs were measured. We verified that head and eye coil translations during the pitch head impulse were within the range of ± 5 cm for a maximum range of $\pm 30°$ of head pitch. The maximum error was 0.3° for a search coil translation of ± 5 cm over $\pm 30°$ angle of coil rotation.

Potential artefacts due to head coil inertia

We measured the possible errors due to the inertia of the head coil mounted on the spectacle frame during pitch head impulses in seven normal subjects. The subjects wore a scleral search coil mounted onto a bite-bar at 2 cm in front of the spectacle mounted head coil. The bite-bar was held firmly in the subject's mouth using a dental mould (GC Hydrophilic Exaflex). The respective head coil velocities from the bite-bar and the spectacle frame were calculated using the method described for obtaining head velocity (see Data analysis, above). The head coil velocities from the spectacle frame were not significantly different ($P>0.05$) from the head coil velocities from the bite-bar at 125°/s and at 200°/s.

Potential artefacts due to visual fixation

The testing of all subjects was conducted in dim lighting conditions. To ensure that the presence of a fixation light did not affect the results, five normal subjects were tested using the same paradigm, first in dim light, then in complete darkness. During the test in complete darkness, the target was extinguished just before the start of each data acquisition trial of 1024 ms duration and approximately 200–300 ms before the onset of the head impulse, so that the head impulse was delivered in complete darkness. The target was turned on immediately at the end of each individual data acquisition trial. A lowess fit (see Data analysis) of the eye velocity as a function of head velocity was calculated for each subject. At head velocity of 125°/s, the mean difference between eye velocity response tested in darkness and in dim light were: downward 0.99 ± 4.99°/s and upward 0.66 ± 12.735°/s. There was no significant difference ($P>0.05$) between eye velocity response at head velocity of 125°/s, tested in darkness and in dim light.

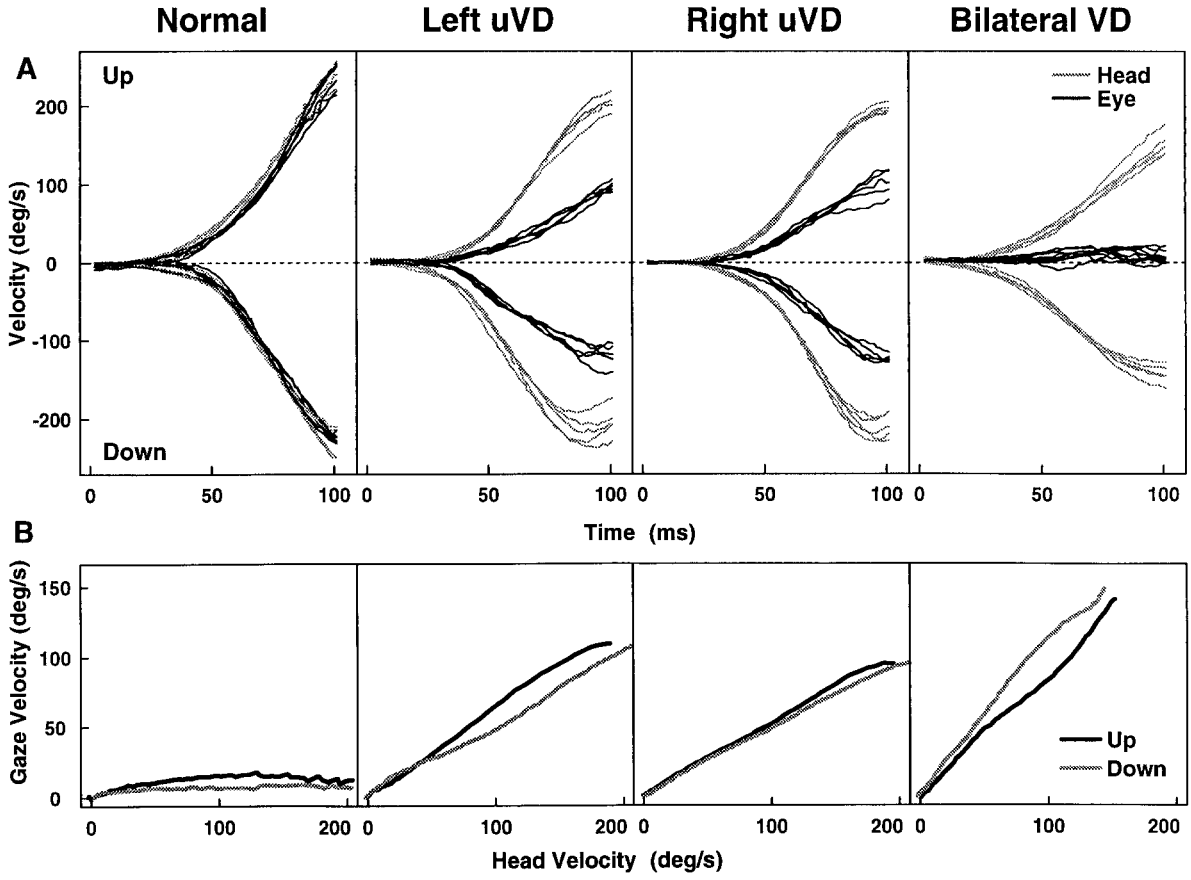


Fig. 4 **A** Superimposition of eye and head velocity traces to 12 (6 upward and 6 downward) pitch head impulses from one normal subject, one left and one right unilateral vestibular deafferented (*uVD*) subject and one bilateral vestibular deafferentated (*VD*) subject. The eye signals are inverted. There is a significant deficit of vertical vestibulo-ocular reflex in the pitch plane (pitch-vVOR) in the left and right uVD subjects and absence of vestibular response in the bilateral VD subject. **B** Graph of mean gaze velocity as a function of mean head velocity for each subject. Note that at a mean head velocity of 125°/s the left and right uVD subjects have mean gaze velocities of about 60°/s, while the bilateral VD subject has mean gaze velocities greater than 100°/s

Results

Normal subjects

Typical head impulses and compensatory eye rotation responses in four different directions: rightwards and leftwards in yaw, upwards and downwards in pitch, from a normal subject, are shown in Fig. 2. The eye signals were inverted for illustration. In normal subjects, compensatory eye rotation responses closely match the head impulse stimuli in position, velocity and acceleration profiles.

Pre- and post-operative vestibulo-ocular reflex responses of a left uVD subject

Pre-operative data from a subject who subsequently underwent left uVD is shown in Fig. 3A. This subject's pre-operative horizontal vestibulo-ocular reflex (hVOR) and pitch-vVOR gains were within the 95% CI of the normal subjects. The patient had a left hearing loss with no loss of lateral semicircular canal function due to an acoustic neuroma. The compensatory eye rotation responses matched the head impulse stimuli in position, velocity and acceleration profiles; they were indistinguishable from those of normal subjects.

Following uVD there was a marked asymmetry in the hVOR: Fig. 3B shows that when the head was rotated to the intact side (rightwards) in the yaw plane, the compensatory eye response was slightly decreased. However, when the head was rotated towards the side of the deafferentation (leftwards), the compensatory eye rotation response had a significantly lower velocity and acceleration than the head stimulus; consequently eye position lagged behind the head position. During upward or downward pitch head impulses, compensatory eye velocity and acceleration were significantly less than the head velocity and acceleration, resulting in a large eye position error during both upward and downward head impulses. The results from this subject were similar to the data averaged across all subjects.

Pitch eye velocity responses of normal, left and right uVD, and bilateral VD subjects

Twelve (6 upward and 6 downward) pitch head impulse stimuli and eye rotation responses from a normal subject, from a left uVD subject, a right uVD subject and a bilateral VD subject are shown in Fig. 4A. Figure 4B shows their mean gaze velocity as a function of mean head velocity. In order to compare these results we chose to report the mean pitch-vVOR gain at a high head velocity. In the normal subject, the compensatory eye velocity closely mirrors the head velocity from the onset to peak during every impulse: at a mean head velocity of 125°/s, mean gaze velocity and pitch-vVOR gain were: upward 16.3°/s and 0.87, downward 6.3°/s and 0.95. However, in both the left uVD and right uVD subjects, the compensatory eye velocity was much less than the head velocity from onset of the head impulse to peak head velocity resulting in a large gaze velocity. At the same mean head velocity of 125°/s, mean gaze velocity and pitch-vVOR gain for the left uVD subject were: upward 81.3°/s and 0.35, downward 63.8°/s and 0.49; and for the right uVD subject were: upward 66.3°/s and 0.47, downward 61.3°/s and 0.51. The results from the bilateral VD subject showed that there was no consistent compensatory eye rotation response to any of the head impulses. At the same head velocity of 125°/s, the mean gaze velocity was very high and the mean pitch-vVOR gain was very low: upward 105.0°/s and 0.16, downward 118.8°/s and 0.05.

Yaw and pitch eye velocity responses in uVD subjects

Figure 5 illustrates the mean head velocity stimulus and eye velocity response in yaw and in pitch for each of a group of 12 uVD subjects (6 left and 6 right). Each mean was based on six trials, which were selected so that the head velocity profiles were as similar as possible. The data from the yaw head impulses in the group of left uVD subjects was inverted to show the responses as ipsilesional or contralesional. Group means $\pm 95\%$ CI are shown for head and eye velocities (Fig. 5B). At a mean head velocity of 125°/s the compensatory eye velocities for each direction were: ipsilesion 44.6 ± 11.2°/s, contralesion 83.4 ± 13.2°/s; upward 77.8 ± 12.1°/s, downward 83.3 ± 9.2°/s. The decrease in ipsilesional and contralesional hVOR gain was statistically significant ($P < 0.05$, $t = 2.20$, two-tailed, $df = 11$). The decrease in mean pitch-vVOR gain for responses to both upward and downward head impulses in pitch was statistically significant ($P < 0.05$, $t = 2.20$, two-tailed, $df = 11$). Figure 5C shows mean gaze velocity during ipsilesion, contralesion, upward and downward head rotation. At a mean head velocity of 125°/s, the mean gaze velocities were: ipsilesion 80.6 ± 6.8°/s, contralesion 41.1 ± 1.6°/s; upward 47.9 ± 7.3°/s, downward 43.9 ± 3.8°/s (group means $\pm 95\%$ CI).

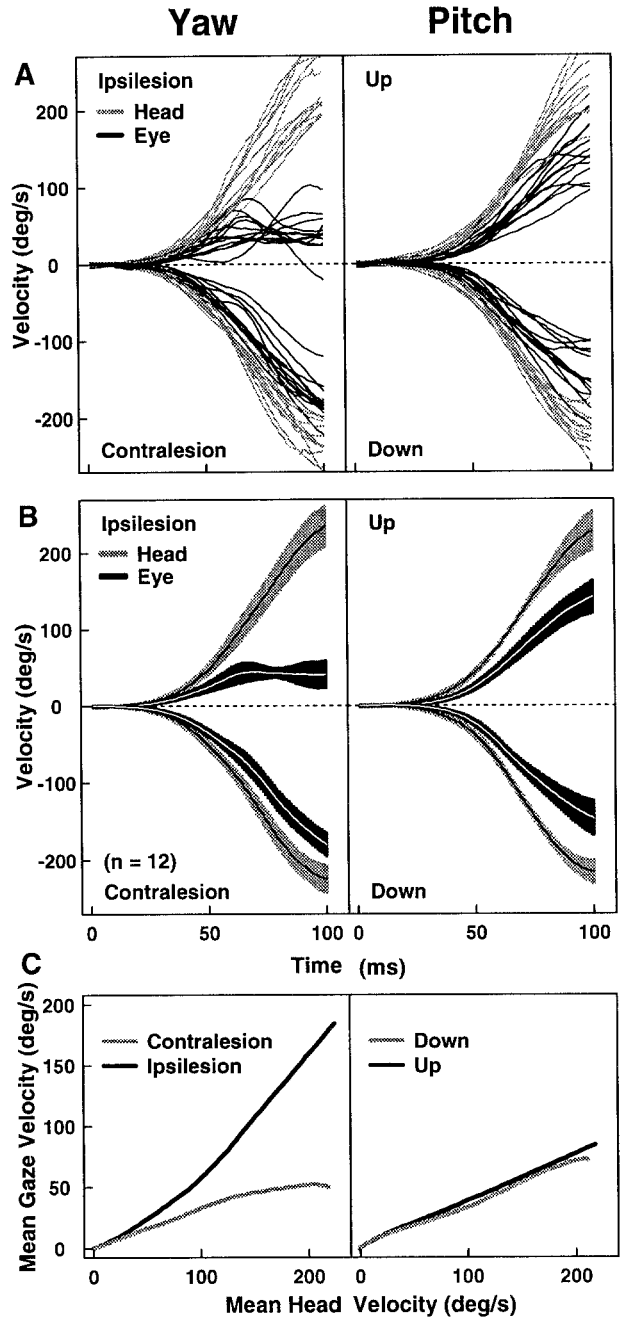


Fig. 5 **A** Superimposed head and eye velocity traces from 12 (6 right and 6 left) unilateral vestibular deafferented (uVD) subjects. The eye signals are inverted. Each mean velocity is based on six head impulses. The data from the yaw head impulses in the 6 left uVD subjects has been inverted to show the responses as "ipsilesion" or "contralesion". **B** Group means and two-tailed 95% confidence intervals of the velocity data across these 12 uVD subjects and **C** mean gaze velocity as a function of mean head velocity. There is a severe deficit in the ipsilesion yaw horizontal vestibulo-ocular (hVOR) and a mild deficit in the contralesion yaw hVOR as previously reported (Halmagyi et al. 1990). During pitch impulses, there is a moderately severe, symmetrical pitch-vVOR deficit

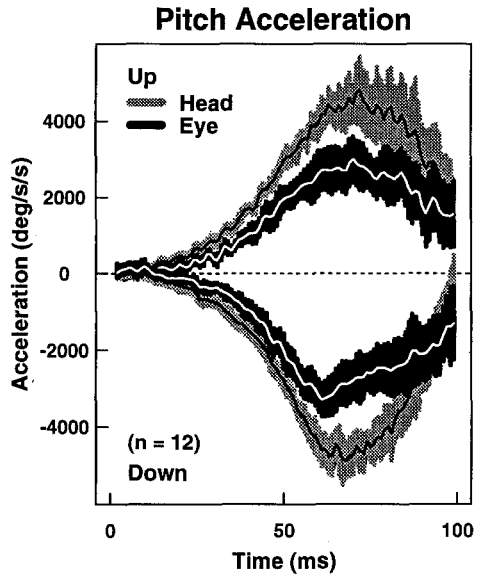


Fig. 6 Group means and two-tailed 95% confidence intervals of vertical head and eye accelerations of the pitch-vertical vestibulo-ocular reflex (vVOR) from the group of 12 (6 left and 6 right) unilateral vestibular deafferented subjects shown in Fig. 5. There is a significant deficit in pitch-vVOR

Fig. 7A–C Mean eye velocity as a function of head velocity in **A** 18 normal subjects and in **B** 15 unilateral vestibular deafferented subjects tested more than 1 year after unilateral vestibular deafferentation; **C** shows group means and two-tailed 95% confidence intervals (*C.I.*) of both these groups. There is a moderately severe, symmetrical pitch-vVOR deficit

Pitch eye acceleration responses in uVD subjects

Group means ±95% CI of vertical head and eye accelerations in pitch are shown in Fig. 6A. The mean head acceleration in this group of subjects was more than 4000°/s² during the head impulses; the eye acceleration response was much lower than the head acceleration for both upward and downward head impulses. At a mean head acceleration of 2700°/s² the mean pitch-vVOR acceleration gains were: upward 0.67±0.09, downward 0.67±0.08. The compensatory eye acceleration at mean head acceleration of 2700°/s² during upward and downward head impulses in these uVD subjects was significantly different ($P<0.05$) from that in normal subjects.

Eye velocity as a function of head velocity in normal and uVD subjects

The velocity data from normal and from uVD subjects tested at 1 year or more after deafferentation were analysed and displayed as each individual's average eye velocity as a function of head velocity (Fig. 7). The grey lines in Fig. 7 represent the mean eye velocity reponses from 18 normal subjects and the black lines represent the responses from 15 (8 left and 7 right) uVD subjects. The right panel of Fig. 7 and Table 1 show the group means ±95% CI of normal and uVD subjects.

The mean pitch-vVOR gains for upward and downward head impulses were significantly lower ($P<0.05$)

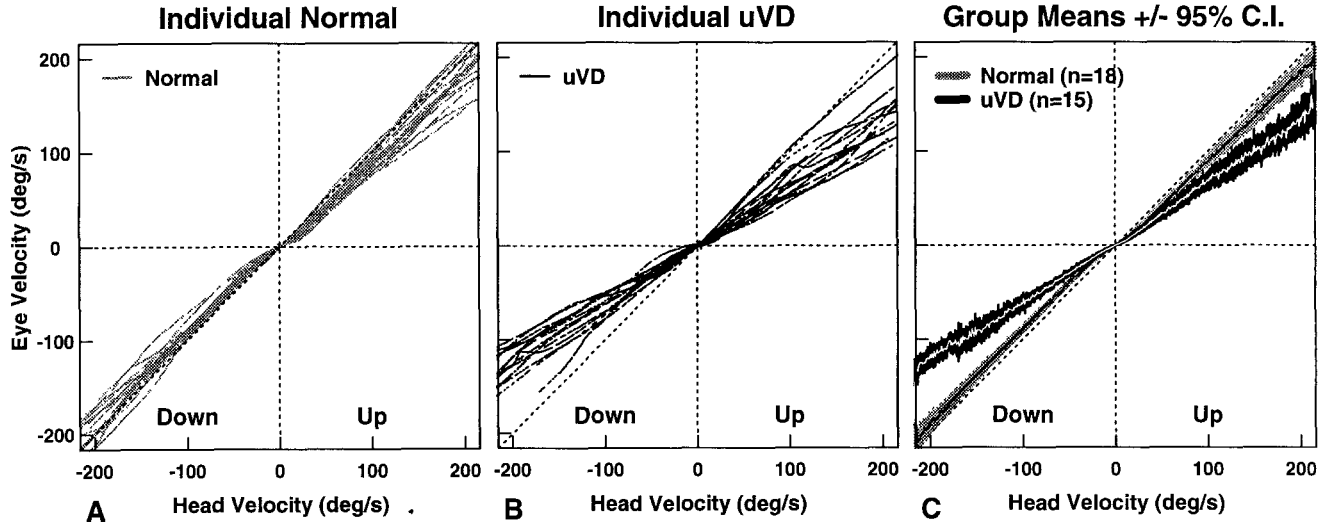


Table 1 Eye velocity as a function of head velocity. Group means ±95% confidence intervals of normal subjects and patients after unilateral vestibular deafferentation (*uVD*). (*vVOR* Vertical vestibulo-ocular reflex)

Subjects	Head velocity (°/s)	Upward		Downward	
		Eye velocity (°/s)	vVOR Gain	Eye velocity (°/s)	vVOR Gain
Normal ($n=18$)	125.0	111.4±7.1	0.89±0.06	113.9±5.1	0.91±0.04
	200.0	184.2±12.0	0.92±0.06	191.7±8.8	0.96±0.04
uVD ($n=15$)	125.0	83.9±8.5	0.67±0.11	78.5±8.5	0.63 ±0.07
	200.0	134.2±14.3	0.67±0.07	116.8±12.6	0.58±0.06

in uVD subjects than in normal subjects. The mean pitch-vVOR gain of the eight uVD subjects tested less than 6 months after uVD was not significantly different ($P > 0.05$) from the nine uVD subjects tested more than 24 months after uVD. The results show that unilateral loss of vestibular function produced a symmetrical deficit in pitch-vVOR gain of about 30%. The deficit was still present in the 15 uVD subjects tested more than 1 year after deafferentation.

The data showed that pitch-vVOR gain for upward and downward head impulses was symmetrical in both normal and uVD subjects. The mean difference between upward and downward pitch-vVOR gains at a head velocity of 125°/s was 0.0125 ± 0.0631 in normal subjects and 0.0071 ± 0.0751 in uVD subjects. The difference between the mean upward and downward pitch-vVOR gain was not significant either in normal subjects ($P > 0.05$, $t = 0.4217$, one-sample t-test, $df = 16$) or in uVD subjects ($P > 0.05$, $t = 0.2049$, one-sample t-test, $df = 20$).

Discussion

Permanent pitch-vVOR deficit after uVD

Previous studies in humans (Allum et al. 1988) and in monkeys (Chae et al. 1990) have shown complete recovery of the pitch-vVOR function following uVD. In contrast our study shows that recovery is incomplete and that there is a permanent 30% residual deficit in the pitch-vVOR gain. This result accords with data which shows that recovery after uVD of other vestibular functions such as ocular torsion (Curthoys et al. 1991), roll-tilt perception (Dai et al. 1989), hVOR (Halmagyi et al. 1990) and postural stability (Black et al. 1989) is also incomplete.

There are several possible reasons why we were able to show a permanent pitch-vVOR deficit after uVD whereas others have not. First, in human studies the uVD was neither complete nor permanent (Allum et al. 1988). Second, in all previous studies only low-frequency, low-acceleration, predictable sinusoidal rotations were used (Allum et al. 1988; Chae et al. 1990). We agree with Collewijn (1989a,b) that compensatory ocular responses to such stimuli are not necessarily an accurate index of the vestibular component of gaze stabilisation, since at such stimulus magnitudes VOR gain can be varied by cognitive factors (Barr et al. 1976, Collewijn et al. 1983).

Adaptive plasticity of the pitch-vVOR following uVD

Normal locomotion can generate pitch head velocities up to 90°/s (Grossman et al. 1988, 1989). During such activities uVD subjects who have a pitch-vVOR gain of about 0.65 would experience retinal image velocities greater than 30°/s. Retinal image velocities of this magnitude not only degrade visual acuity (Westheimer and McKee 1975; Demer and Amjadi 1993) but also serve as a powerful stimulus for adaptive plasticity of vVOR gain. Retinal slip produced optically by inverting prisms (Melvill-Jones and Gonshor 1982), magnifying or minifying lenses (Collewijn et al. 1983; Istl-Lenz et al. 1985; Melvill-Jones et al. 1988; Lisberger 1988) have been used experimentally as stimuli for vestibulo-ocular reflex adaptive plasticity. These experiments have shown that vestibulo-ocular reflex gain can be recalibrated in normal subjects with bilateral vestibular inputs. Why then have these adaptive mechanisms not boosted the vVOR gain in our uVD subjects to overcome retinal image velocities greater than 30°/s? One reason can be that uVD not only produces a permanent deficit in the vestibulo-ocular reflex, but also impairs the vestibulo-ocular reflex adaptive mechanism. This suggestion is supported by the work of Maioli and Precht (1985), who showed that the vestibulo-ocular reflex adaptive plasticity control mechanism in cats, although present, does not participate fully in the compensation process to correct for the asymmetrical hVOR gain after uVD.

Strategies of pitch-vVOR compensation in uVD subjects

We found that uVD subjects made catch-up saccades (Segal and Katsarkas 1988; Melvill Jones et al. 1988) to supplement the deficient pitch-vVOR gain, thus minimising retinal position error during passive head rotations. These saccades usually occurred 200–500 ms after onset of the head impulse (Fig. 1A). It is likely that there is organised recruitment of other sensory-motor, non-vestibular systems such as saccadic, optokinetic, proprioceptive, cervical as well as voluntary inputs (Tomlinson et al. 1980; Collewijn 1989a,b; Leigh and Brandt 1993) to substitute for the deficiencies in pitch-vVOR function during gaze control.

Up-down symmetry of pitch-vVOR

Our study confirms earlier reports that there is no significant up-down asymmetry of the pitch-vVOR (Baloh et al. 1986; Baloh and Demer 1991; Demer 1992) in humans as well as in monkeys (Correia et al. 1984) during upright pitch head rotation. In our preliminary results with 16 subjects (Halmagyi et al. 1992), we did find a trend towards lower upward rather than downward pitch-vVOR gain. The present larger study of 42 subjects (19 normal and 23 unilateral deafferented subjects) found no systematic pitch-vVOR up-down asymmetry in either normal or uVD subjects, although there were some asymmetries in certain individuals similar to that reported by Baloh and Demer (1991).

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