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III. VESTIBULO-OCULOMOTOR FUNCTIONS

EARLY COMPONENTS OF THE HUMAN ROTATIONAL VOR: LATENCY AND GAIN

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Passive rotation of the head is invariably accompanied by compensatory eye rotation that works toward stabilization of the gaze. The earliest components (witLin 100 ms of stimulus onset) of this compensation are dominated by the vestibulo-ocular reflex (VOR), which is characterized by oligo-synaptic connections and common spatial co-ordinates between the semicircular canals and the eye muscles. These early components, that should be especially informative about the function of the pure VOR and the vestibular organ, have been only sparsely addressed in human subjects. We used a reactive torque-driven helmet, in combination with the magnetic scleral sensor-coil technique, to record head and binocular eye movements during the early phase of the VOR in response to well-controlled passive head rotation with a sudden onset and an approximately constant acceleration on the order of 1000 deg/s^2. Some of our results, in both normal and labyrinth-defective subjects, have been reported before. Here I shall concentrate on recent results that were obtained with a high sampling frequency (1000/s) in a series of normal subjects. Head velocity increased linearly as a function of time during the first 50 ms (or longer, depending on the subject). Eye velocity also accelerated linearly as a function of time. Linear regressions to these functions (r^2 typically 0.99) yielded both the VOR delay (interval between their intersections with the time-axis) and the average early VOR gain (ration between their slopes). Delays were about 10±2 ms (range 6-15); early gains were about 1.1±0.1 (range 0.8-1.30). These values did not differ between ipsi- and contralateral rotation with respect to the side of the eye. The moment-to-moment gain values (V_{eye} t /V_{head} t - 1 at) rose, after the latency period, typically to values above unity and approached unity after about 100 ms. During the latency period, a majority of subjects showed anticompensatory eye movements, that started simultaneously with the head movements and reached several deg/s. It is hypothesized tiat this is a purely mechanical response, caused by off-center rotation of the eye, resulting in a significant linear component of the acceleration of the orbital contents. The latter hypothesis will be tested in experiments with controlled variation of the axis of head rotation.

CROSS AXIS VOR INDUCED BY PURSUIT TRAINING IN MONKEYS: FURTHER PROPERTIES OF ADAPTIVE RESPONSES

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In every day life, the vestibulo-ocular reflex (VOR) and smooth pursuit eye

movement interact with each other to optimize visual acuity. To examine how the VOR is affected by prolonged interaction of these two systems, we used the "cross axis" procedure that was originally designed to interact vestibular and optokinetic stimuli in cats (Schultheis and Robinson, 1981). By modifying the process in monkeys to incorporate smooth pursuit instead of optokinetic stimuli, we showed that pursuit training during VOR is effective in inducing the adaptive cross-axis VOR that appears only after training and that is tuned to the parameters of the training stimulus (Fukushima et al., 1996). To obtain further information on the pathways and possible mechanisms for cross-axis VOR induced by pursuit training, in this study we examined 1) latency- of cross axis VOR and 2) frequency response characteristics evoked by pitch vs yaw rotation induced by phase shift training.

Four Japanese monkeys were initially kained for standard ocular tracking tasks. During cross axis training, monkeys were rotated either in the pitch or yaw plane while moving the target spot orthogonally to the rotation plane using chair position signals. To examine latencies of the cross axis VOR, the monkeys were trained to pursue the vertically moving target during rapid yaw rotation (from 0 to 40 deg/s over 90 ms, period of constant velocity <1 s and back to 0 deg/s). Eye movements were examined by rotation alone without the target in complete darkness. Phase shift training was done by rotating the animal sinusoidally at 0.5 Hz (10 deg) while presenting the target moving either 90 deg lead or 90 deg lag to the chair, and eye movements were examined by rotation alone in complete darkness at 0.1-1.0 Hz (10 deg).

Mean latency of the collinear VOR induced by rapid yaw rotation in complete darkness was 15 ms, whereas mean latency of the adaptive cross axis VOR was 23 ms, suggesting that longer and more complex pathways are involved for the adaptive responses. After the phase shift training, chair rotation at the training frequency in complete darkness induced phase- shifted cross axis VOR. Phase and gain of the phase-shifted responses induced by yaw rotation and pitch rotation were similar at frequencies above 0.5 Hz, but were different below 0.3 Hz, suggesting an otolith contribution for the pitch-evoked responses. Computer simulation using an existing model (Miles et al., 1985) suggests that the frequency response characteristics of phase-shifted cross axis VOR could easily be explained by adding another integrator in the adaptive VOR pathway. We also recorded horizontal gaze-velocity-Purkinje cells in the cerebellar floccular lobe that did not respond to pitch rotation before training but clearly responded after horizontal pursuit training coupled with pitch. These results suggest that this integrator may be rq~ated to smooth pursuit.

DYNAMICS OF THE HORIZONTAL VOR EVOKED BY HIGH-FREQUENCY, HIGH-ACCELERATION HEAD ROTATIONS IN SQUIRREL MONKEYS

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We have identified frequency- and velocity-dependent nonlinearities in the

horizontal VOR evoked by high-frequency, high-acceleration head rotations in the squirrel monkey. These nonlinearities are noted in responses to yaw rotations in normal animals and are accentuated following lens-induced magnification of the VOR and after unilateral plugging of the three semicircular canals.

We studied the herizontal VOR (scleral search coil recordings) evoked by sinusoidal head rotations (2 n 20 Hz) and steps of head acceleration (3000O/s2) given in darkness in S squirrel monkeys. Gain remained constant with increasing frequency .83±.06, mean (s.d.) for sinusoidal rotations with an amplitude of 20°/s and a small phase lag was noted at the highest frequencies (9.9±1.6° at 20 Hz). Gain increased with velocity at frequencies >2 Hz. At 4 Hz, gains for 20 and 100°/s rotations were .83±.05 and .99±.04, respectively ($p < .01$). A similar nonlinearity was noted in the responses to acceleration steps. Gain during the acceleration (Ga = 1.04±.08) was greater than gain at the velocity plateau (Gv) which averaged .91±.04 ($p < .01$).

Adaptation of the horizontal VOR to 2.2X magnifying spectacles showed an analogous relationship to frequency and velocity of head movement. Ga after animals had worn these spectacles for 4 days increased to 2.04±.16 whereas Gv rose only to 1.42±.06 ($p < .001$). For sinusoidal rotations, gain decreased from 1.49±.08 at 0.5 Hz to 1.07±.06 at 15 Hz, and a phase lag of -15.1±1.0° noted at 15 Hz. Responses to higher velocity rotations at 2 ñ 6 Hz showed a gain increase comparable to that observed in the data before lens adaptation.

Gain decreased to .54±.04 after unilateral plugging of the three semicircular canals and remained constant with frequency for sinusoidal stimuli with a velocity amplitude of 20°/s. An asymmetry in half-cycle gain was noted for rotations at frequencies >2 Hz as velocity increased toward 100°/s. This asymmetry resulted from an increase in half-cycle gain for contralesional rotations with increasing head velocity. At 4 Hz with velocity amplitude of 20°/s, gain was .61 and .57 for contra- and ipsilesional rotations, respectively. At 4 Hz with velocity amplitude of 100°/s, gain was .80 for contralesional rotations and .55 for ipsilesional rotations. These responses at 4 Hz, 100°/s also displayed nonlinear properties with increased distortion and a shift in the zero-crossing of the eye velocity.

Asymmetries were also seen in responses to steps of angular acceleration after canal plugging. Ga measured during the period of acceleration for contra- and ipsilesional rotations averaged .9O±.16 and .53±.04, respectively ($p < .001$). Gv measured from eye movements at the plateau of head velocity was symmetric: Gv for contralesional rotations = .66±.10; Gv for ipsilesional rotations = .58±.11 ($p > .29$).

We have modeled these data based upon linear and nonlinear inputs to the central pathways controlling the VOR. The linear inputs are described by a ~ansfer function representing the known dynamics of regularly discharging vestibular-nerve afferents. The nonlinear pathway is described by a transfer function containing a term with the square of head velocity passing through a pole and zero, the values of which were calculated to fit the normal data at higher frequencies and velocities. The responses following lens-induced adaptation are modeled by selective modi-

fication of the linear and nonlinear pathways. Adaptation of the signal through the linear pathway is low-pass filtered. The asymmetries and nonlinearities noted after canal plugging are predicted from the simulations based upon elimination of inputs from the nonlinear pathway on the ipsilesional side and selective adaptation of the linear and nonlinear pathways on the contralesional side.

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RESPONSES TO DIFFERENT TYPES OF ROTATIONS

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The responses to centric rotations are elicited from the semicircular canals and usually recorded with ENG. The frequency of the swings is important as low frequencies elicit responses influenced by CNS modulating influences, and thus high frequency swings are of importance to unveil a peripheral loss. The swing frequency pattern is of importance, shown by an investigation of patients with compensated unilateral loss having normal responses to sinusoidal swings but a pathological low gain for pseudo randomized stimulation. The visual influence during rotations may unveil pathology, e.g. abnormal visual suppression in CNS lesions, best investigated during rotation. Animal experiments in rats show a loss of visual inhibition after neck muscle severing, stressing the importance of neck inflow on the vestibulooculomotor system. Eccentric rotation is used to show if, in a unilateral peripheral lesion, not only the canal function is lost but also the otolithic one.

EFFECTS OF COGNITIVE FACTORS ON VOR ACTIONS UNDER NATURAL CONDITIONS

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The Maryland Revolving Field Monitor was used to record gaze accurately under natural conditions as human subjects performed tasks of particular relevance to our species. Conditions were considered to be natural because the subjects were seated with their heads free to move as they used binocular gaze to perform tasks requiring the use of tools. These are the kinds of tasks that humans, and only humans, can plan and execute skillfully.

We will show how the head, the eyes and binocular gaze were coordinated as such natural tasks were performed. Videos of the subjects performing each task will be shown along with visualizations of their head movement and gaze data.

We found that head movements and gaze were coordinated more simply and efficiently than one might expect from our oculomotor literature, which is based primarily on data collected under analytical, but highly unnatural, conditions.

We believe that observations, like these, may make it possible to determine the relative importance of one or another oculomotor action as the torso, head and eyes work together in everyday life. Knowing this could have practical, as well as heuristic, value. It would allow us to allocate research resources in proportion to each oculomotor subsystem's contributions to the human condition when humans do what they, and only they, do best.

ACTIVITY OF FLOCCULAR PURKINJE CELLS IN AWAKE, LTD DEFICIENT MICE (L7-PKCI MUTANTS)

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Specific expression of the protein kinase C inhibitor, PKC[19-31], in Purkinje (P) cells blocks cerebellar long-term depression (LTD), and selectively eliminates adaptation of the vestibuloocular reflex (De Zecuw et al., *Neuron*, 1998). The findings in these L7-PKCI transgenic mice support the idea of a causal relationship between LTD and cerebellar motor learning.

To further test this hypothesis, we started investigating the simple-spike (SS) and complex-spike (CS) activity of P-cells in the flocculus of awake, wild-type and L7-PKCI mice during whole-body rotations. Single-unit P-cell recordings were identified by determining the pause in SS discharge after CSs (climbing fiber pause).

^ The results indicate that P-cells in wild-type and mutant mice exhibit comparable spontaneous SS-rates varying between 20-70 spks/s. The spontaneous CS activity varied between 0.4-1.0 spks/s, except in part of the mutant P-cells. The mean CS activity in these latter cells was higher because they showed two different CSs, as inferred from their waveform, polarity and climbing fiber pause.

Presumably, these neurons reflect the presence of multiple CF innervation in L7-PKCI mice (50 %). During sinusoidal vestibular stimulation in the light and the dark, wild-type and mutant P-cells showed a regular and comparable modolation of their SS discharge. Type I and type II responses were observed in both types of mice.

These preliminary data suggest that the loss of cerebellar LTD in L7-PCKI mice does not result in major abnormalities of floccular P-cell SS responses, despite a difference in CF input. We are now investigating their discharge properties in more quantitative detail.

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ON HOW INHIBITORY BURST NEURON FIRING FREQUENCY CODES THE DYNAMICS OF EYE, HEAD AND GAZE MOTION IN THE HEAD-FIXED AND HEAD-FREE PRIMATE

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We used system identification techniques to relate inhibitory burst neuron (IBN) discharges to the dynamics of either eye, head or gaze motion during head-fixed and head-free gaze shifts in the monkey. (We have discussed in a previous publication how this technique can be used to compute objectively the discharge latency). For saccades performed head-fixed the most important parameters for describing the firing frequency, B(t), were eye velocity (E'), saccade amplitude (DE) and a bias term (r). For our population of 28 IBNs the average discharge was given by: B(t)=282 - 4.1DE+0.84E'(t-td) where td is the latency. For gaze-shifts performed head-free the firing frequency of our IBNs was generally dependent on head velocity (H'), and the population average was now B(t) = 276-1.0DE+0.54E'(t-td)+0.25H'(t-td). The amplitude of the H' coefficient was significantly less than that of the E' coefficient, and the E' coefficient head-fixed was always higher than that head-free. Five IBNs had no head-velocity sensitivity, but their eyevelocity sensitivity head-free was still lower than that obtained head-fixed. IBNs can be subdivided, on the basis of their latency, into short lead IBNs (SLIBNs) and long lead IBNs (LLIBNs). Head-fixed, there was no significant difference between these two cell types; both were equally well described by the above equation: SLIBNs were not "closer", to the output than LLIBNs. Head-free, LLIBNs had a smaller head-velocity sensitivity than SLIBNs.

Conclusion: if excitatory burst neurons and IBNs carry similar signals, then the population H', DE and bias signals must be offset at the level of both the abducens nuclens and the integrator.

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PRIMARY POSITION DISCRIMINATES BETWEEN TILT AND TRANSLATION

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We have previously shown that fast phase axis orientation and primary eye position of the vestibulo-ocular reflex (VOR) are dynamically controlled by otolith signals during head rotations that involve a reorientation of the head relative to gravity (Hess and Angelaki, *J. Neurophysiol.*, **78**: 2193-2202, 1997). Because of the inherent ambiguity associated with primary otolith afferent coding of linear acceleration during head translation and tilts, a similar organization might also underlie the VOR during translation. The ability of the oculomotor system to correctly distinguish gravity from translational accelerations in the dynamic con-

trol of primary eye position has been investigated here by comparing the eye movements elicited by sinusoidal lateral and fore-aft oscillations (0.5 Hz±40 cm, equivalent to ±0.4 g) with those during yaw rotations (180°/s) about a vertically-tilted axis (23.6° tilt resulting in 0.4 g peak linear acceleration in the plane of rotation).

In contrast to a significant modulation of primary eye position as a function of linear acceleration (gravity) during rotation, translation of the head elicited no consistent change in fast phase axis orientation during either lateral or fore-aft oscillations. Accordingly, there was no significant change in the torsional variability of eye positions when expressed relative to a head-fixed compared to a spatially transformed coordinate system. These findings suggest that the spatial modolation of primary eye position and fast phase axis orientation depend on head orientation relative to gravity based on a central mechanism that discriminates between gravitational accelerations due to dynamic head tilts and inertial accelerations due to translation.

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SEMICIRCULAR CANAL CONTRIBUTION TO THE INERTIAL DETECTION OF LINEAR ACCELERATIONS

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According to Einstein's equivalence principle, inertial accelerations resulting from translational motion are physically indistinguishable from gravitational accelerations experienced during tilting movements. Nevertheless, despite ambiguous sensory representation of motion in primary otolith afferent signals, primate oculomotor responses are appropriately compensatory for the correct translational component of the head movement. The neural computational strategies used by the brain to discriminate the two and reliably detect translational motion were investigated in the primate vestibulo-ocular system. The experimental protocols consisted of either linear translations, roll tilts or combined translation/tilt paradigms. Results using both steady-state sinusoidal and transient motion profiles delivered either in complete darkness or during near target viewing demonstrated that not only otolith but also semicircular canal signals are necessary sensory cues for the discrimination between different sources of linear acceleration and the accurate detection of head translation. When the semicircular canals were inactivated, horizontal (translational) eye movements could no longer be correlated with head translation. Instead, translational eye movements totally reflected the erroneous primary otolith afferent signals and were correlated with the resultant acceleration, regardless of whether it resulted from translation or tilt. Therefore, at least at the frequencies where the vestibulo-ocular reflex is important for gaze stabilization (> 0.1 Hz), the oculomotor system discriminates between head translation and tilt

primarily by sensory integration mechanisms rather than frequency segregation of otolith afferent information. A nonlinear neural computational scheme is proposed where not only linear acceleration information from the otolith receptors but also angolar velocity signals from the semicircular canals of the inner ear are simultanecusly used by the brain to correctly estimate the source of linear acceleration and elicit context-appropriate oculomotor responses.

3D ANALYSIS OF THE EYE MOVEMENTS DURING OVAR

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To investigate the dynamic otolith function during off vertical axis rotation (OVAR), three dimensional analysis of the eye movements was performed.

Three dimensional analysis was carried out by the video-oculographic techniques developed by us. Thirty healthy adult volunteers participated in this study. The subjects were seated on the rotation chair and their bodies were fixed with a body harness and soft rnbber to the chair safely. The counter clockwise rotation with 4 deg/sec2 was applied until the rotation speed reached 60 deg/sec and after that the constant velocity was maintained for 60 minutes. The eye movements during the constant velocity rotation, were analyzed three dimensionally.

Sinusoidal modulation by OVAR was clearly observed in all three components. Horizontal nystagmus was evoked towards the left, but no clear nystagmus was identified in vertical and torsional components. Maximum amplitude of horizontal eye movement was observed in the right and left head down position, whereas that of the vertical eye movement was elicited in the nose down and up position. Maximum torsional eye movement was seen when the head position was between frontal and sagittal planes. These results indicate ttat the torsional eye movement during OVAR is not simply induced by a counter rolling response.

HUMAN THREE DIMENSIONAL EYE MOVEMENTS IN RESPONSE TO INTERAURAL LINEAR ACCELERATION DURING OFF CENTER YAW ROTATION ON A CENTRIFUGE

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We used 3-d search coils to measure nystagmus caused by off-center yaw rotation (yaw centrifugation) in normal healthy human subjects (n=7). Each subject was seated with head erect on the arm of a fixed-chair human centrifuge, lm away from the center of the rotation, and positioned to be facing along a tangent; either facing the direction of motion (facing-motion) or opposite to the direction of rotation (back-to-motion). In tota1 darkness each subject as accelerated at one

of 3 different steps of angular acceleration (5, 10 or 15 deg/s/s) from 0 deg/s to a constant velocity of 200 deg/s. Both yaw right and yaw left angular accelerations were studied. During rotation a centripetal linear acceleration (increasing parabolically from 0 to 1.24g units) was directed along the subject's interaural axis resulting in a shift of the resultant gravitoinertial acceleration (GIA) by 51 deg in the subject's roll plane and an increase of the total GIA magnitude from 1 g to 1.59 g. The magnitude of the interaural linear acceleration increases relatively slowly whereas the magnitude of the angular acceleration is constant during the angular acceleration.

During the angular acceleration off-center, torsional and vertical eye velocities were present in addition to the horizontal eye velocity component. The three angular acceleration steps sbow the canal dependence of the torsional eye velocity: it is present very early during the step of angular acceleration, before the interaural linear acceleration has attained a "threshold" value of about 0.3g units. The vertical eye velocity component is due to otolithic input since it only appears midway through the stimulus, causing the axis of eye velocity to shift in the roll-plane slowly and modestly in the direction of the GIA. We attribute the discrepancy between these human results and monkey results from comparable studies as being due to the relatively poor velocity storage mechanism in human subjects. In the "Raphan et al. model" it is this velocity mechanism which mediates the otolithic modulation of canal responses. Our results confirm that the axis of eye velocity of humans is essentially head-referenced whereas in monkeys the axis is essentially space-referenced.

MECHANISMS OF ADAPTATION TO UNILATERAL LABYRINTHINE LOSS

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It is known that asymmetric VOR responses are elicited in pat''ents with unilateral vestibular loss (UVL) during rapid head perturbations. These asymmetric responses are created by nonlinearities of vestibular afferent dynamics and range. However, it is unclear how these compensatory eye movements are triggered. We applied rapid head perturbations (500-10,000°/s2, 50-350°/s, ±15-30°) to 9 normal subiects, 5 patients with chronic UVL and 12 patients with acute UVL. Seated subjects were asked to fixate a stationary target in space, an imagined target, or perform mental distraction tasks in the dark. Three-dimensional eye and head orientations were recorded using a magnetic search coil system. To characterize the eye movement discontinuities (within the longer time-varying trajectory), we applied wavelet analyses techniques to the signals. Wavelets allow us to localize better the short amplitude onsets and match better velocity and acceleration trajectory patterns to our wideband signals. We found that these patients adapt to the asymmetric VOR with compensatory eye movements generated independently of vision and voluntary effort. These eye movements contain both slow and fast

corrections (discontinuities). Our analysis showed that after the onset of the head movement, first a low-velocity correction is triggered around peak head acceleration and reflects the head velocity trajectory; later a high- velocity correction is triggered around peak head velocity and does not reflect the head velocity trajectory. The first correction may be afferent driven and acts to diminish the gaze velocity error. The second correction may be centrally programmed and acts to diminish gaze position error. These adaptive corrections appear to be developed soon after the vestibular lesion, and sharpen their temporal patterns relative to the length of vestibular adaptation.

CIRCULAR HEAD-SHAKING: A NEW WAY OF TESTING THE VERTICAL CANALS?

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To get a better understanding of vestibular stimulation during large head movements, we have tested 6 healthy subjects during circular headshaking. This kind of head movement elicits a powerful stimulation of all six semicircular canals, similar to a velocity step about the nasooccipital axis, but without the requirement of a mechanical turntable. We have recorded 3dimensional eye position and head position at 100 Hz. Analysis of eye- and head-movements shows that the vertigo experienced by most subjects is caused by the stimulation of the canals during the abrupt termination of the head shaking: the 3-dimensional eye movements predicted purely by the stimulation of the canals match the recorded eye movements well. The mechanical properties of the semicircular canals are the decisive component, and the processing of the canal signals by the brain stem ("velocity storage") contributes only little to the eye movement generation. Since this stimulus leads to excitation of all canals on one side, and inhibition of all canals on the opposite side, this paradigm might be a valuable test for the functional status of the semicircular canals.

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HUMAN 3-D EYE MOVEMENTS SHOW THAT SEMICIRCULAR CANAL HEAD IMPULSES DETECT ABSENT FUNCTION OF INDIVIDUAL CANALS

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We studied the human vestibulo-ocular reflex (VOR) generated by the anterior and posterior semicircular canals (SCCs). The stimulus was the head "impulse": a brief, unpredictable, passive, high-acceleration (up to 4000 deg/s/s), low-amplitude

(20 to 30 deg) head rotation. In order to maximally stimulate an anterior or posterior SCC, we delivered the head impulses in a diagonal plane, approximately co-planar with the canal being tested. We recorded head and eye position in three dimensions with scleral search coils in nine normal subjects, seven patients following unilateral surgical vestibular neurectomy, and three patients following unilateral posterior SCC occlusion. In the post-surgical patients we demonstrated a severe, permanent VOR gain deficit (0.2-0.3) for head impulses directed toward any single non-functioning SCC. The specificity of the test depends on the geometry of the SCCs. The SCCs are close to orthogonal to each other, and each canal is approximately co-planar with a SCC on the opposite side. A head impulse in the plane of one SCC pair will therefore maximally stimulate that pair only. The sensitivity of the test depends on the directional polarization of primary vestibular afferents, as implied by Ewald's second law. A head impulse toward an inactivated SCC elicits a deficient "off" direction response from its co-planar SCC. The diagonal head impulse is the first test of individual vertical SCC function in humans, and together with the horizontal head impulse, forms a comprehensive battery of semicircular canal plane tests.

PROBING 3-D VESTIBULAR RESPONSES WITH ALCOHOL

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Normally, the semicircular canals selectively transduce angular velocity and are insensitive to gravitational orientation and linear acceleration. In acute alcohol intoxication, a specific gravity differential occurs between the cupulae and the endolymph, rendering the cupulae sensitive to gravity (buoyance mechanism). This results in positional alcohol nystagmus (PAN). We reevaluated PAN in 8 normal subjects by means of 3-D eye movement analysis (dual search- coils). Forty minutes after intake of 0.8 g alcohol / kg bodyweight the subjects were positioned such that the lateral canals were earth vertical. From this position they were rotated about an earth-horizontal axis in the plane of the lateral canals to either 45° or 90° right ear or left ear down and eye movements were recorded in each position for a minimum of 40 sec. While the torsional and horizontal components of the response could be explained by the buoyancy mechanism, the vertical component was in most cases and head positions opposite to the predicted direction. This problem could be solved by assuming an additional vertical bias velocity (all cases slow phase down) induced by the alcohol intoxication. After correction for this bias, the modulation of the eye movement direction was as expected from a buoyancy mechanism that applies to all six cupulae. The bias may represent a toxic effect in central vestibular pathways producing a tone imbalance of the vertical VOR in pitch.