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Amplitude and Frequency Prediction in the Translational Vestibulo-ocular Reflex

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Abstract

The goal of this study was to assess the effect of amplitude and frequency predictability on the performance of the translational vestibulo-ocular reflex (tVOR). Eye movements were recorded in 5 subjects during continuous vertical translation that consisted of a series of segments with: 1) 3 amplitudes at constant frequency (2 Hz) or 2) 3 different frequencies (1.6, 2, 2.5 Hz). Stimulus changes were presented in a pseudo-random order. We found that there was little change in the tVOR immediately after an unexpected stimulus change, as if eye velocity were being driven more by an expectation based on previous steady-state motion than by current head translation. For amplitude transitions, only about 30% of the eventual response change was seen in the first half cycle. Similarly, a sudden change in translation frequency did not appear in eye velocity for 70 ms, compared to a 8 ms lag during similar yaw rotation. Finally, after a sudden large decrease in frequency, the eyes continued to track at the original higher frequency, resulting initially in an anti-compensatory tVOR acceleration. Our results elucidate further the complexity of the tVOR and show that motion prediction based on prior experience plays an important role in its response.

Keywords

eye movements; vestibular; otolith; translation; visual-vestibular interaction

1. INTRODUCTION

The translational vestibulo-ocular reflex (tVOR) generates eye movements that partially compensate for linear motion of the head. There are several characteristics of the tVOR that distinguish it from the rotational VOR (rVOR). First, in humans at least, it is under-compensatory: the eye movement is always less than what would be necessary for full gaze stabilization. This is true for regular sinusoidal head motion [9] as well as for abrupt translations [11] and for complex continuous motion that consists of a sum of sinusoids [13]. Second, non-vestibular contributions to the tVOR are considerable. For example, due to geometric considerations (eye rotations compensate for head translations), the distance to the object being viewed modulates the amplitude of the tVOR by an order of magnitude or more [12]. Vision also seems to play an important role, as responses to translation are much

lower in the dark than in an illuminated room [9]. Finally, knowledge of target behavior affects the amplitude of the tVOR. If the object being viewed is expected to move with the head, in which case the tVOR should be suppressed, then the initial tVOR gain is lower than it is when the object is expected to remain still [10].

Previous work has also suggested that the predictability of head motion may also have an important influence on the tVOR, unlike the rVOR, for which eye velocity simply tracks head movement. For example, during sum-of-sines (SOS) translation, the tVOR demonstrates a reduced response to the low-frequency components of the stimulus, compared to the response for single frequency motion [13]. In the present study, we tested more directly the effect of motion predictability on the tVOR by examining the response after abrupt and unpredictable changes of the amplitude or frequency of sinusoidal vertical translation.

2. METHODS

2.1 Subjects

Five neurologically normal subjects without a history of vestibular disease were included in this study. Data recorded from a sixth subject could not be analyzed due to artifact from very frequent continuous blinking. Before participating, all subjects gave written informed consent according to a protocol that was approved by the Institutional Review Board of the Louis Stokes Cleveland Department of Veterans Affairs Medical Center.

2.2 Testing Apparatus and Eye Movement Recording

Subjects sat with head restrained in a chair that was mounted to a 6 degree-of-freedom motion platform (Moog 6DOF-2000E, E. Aurora, NY) whose position was controlled by a computer based on a pre-defined motion profile. Instantaneous head position was recorded by an infrared based motion tracking system (Vicon, Oxford, UK), with reflective markers placed over the protuberance of the zygomatic bone bilaterally. A series of markers fixed relative to the platform measured chair motion. Eye movements were recorded using head-fixed binocular video-oculography (I-scan, Woburn, MA), recorded at 120 Hz.

Eye movements were recorded during vertical translation and yaw rotation. For translation, subjects were instructed to maintain fixation of an earth-fixed near target that was 12.7 ± 2.6 cm (mean $\pm$ s.d.) from the eyes, in an illuminated room. All subjects were able to maintain convergence on this near target throughout the motion. For rotation, subjects looked at a target on the wall that was about 2 m away. The choice of different fixation distances for translation and rotation was deliberate and based on a fundamental geometrical difference between the two reflexes. Because the tVOR compensates for a head translation with an eye rotation, the response varies inversely with distance, and there is very little eye movement when the viewing distance is far away. On the other hand, the rVOR is best tested during far fixation. Head rotation with near fixation evokes a more complex response that must also account for translation of the orbits relative to the target.

2.3 Stimuli

The motion stimulus used to evaluate responses to transitions of vertical translation amplitude is shown in Figure 1. It consisted of a continuous sequence of 2-Hz vertical oscillations in 4 cycle segments that had one of three amplitudes (see figure legend for stimulus details). Segments with the middle amplitude were over-represented, because the focus of the analysis was on transitions from this amplitude to one of the other two. Segments were arranged according to amplitude in a pseudo-random order. Thus, although the timing of the transitions was regular (every 4 cycles), the direction of the amplitude change could not be predicted by the subject. In order to compare eye movement responses to rotation to those evoked by head translation, the same stimulus sequence was applied to yaw, scaled so that the peak rotational velocities were approximately 11, 19, and 30 °/s.

To study transitions of motion frequency, we used a different continuous stimulus that was constructed of segments of three individual frequencies (1.6, 2.0, 2.5 Hz) and similar amplitude. Again, there were more segments with the middle frequency, and the analysis compared transitions from this frequency to each of the other two. Just as for amplitude transitions, the same profile was used with different scaling for both vertical translation and yaw rotation. Finally, we examined qualitatively the responses to a larger decrease in frequency (from 2.5 to 1.0 Hz). For this stimulus, because there were only two frequencies, we rendered the timing of the transitions unpredictable by varying the number of cycles in each segment.

The choice to compare yaw rotation (evoking a horizontal eye movement) to vertical translation (evoking a vertical eye movement) was made for several reasons. We tested yaw rather than pitch because pitch from the upright position involves a change in the orientation of the head relative to gravity and is thus a combined canal and otolith stimulus. Moreover, pitch about the interaural axis is less feasible than yaw because it requires much larger excursions of the motion platform. We tested the vertical tVOR because sustained vertical translation is easier for subjects to tolerate (especially at frequencies as high as 2 Hz). In a prior study [13], the horizontal and vertical tVOR showed similar effects of stimulus predictability.

2.4 Data Analysis

Data were analyzed using custom programs written by the authors in MATLAB™ (Mathworks, Natick, MA) and Python (www.python.org), using the scipy (www.scipy.org), numpy, and matplotlib (www.matplotlib.org) packages. Eye position signals were behaviorally calibrated using a fixation paradigm, digitally filtered (15 Hz) for noise reduction, and differentiated to yield eye-in-head velocity. Eye positions recorded during slow horizontal and vertical trapezoidal motion were used to calculate the ideal required eye movement based on the position of the head markers. VOR analysis was performed on data recorded from the right eye.

For both amplitude and frequency prediction paradigms, we isolated and combined ideal and actual head velocity segments for transitions from the middle amplitude or frequency to each of the other two amplitudes or frequencies. Segments corresponding to the same type of

transition were aligned to the time of the transition, and the median of all the trials was calculated. Responses were compared using a paired t-test (function `ttest_1samp` in `scipy.stats`), using $\alpha=0.05$.

For frequency transitions (Figure 5), we determined the point of divergence for the two different trial groups using a point-by-point paired t-test, starting beyond the transition and moving backward. The time at which the p-value of this t-test exceeded 0.05 was defined as the divergence time. The divergence time of ideal eye velocity was then subtracted from that of the actual eye velocity, as a measure of latency. Additional details regarding data analysis are provided in the Results section and the figure legends.

3. RESULTS

3.1 Amplitude prediction

Responses to transitions of stimulus amplitude are shown for one subject in Figure 2. The key finding is that eye velocity showed little effect of the change in head motion amplitude during the first half-cycle after the transition (arrows). Although there is already a large difference in peak head velocity and, therefore, in the ideal eye velocity (upper panel), actual eye velocity is nearly the same in both cases (lower panel). Thus, the eye movement immediately after the transition appears to be dominated by the prior steady-state motion of the head. Only later does eye velocity fully adjust to reflect the new head velocity. For this subject, the difference in median eye velocity was only about 8 °/s at the first post-transition peak but had grown to 25 °/s at steady state. Thus, only about 32 % of the eventual eye velocity difference was present in the initial half-cycle.

All subjects showed a similar response (Figure 3). To quantify this effect, we calculated for each subject the ratio of the peak eye velocities for the initial post-transition half cycle and for the steady state (beginning of 4th cycle after transition, $t \approx 1.6$ s in Figure 3). The fact that eye velocity in the first half cycle after the transition does not scale with head velocity is reflected in the corresponding tVOR gains, defined as the ratio of actual to ideal peak eye velocity [9]. For transitions in which head velocity increases, tVOR gain decreases (the denominator increases, while the numerator remains nearly the same). In contrast, when head velocity decreases, the gain initially increases, until the eye slows to reflect the new lower head speed. To quantify this effect, we calculated a gain ratio for the peak of each positive half-cycle:

$$\text{gain ratio} = g_{23} / g_{21}$$

where g_{21} is the gain at a particular peak for trials with a transition from the middle to the smallest amplitude, and g_{23} the gain for trials from the middle to the largest amplitude. If eye velocity always follows head velocity, then this gain ratio would remain close to unity. Instead, the gain ratio dropped by approximately 40 % for the first half-cycle after the transition (Figure 4, left panel). By the next stimulus cycle, eye velocities had diverged to reflect the new head velocity, and the gain ratio had returned to its pre-transition level near unity. The delay in the response to unpredictable changes in head velocity is unique to the

tVOR. When the same amplitude transitions were applied during yaw rotation, eye velocities diverged more quickly after the transition (Figure 3, right panels), and the gain ratio did not decrease (Figure 4, right panel).

The percentage of the tVOR gain attributable to steady-state prediction can also be estimated by calculating the “gain” of the response to the amplitude change and then comparing it to the gain at steady-state. To do this, we calculated a gain based on the ratio of the difference in recorded eye velocity to the difference in ideal eye velocity at the initial post-transition peak (peak 0 in Figure 3):

$$g_{\Delta} = \frac{V_{E_{30}} - V_{E_{10}}}{V_{I_{30}} - V_{I_{10}}}$$

where V_E is recorded eye velocity, V_I is ideal eye velocity, and the subscripts 3 and 1 refer to the largest and smallest amplitude translations, respectively. Based on median values for each subject (Figure 3), g_{Δ} was 0.17 ± 0.15 . In contrast, tVOR gains measured at steady state in the same subjects were more than three times greater (0.57 ± 0.15).

3.2 Frequency prediction

The tVOR and rVOR also differ in their responses to changes of stimulus frequency. This can be shown by comparing the time after the transition at which the eye velocities for the two new frequencies diverge to the time of divergence of the head velocities (Figure 5). Similar to amplitude transitions, it took longer for unpredictable frequency changes to be seen clearly in the tVOR (70 ms) than for the rVOR (8 ms).

Finally, sudden large changes in stimulus frequency clearly illustrate the effect of prediction in the tVOR. When the frequency of head motion decreased abruptly from 2.5 Hz to 1.0 Hz, the eyes initially continued to move as if there had been no frequency change, including a deceleration that was unrelated to actual head motion but was instead in the direction opposite to the required eye acceleration (Figure 6).

4. DISCUSSION

Our results show that expectation based on prior experience contributes substantially to the tVOR. When regular sinusoidal head motion is interrupted by a sudden change in amplitude or frequency, there is a considerable delay before the full effect of this change is seen in the evoked eye movement. At first, the eyes continue to move as if responding to anticipated rather than actual head translation. This is true regardless of absolute response gain and was seen in all of our subjects. Such behavior is very different from that of the rVOR, for which eye velocity tracks even unpredictable head velocity much more precisely.

The tVOR gain appears to scale with the degree of motion predictability. The highest gains are seen for regular sinusoidal translation. Lowest are the gains for abrupt translation [11] and for sudden changes in ongoing motion (0.17 in the present study and only 30% of the steady-state gain). The tVOR in response to a SOS stimulus with intermediate predictability

fell between these values. The gain for the 2 Hz component was 75% of the steady-state gain for 2 Hz but with a larger phase lag [13].

Our findings have several important implications. First, they emphasize further the fact that the tVOR, although dependent on otolith input, is not a simple linear vestibular reflex. The gain is dynamic and may depend on past as well as current head motion. At steady-state, expectation appears to dominate and the tVOR gain is as much as 3 times greater than the gain of the response to abrupt perturbations. Thus, even more so than for the rVOR, the tVOR is stimulus-dependent and may be as much a measure of central vestibular and motion processing as it is of primary otolith function.

Prior work has shown that normal tVOR gains vary among individuals, even at steady-state, when motion is predictable [9]. This was also true for the subjects of this study and was the reason that we normalized the responses for analysis (Figure 3). Despite this overall variability, however, in each individual subject the predictive component of the tVOR appears to be driving the response to a particular gain relative to the ideal eye movement. In the current study, once the steady state was reached after amplitude transitions (Figure 3), the tVOR gain ratio was no different from unity, i.e., the gains at steady state for all stimulus amplitudes were equal.

The criteria for tVOR gain to be set at a particular value remain uncertain, but visual motion feedback appears to be playing a central role. For example, in humans, the tVOR gain is considerably lower in the dark than in the light [9]. Gain is also reduced when a stroboscopic device permits vision but eliminates retinal slip [8]. Moreover, manipulating vergence angle with optical prisms to simulate a change in viewing distance did not affect steady-state eye velocity, possibly because the required eye movement based on visual feedback does not change [9]. Finally, although eye velocity does increase with image magnification, the increase is consistent with visual feedback and is proportional to the increase in required eye velocity [8].

The presence of prediction in the tVOR is similar to what has been described for foveal pursuit (a recent review of prediction and other cognitive contributors to pursuit can be found in Fukushima, et al. [6]). For example, if a moving stimulus is extinguished during steady tracking but is expected to reappear, pursuit eye movements continue [2; 3]. Anticipation is also seen in the tracking of sinusoidal stimuli [1], as we have found here for the tVOR. Finally, other studies have shown that prior experience influences visual tracking over a longer time scale [14]. The finding of prediction in the tVOR provides additional evidence of the close relationship between these two types of eye movement. It also suggests that brain areas that are presumed to contribute to pursuit prediction, such as the cerebellum [7] and frontal cortex [5] may also be responsible for prediction in the tVOR.

Although the tVOR bears a number of similarities to visual tracking, and visual feedback seems to play a role in setting the tVOR gain, it is unlikely that the tVOR is simply a visually driven eye movement, without any otolith contribution to the response. First, although tVOR gains are lower in the dark, there is still a response in the absence of visual feedback, including to abrupt, unpredictable stimuli [4; 11]. Second, even when vision is

present, the latency is too short for the reflex to be attributed to visual tracking alone. This was also true for the responses to frequency transitions seen in this study: the decrease in frequency was at least partially reflected in the eye movement within about 70 ms. Finally, the frequency response of pursuit and the tVOR differ. For a given frequency of motion (e.g., 2 Hz), the tVOR has a higher gain and a lower phase lag than does foveal pursuit of a comparable visual stimulus when the head is still [9].

While it is unlikely that the tVOR is driven purely by visual inputs, much of its behavior must still depend on central processing. In particular, it would be difficult to attribute the tVOR prediction demonstrated here to response characteristics of the labyrinth. A peripheral explanation of our findings would imply that that otolith macula does not fully change its amplitude (Figure 2) or frequency (Figure 6) of oscillation for more than 100 ms following a change in head motion. Moreover, a response such as that shown in Figure 6 would require that the motion of the macula sometimes be in the direction opposite to that expected from head translation.

Anticipation of motion amplitude and frequency is only one form of prediction in the tVOR. The response is also influenced by expectations regarding the motion of the object being viewed. Ramat, et al. [10], showed that brief translations along the interaural axis elicit larger eye velocities when the subject expects that the target will remain fixed in space, compared to when it will move with the head [10]. Unpredictable target motion evokes an intermediate response. Finally, in the same study, it was also shown that being able to predict the direction of head translation enhances the response, similar to our finding that the tVOR reflects expected as well as actual head motion.

In summary, the tVOR is a complex eye movement that is driven by translational head movement but is also highly dependent on non-vestibular signals and central motion processing, including a predictive component that is based on prior experience and expectation. This prediction is similar to that which is seen in visual tracking, and it is likely that there is overlap in the pathways that mediate prediction for pursuit and the tVOR. These aspects of the tVOR have the potential to provide additional measures, not only for assessment of the integrity of otolith inputs, but also of higher-order cognitive processes related to the experience, perception, and anticipation of movement.

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Figure 1.

Platform motion profile used for assessment of amplitude prediction. The stimulus consisted of a continuous 96 second 2-Hz oscillation that was divided into 48 segments of 4 cycles each. Each segment had one of three peak amplitudes (approximately 0.5, 0.88, or 1.4 cm; 6.5, 11, or 17 cm/s; 0.08, 0.14, 0.23 g).

Figure 2.

Responses from one subject to stimulus amplitude changes. The upper panel shows the calculated ideal velocity and the lower panel the recorded eye velocity. Data from two groups of transitions are synchronized to the time of the amplitude transition ($t=0$) and superimposed: 1) transitions from the middle to the smallest amplitude (gray lines) and 2) transitions from the middle to the largest amplitude (black lines). For each set of trials, dashed lines represent the responses around individual transitions and the solid lines the medians of each group. The arrows indicate the first velocity peak after the amplitude change. Note that despite the large difference in the ideal eye velocity at the time of this first peak, the recorded eye velocities are nearly identical and are very similar to those at steady-state before the transition.

Figure 3.

Median responses to amplitude transitions in all 5 subjects during vertical translation (left panels) and yaw rotation (right panels). Due to differences in the absolute magnitudes of ideal eye velocity (due to small differences in the distance of the target from the eyes) and actual eye velocity (due to differences in gain), we normalized each velocity trace to the peak velocity of the initial half-cycle. This allows for comparison of responses between the two different amplitude transitions for the whole group of subjects. As in Figure 2, black traces represent middle-to-high and gray traces middle-to-low amplitude transitions.

Figure 4.

Gain ratios around the time of amplitude transitions for the tVOR (left panel) and rVOR (right panel). For each positive half-cycle we determined the ratio of the gain of amplitude-increasing trials to that of amplitude-decreasing trials. Each individual gain was calculated as the ratio of peak actual to peak ideal eye velocity for one subject. The mean and 95% confidence intervals are shown for the group of 5 subjects for each cycle. Cycle 0 is the first one after the amplitude transition (arrow in Figure 2).

Figure 5.

Median eye velocities in response to frequency transitions from 2.0 Hz to either 2.5 Hz (black traces) or 1.6 Hz (gray traces). The right panels show the same data as the panels on the left, but magnified to show more clearly the behavior around the time of the transition. Similar to the analysis of responses to amplitude transitions (Figure 3), median velocities were normalized, this time to the peak value immediately preceding the transition. Note that the required ideal eye velocities diverge in response to the frequency difference much earlier than do the actual eye movements (arrows). For the tVOR, this latency was 70 ms, whereas for the yaw rVOR it was only 8 ms.

Figure 6.

Normalized median eye velocities for each subject around a single frequency transition from 2.5 Hz to 1.0 Hz. The required eye velocity is shown in gray and the recorded eye velocity in black. After the transition, the eyes initially followed the original 2.5 Hz trajectory, rather than that corresponding to the new lower-frequency head motion. Note that although post-transition eye velocity appears to be greater than ideal, this is a consequence of the independent normalization of required and actual velocity traces. The tVOR gain was higher at the lower frequency, but it was not greater than unity.