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SUMMARY PAGE

THE PROBLEM

Development of simple procedures adaptable for use in operational settings for assessment of vestibular function and visual-vestibular interactions.

FINDINGS

The vestibulo-ocular reflex (VOR) generated by voluntary head movements keyed to a tone varying sinusoidally in pitch was studied in 13 men. Modulation of pitch at frequencies ranging from 0.1 to 5.0 Hz yielded systematic variation in head movement frequencies, although at higher frequencies head frequencies fell below requested frequencies. Three conditions of visual stimulation were used. When an Earth-fixed visual target was visible, VOR gain [(maximum eye velocity) : (maximum head velocity)] in each half cycle was slightly but significantly greater than VOR gain in darkness at all frequencies except 0.1 Hz. With a head-fixed target, VOR gain was substantially less than VOR gain in darkness at all requested frequencies below 2.0 Hz. The finding that visual suppression becomes ineffective at frequencies above 1.0 Hz parallels results obtained in other laboratories during passive whole-body oscillation. Results indicate that the procedures appear feasible for further evaluation as part of a clinical test battery.

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INTRODUCT ION

Visual pursuit tracking of moving objects is poor at angular velocities and frequencies that commonly occur in natural voluntary head and body movement (3,8,11,18,19,22). Since many head and body movements relative to the Earth exceed the limits of visual pursuit, it follows that reflexive stabilization of the eye may play an important role in sustaining clear vision in many conditions of life. Manifestations of recent dysfunction of the vestibular system (or its central processes) are blurring of vision, nausea, and apparent motion (oscillopsia) of viewed objects during head turns. Several authors have suggested that self-produced, i.e., voluntary, head oscillation may be useful in generating the vestibuloocular reflex in a fashion that lends itself to quantitative analysis which, in turn, may prove useful in assessing individuals with labyrinthine disorders (1,7,10).

The present report describes preliminary work concerned with the development of methodology for: 1) generating voluntary head movements in yaw at various frequencies under several conditions of visual stimulation, 2) measuring head movements and eye movements, and 3) quantifying relationships between head movements and eye movements. The basic plan of this research is to compare the relationships obtained between selfgenerated head movement and eye movement under different conditions of visual stimulation with results that have been previously obtained in other studies wherein head movements were produced by whole-body passive oscillation over a similar frequency range. Subsequently, the effects of equilibration disorders on oculomotor control during voluntary head movements will be compared with normative data from healthy subjects.

Three conditions of visual stimulation during eye movement recording used in the present study were: 1) eyes open with the subject attempting to fixate an Earth-fixed target light while the head was turned (visual augmentation of the vestibulo-ocular reflex); 2) eyes open in the dark with the subject attempting to fixate an imagined stationary (Earthfixed) point while the head was turned; 3) eyes open with the subject attempting to fixate a target light fixed relative to the head while the head was turned (visual suppression of the vestibulo-ocular reflex).

PROCEDURE

SUBJECTS

Thirteen individuals ranging in age from 19 to 56 years, with no known vestibular or oculomotor disorders, served as subjects. In addition, two referrals with signs of vestibular dysfunction were tested.

APPARATUS

Electrodes, suitable for electro-oculography (EOG), were taped on outer canthi of each eye with reference on nasion. D.C. amplification of the EOG signal was used for chart and tape recording of horizontal eye movements. A lightweight head frame from a welder's helmet, fitted snugly to the head, was attached to a freely rotating potentiometer to yield z-axic (16) head angular position signals which were recorded on magnetic tape along with EOG. A light at the apex of the head frame served to project a small spot onto a screen located 1.0 m in front of the subject. This provided a head-fixed visual target during head movement for the condition in which visual suppression of reflexive eye movements was studied.

A calibration board, with a red light-emitting diode (LED) at center and at left and right 10 deg, 20 deg, 30 deg positions, was placed 1 m in front of the subject's nasion with the subject seated comfortably.

METHOD

At least 20 minutes of subdued light condition preceded each experiment in order to minimize variations in EOG potentials due to dark adaptation. Sound cues for head oscillation were pre-recorded on a cassette tape along with voice instructions for the subject. The sound cue was a rising and falling tone (frequency modulated carrier) with a midfrequency of 700 Hz and varying from 400 Hz to 1,000 Hz with sinusoidal modulation. Modulation frequencies of 0.1, 0.2, 0.5, 1, 2, 3, 4, and 5 Hz provided the cues for head oscillation at each of these frequencies, according to the sequence described in Table I.

Table I

Frequency of Modulation of a Tone That Served as the Head Movement Cue

Cue Frequency	Duration of Cue
1 Hz	15 sec
2	15
3	15
4	8
5	8
1	15
0.5	15
0.2	15
0.1	70

Each cue was preceded by a 5-second silent period. The subject was asked to listen carefully to the rising and falling tone and move his head from side to side, about 20 degrees each way, keeping in time with the tone so that his head would always move in the same direction with a rising tone and in the opposite direction with a falling tone. If the subject did not achieve a satisfactory match to 1 Hz cue, the run was stopped and restarted after further instruction was given. Other than this, no practice was given.

Three trial runs made up a test session. In each run the whole sequence of cue frequencies was presented in a dark room with or without target lights as follows: The first run (Run 1) was with an Earth-fixed carget in the form of the center LED on the calibration board in a. otherwise dark room. The subject was asked to fixate this target throughout the run, thereby providing a run with synergistic vestibular and visual input. For the second run (Run 2) the subject was asked to fixate upon a point in the darkness at the imagined position of the center light. In the third run (Run 3) the head-fixed light was turned on and the subject was asked to fixate upon the projected spot and follow it as closely as possible while it moved from side to side with oscillations of the head. This provided a head-fixed target for visual suppression of the vestibulo-ocular reflex. EOG calibrations were recorded prior to each run (which lasted about 3.5 min) and after Run 3. Head position calibration was recorded prior to Run 1 by superimposition of the projected spot upon the left-and-right 20-degree LEDs, successively.

Analog signals were recorded on two channels of a Philips Mini Log 4 four-channel cassette tape recorder, using frequency modulation recording. A third channel carried spoken comments.

At analysis time, the analog tapes were replaced for analog-todigital (A/D) conversion by a two-channel, 12-bit A/D converter under control of a Data General NOVA 1200 digital computer. Converted data were then stored in digital form on digital cassette tapes. Programs were written in BASIC and NOVA assembly language to perform analysis of the data. Head and eye position signals were digitized according to the following table (Table II).

Table II

Cue Frequency Hz+	Sample Rate Per Second*	Sample Time Seconds	Number of Points	Number of Cycles
1	50	10	500	10
2	100	10	1000	20
3	143	7	1000	21
4	200	5	1000	20
5	250	4	1000	20
1	50	10	500	10
0.5	25	12	300	6
0.2	10	30	300	6
0.1	5	60	300	6

Sampling Rate for Digitizing Head and Eye Position Signals for Each Cue Frequency#

#The sample time and rate yield 50 points per cycle at nominal cue frequencies. *each channel (head,eye)

+nominal. Actual number usually differs above 1 Hz.

Considering one subject only, each of the three runs was handled identically. Nine cue frequencies yielded nine head movement files and nine corresponding eye movement files of digital data which were stored on digital cassette. Noise and saccadic eye movement signals were removed from these files by digital filtering with two iterations of a 3-point digital low pass filter with zero phase shift (21) according to the equation:

 $h'_{i} = (h_{i-2} + 2H_{i-1} + 3h_{i} + 2h_{i+1} + h_{i+2})/9 *$

This procedure resulted in a filter with a -3 db frequency of (0.13 x sample rate). Hence, with a 1 Hz cue frequency, sampled data converted at 50 points per second were filtered with a -3 dB frequency of 6.5 Hz.

Filtered head and eye position data for each case were analyzed for values of maximum positive and negative slope, corresponding to maximum head and eye velocity to the left or to the right. To determine the maximum slope, seven adjacent points were fitted by the method of least squares to a straight line, and the slope of the line was compared with previous slopes. The maximum slope values were obtained by determining at which data points along the curve the slope of a best-fitting 7-point straight line was maximum. Potential maxima less than 7 points from previously determined maximum were rejected.

When the maximum slopes had been obtained, means and standard deviations were computed for each group i.e., for all maximum positive head velocities, for all maximum negative head velocities, et cetera. Finally those values which lay outside two standard deviations of the mean velocity for each cue frequency were eliminated and new means computed.

Actual frequencies of head oscillation were determined for each cue frequency by determining the mean of the intervals between successive maximum positive head velocities. Mean gain for each cue frequency was obtained by dividing mean maximum positive eye velocity minus mean maximum negative eye velocity by mean maximum positive head velocity minus mean maximum negative head velocity; i.e., peak-to-peak eye velocity divided by peak-to-peak head velocity.

The accuracy of our methods was limited by the physical devices used for calibration, head position transduction, and EOG detection. Eye position calibration was accurate to within 1 mm in 160 mm on the calibration board, while the head-fixed light calibration was limited in accuracy by the size of the projected spot to about 5 mm in 160 mm. EOG calibration accuracy on the chart was approximately 5 percent, and we calibrated before each run. We made no attempt to average calibrations if there was a pre/post change, but we rejected an experiment if the EOG calibration drift exceeded 10 percent during a run. Accuracy of head position movement was probably limited by the tightness of fit of the

*where h, is the ith sample and h', is its filtered replacement.

head frame. A linear potentiometer accurate to 0.1 percent was used as the head position indicator, and again, head calibration accuracy on the chart was approximately 5 percent. Slippage of the head frame and any consequent errors in head movement measurement were not determined, but the tightness of the head frame was ensured before testing by manual manipulation. Slippage would likely involve skin movement anyway, and this cannot be prevented, except by addition of a biteboard attachment. The desirability of this added precaution will be determined in subsequent studies.

RESULTS

Typical recordings of head and eye position signals for all requested frequencies of the three runs are shown in Figures 1, 2, and 3. As is obvious in the lower frequency oscillations, head and eye signals are out of phase by approximately 180 degrees as expected.* With the Earthfixed target (Run 1, Figure 1), and in the dark (Run 2, Figure 2), it can be seen that the head/eye position relationship does not appear to change significantly over the range of oscillation frequencies used; however, velocity information is not explicit in these illustrations. In Figure 3 (Run 3) the effect of visual suppression by the head-fixed target is evident at the lower frequencies as is the gradual loss of suppression as oscillation frequency increases. From Figures 1 - 3, it is apparent that the head movements departed substantially from sinusoidal form at requested frequencies of 4 and 5 Hz.

Typical plots of maximum eye velocity versus maximum head velocity for all subjects in each of the three runs are shown in Figure 4. Many subjects maintained an essentially linear relationship in Runs 1 and 2 for velocities up to, and occasionally exceeding, 500 deg/sec in both directions. Nonlinearity, due to visual suppression at low velocities in Run 3 <u>data</u>, resulted in a characteristic reverse S-shaped curve. Eye velocity versus head velocity gains for all subjects at each requested frequency were averaged and standard deviations computed. These are presented in Figures 5, 6, and 7 for Runs 1, 2, and 3, respectively. Bars indicate one standard deviation each side of the mean gain for each mean head oscillation frequency.

The mean gains in Run 1 were greater than the mean gains in Run 2 when results for corresponding frequencies were evaluated by <u>t</u>-tests for paired measures (see Table III). Only at the 0.1 Hz frequency did the mean difference in gains for corresponding frequencies on Run 1 and Run 2 fail to approach statistical significance. Thus, the condition (Run 1) which provided synergistic visual and vestibular inputs yielded higher gains than the condition (Run 2) in which visual stimulation was absent, albeit the gains were not very much different. With a headfixed target, meant to visually suppress the vestibulo-ocular reflex (Run 3), all gains at 1 Hz and below were significantly less than in Runs 1 and 2.

*Phase analysis is in progress and will be dealt with in a separate report.

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Statistical Comparisons of Mean Gains [(maximum eye velocity : maximum head velocity)] at Each Requested Frequency in Runs 1, 2, and 3

Request	ed Frequency	0.1	0.2	0.5	1.0	1.0	2.0	3.0	3.0	5.0
Run 1	Lained Frequency Mean Gain (S.D.)	1.019 (.153)	1.005 (.150)	1.034 (.145)	1.129 1.129 (.214)	1.058 (.136)	1.120 (.246)	1.113 (.240)	3.4 1.17 (.254)	<u> </u>
Kun 2	Mean Gain (S.D.)	1.032 (.230)	.393	.895 (.192)	.840 (.116)	.827	.905 (.166)	.876	.950 (.251)	1.078 (.561)
Run 3	Mean Gain (S.D.)	.331 (.239)	.255 (.194)	.308	.445	.529	.788 (.203)	.908 (.227)	.962 (.411)	1.006 (.332)
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Run 1 -	Run 2 <u>t</u> (paired scores) (df)	24 (12)	2.22 * (12)	2.22 * (12)	4.20** (12)	3.97**	3.13** (12)	4.02 ** (11)	3.64** (11)	3.89 ** (11)
Run 2 -	Run 3 <u>t</u> (paired scores) (<u>df</u>)	13.51*** (12)	10.49*** (12)	9.51*** (12)	7.03 ** * (12)	4.06** (12)	1.61 (12)	49 (11)	28 (11)	.54 (11)
Run 1 -	Run 3 <u>t</u> (paired scores) <u>(df</u>)	12.17*** (12)	12.55 *** (12)	16.49*** (12)	8.82*** (12)	7.99*** (12)	3.96** (12)	2.77 * (12)	1.68 (12)	3.13* (12)
*p < .05										

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Mean attained head frequencies at each requested frequency were very close in Runs 1, 2, and 3, and slight differences were not statistically significant. No significant differences between mean head frequencies at each requested frequency were found in comparing Runs 1, 2, and 3. As is apparent in Figure 8, obtained frequencies were progressively less than requested frequencies between 2 and 5 Hz, and standard deviations were large at 4 and 5 Hz. Only three subjects achieved a frequency of 5 Hz.

DISCUSSION

The method used to control the fundamental frequency of the head movements appeared to be reasonably effective from 0.1 to 2.0 Hz, but above 2 Hz effective control diminished, suggesting that our higher frequencies exceed natural limits, at least with the procedure we used. As expected, subjects reduced amplitude of head oscillation at the higher frequencies since, for example, at 5 Hz, + 20-degree excursions would yield peak angular accelerations of almost 20,000 deg/sec², assuming approximate sinusoidal waveforms. It is possible that brief training to reduce the amplitude of head movements to practiced limits as frequency is increased would yield a better match between requested 4 and 5 Hz frequencies and attained frequencies. This would more nearly duplicate the stimulus parameters used by Benson and Barnes (8) with their passive (turntable) stimulus sequence in which amplitude was diminished systematically as frequency was increased so as to maintain a fixed-peak angular velocity. We chose, however, to ask subjects to maintain maximum comfortable amplitude as frequency increased, in order to observe relations between head and eye movement at high peak head velocities. Noteworthy in our data is the fact that most subjects yielded very good eye velocity matches to head movement waveforms even when peak velocities were of the order of 400-500 deg/sec. Considering the findings of Atkin and Bender (1), it is possible that only higher velocities of head movement will provide a measure of reduced vestibular function and permit discrimination of unilateral dysfunction.

At our lower frequencies, 0.1 and 0.2 Hz, the mean obtained frequency closely matched the requested frequency. However, the head movement waveform was not always smooth and appeared, in some cases, more triangular than sinusoidal. These frequencies involve controlled head velocities that are slow relative to natural voluntary head movements, and it probably requires more voluntary effort than the intermediate frequencies in our stimulus sequence. The subject thinks his way through this movement in contrast with "releasing" a natural head shake. It appears, therefore, that our methods should be supplemented by alternative procedures at the low and high ends of the frequency range we attempted to explore.

The mean gains (eye velocity/head velocity) found in Run 1, which involved synergistic visual and vestibular oculomotor control inputs, were 1.0 or slightly greater than 1.0 for all Trequencies except the requested frequency of 5 Hz in which the mean gain increased to 1.41. The actual mean attained frequency here was 3.92 Hz. This tendency for gain to increase when frequencies are of the order of 4 Hz is consistent with results of Benson et al. and Barnes (3,8) who found, with passive oscillation of subjects in the dark, progressive increase in gain between 1 and 5 Hz, and with findings of Keller (17) in passively rotated monkeys whose VOR increased from unity at 2 Hz to a mean of 1.3 at 4 Hz. However, in our observations, the average obtained frequency did not reach the nominal frequencies of 3, 4, and 5 Hz (see Figure 8), and moreover, the increase in gain at the nominal frequency of 5 Hz is attributable to a few subjects who showed a substantial increase. The increase in gain at 5 Hz was not statistically significant for our 13 subjects; relative to this point, it is important to bear in mind that only a few subjects attained the 4 and 5 Hz frequencies, so the standard deviations of gains at the higher frequencies were large for Runs 1, 2, and 3.

The mean gain in Run 2, conducted in the absence of visual stimulation, was 0.92 over all frequencies. Again, the mean gain at the nominal 5 Hz was greater than the mean gain at all other frequencies, but it was only slightly greater. Mean gains ranged between 0.83 and 1.08, although the mean differences between various frequencies were of questionable statistical significance.

Generally, the mean gains in Run 1 were greater than the mean gains in Run 2. In fact, all mean gain differences between Runs 1 and 2 were statistically significant with the exception of the 0.1 Hz comparison (see Table III). Curiously the lowest gain occurred at 1 Hz in Run 2, suggesting that perhaps one control system may lose influence as another ascends in importance. In this connection and of potential importance is the relatively high gain found in Run 2 at 0.1, 0.2, and 0.5 Hz. These gains are higher than those found by Hixson (15), Benson and Barnes (8), and Barnes and Forbat (4) during passive oscillation over a comparable frequency range. Since our data were obtained during voluntary oscillation of the head on the neck, there are at least two possible interpretations of this high gain in the dark at these low frequencies: 1) proprioception from involvement of the neck muscles enhances the VORoculomotor response during voluntary head movement (4,9); or 2) initiation of voluntary head movement may first increase the ampullary tonic afferent activity through efferent control (12) which would allow more dynamic range before units are silenced. Here, however, it is important to consider the findings of Barr et al. (5) who found that passive angular oscillation in darkness over a frequency range of 0.1 to 0.8 Hz yielded mean gain of about 0.95 when subjects imagined a target fixed in space and attempted to look at the imagined target as the head oscillated relative to it. Similar use of imagined Earth-fixed targets was employed by Vidic et al. (20) during linear oscillation. Since our subjects were instructed in the same way, this presents a third alternative; viz., 3) the high gains observed in our subjects may have been attributable to this goal-directed voluntary behavior in Run 2, and cur mean gain in Run 2 of 0.92 is very similar to the 0.95 found by Barr et al. These alternatives are not mutually exclusive.

Gains in Run 3, in which a light spot projected from the head moved with the head, thereby yielding a "head-fixed image" that could be expected to suppress the vestibulo-ocular reflex, were considerably lower than gains obtained in Runs 1 and 2 for frequencies from 0.1 Hz through 1.0 Hz and were intermediate between those found by Barr et al. for real and imagined head-fixed targets during passive oscillation. Possibly the voluntary action and/or contribution of neck action in generating our oscillatory motion reduced the visual suppression of the vestibulo-ocular reflex, or alternatively, upped the gain of the VOR. It is interesting also that for frequencies 2 Hz and above, our gains with a head-fixed target increased and achieved 1.00 at 4.0 Hz (nominal 5 Hz). This is sident to findings of Barnes et al. who found visual suppression of the VOP very effective between 0.1 and 1.0 Hz, but increasingly less effective above 1.0 Hz. Whereas our mean gain was consistent with the findings of Barnes et al. and Benson (3,8) in the higher frequencies, it is higher than that reported by Barr et al. (5) in their "high frequency" observations with a head-fixed target (gain = 0.60) or with imagined head-fired (gain 0.64) Cargets. Note, however, that Barr et al. used a single transient in which 60 deg/sec peak velocity was attained in 0.3 sec for their "high frequency" stimulus, but this single transient involves a mean peck acceleration of about 3.5 rad/sec² and a duration comparable to the period of a 0.8 Hz sinusoidal stimulus. Moreover, it was not a repeating cyclic stimulus but rather a single complex stimulus waveform. While this waveform undoubtedly contains high-frequency components as harmonics, it should not necessarily be expected that the "high frequency" stimulus of Barr et al. should yield results corresponding to our results or those of Benson in the 2 to 5 Hz range with a head-fixed target.

A last point of consideration in the evaluation of the relative magnitude of the eye/head velocity gains measured in the present study involves the time-domain method selected for gain analysis. That is, gains were calculated based on measures of the instantaneous eye and head velocities at selected intervals within each periodic waveform. Because the head motions at the higher frequencies were distorted, i.e., nonsinusoidal, each stimulus necessarily contains harmonic contributions to the fundamental head oscillation frequency. For this reason, the word gain as used in the present paper is not used in the strict engineering theory sense, and a later report will compare frequency and time domain analyses of responses to active head oscillation.

There have been several indications that self-generated head movements may provide a means of quantitative assessment of vestibular and other equilibration disorders (1,2,5,6,13,14). Although the present observations were carried cut for purposes of procedural development, during our experiments two individuals with apparent clinical signs volunteered for testing. One of these individuals, an airsickness referral, had been found to have below normal visual suppression of vestibular nystagmus during sinusoidal passive whole-body oscillation at 0.04 Hz with peak velocities of + 120 deg/sec His pendular eye tracking was also considered below normal limits. This subject yielded gain ratios on all three runs that were well above the limits of expected chance variation. The other individual had experienced episodic vertigo. ENG caloric testing indicated a 12 percent ear difference (considered within normal limits), a weak positional rystagmus in head-left position (considered WNL), and a directional difference in optokinetic nystagmus (leftward tracking was superior to rightward tracking). While this standard form of clinical

testing failed to yield clearly abnormal results, this vertigo referral was the only individual we tested whose gain ratios in Run 2 consistently exceeded those in Run 1. As noted earlier, gains in Run 1, with visual augmentation of the VOR, consistently exceeded gains in Run 2 in our "normal" subjects. The limited information presented on these two subjects is not intended as evidence of the validity of the procedure under study, but it is mentioned, at this stage, only as an interesting casual observation.

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Figure l

Recordings of head and eye position during head oscillation while viewing an Earth-fixed target. Frequencies indicated are the cue (i.e., requested) frequencies.



Recordings of head and eye position during head oscillation in the dark



Recordings of head and eye position during voluntary head oscillation while viewin a head-fixed target



Figure 4

Maximum eye velocity versus maximum head velocity for all subjects. Each dot represents the mean at one frequency for one subject.



Maximum velocity gains (eye/head) with an Earth-fixed target versus mean attained oscillation frequency for all subjects. Horizontal bars indicate one standard deviation on each side of the mean. The connecting line intersects the two points at 1 Hz.

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Maximum velocity gains (eye/head) in the dark versus mean attained oscillation frequency. Horizontal bars indicate one standard deviation on either side of the mean gain. The connecting line intersects the two points at 1 Hz.

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Figure 7

Maximum velocity gains (eye/head) with a head-fixed target versus mean attained frequency for all subjects. Horizontal bars indicate one standard deviation on each side of the mean. The connecting line intersects the two points at 1 Hz.

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Mean obtained head oscillation frequency for all subjects versus requested (cue) frequency. Horizontal bars indicate one standard deviation above and below each mean head frequency.

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