Anticipatory VOR Suppression Induced by Visual and Nonvisual Stimuli in Humans

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Barnes, G. R. and G. D. Paige. Anticipatory VOR suppression induced by visual and nonvisual stimuli in humans. J Neurophysiol 92: 1501–1511, 2004. First published December 3, 2003; 10.1152/jn.00611.2003. We compared the predictive behavior of smooth pursuit (SP) and suppression of the vestibuloocular reflex (VOR) in humans by examining anticipatory smooth eye movements, a phenomenon that arises after repeated presentations of sudden target movement preceded by an auditory warning cue. We investigated whether anticipatory smooth eye movements also occur prior to cued head motion, particularly when subjects expect interaction between the VOR and either real or imagined head-fixed targets. Subjects were presented with horizontal motion stimuli consisting of a visual target alone (SP), head motion in darkness (VOR), or head motion in the presence of a real or imagined head-fixed target (HFT and IHFT, respectively). Stimulus sequences were delivered as single cycles of a velocity sinusoid (frequency: 0.5 or 1.0 Hz) that were either cued (a sound cue 400 ms earlier) or noncued. For SP, anticipatory smooth eye movements developed over repeated trials in the cued, but not the noncued, condition. In the VOR condition, no such anticipatory eye movements were observed even when cued. In contrast, anticipatory responses were observed under cued, but not noncued, HFT and IHFT conditions, as for SP. Anticipatory HFT responses increased in proportion to the velocity of preceding stimuli. In general, anticipatory responses were similar in cued SP, HFT, and IHFT conditions and were appropriate for expected target motion in space. Anticipatory responses may represent the output of a central mechanism for smooth-eye-movement generation that operates during predictive SP as well as VOR modulations that are linked with SP even in the absence of real visual targets.

INTRODUCTION

The vestibuloocular reflex (VOR) normally operates in concert with visually driven eye-movement systems, particularly smooth pursuit (SP), to stabilize retinal images during natural behavior. Visual and vestibular mechanisms interact to complement or counteract each other. Regarding the latter, SP is often used to suppress the VOR during combined eye-head tracking of moving targets or in the laboratory during suppression of the VOR that occurs when fixating a head-fixed target (HFT) during whole-body rotation. Extensive behavioral experiments have shown that pursuit and VOR suppression share many common features, including similar limitations in their frequency response and the susceptibility to velocity saturation (Barnes et al. 1978; Lau et al. 1978; Paige 1983; and Paige et al. 1998). However, there is also evidence that visual feedback during head motion is not the sole source of VOR suppression.

The earliest demonstrations of this were by Gauthier and Robinson (1975) and by Barr et al. (1976), who showed that subjects could partially suppress the VOR in the dark by attempting to fixate an imagined HFT. The debate about the relative contribution of these visual and nonvisual mechanisms of VOR suppression was fuelled by evidence from clinical studies showing dissociation between pursuit and VOR suppression in some patients (Chambers and Gresty 1983; Ranalli and Sharpe 1988). But there was also a strong theoretical argument made by Robinson (1982), suggesting that during active head movements an alternative source of information, such as neck afferent feedback or an efference copy of the vestibular outflow, might be used as a substitute or a supplement for visual feedback. Since then, further evidence for nonvisual VOR suppression has been obtained (Barnes and Eason 1988; Huebner et al. 1992; McKinley and Peterson 1985), and the behavior of neurons in the brain stem has been examined in an attempt to determine the source of the nonvisual signal (Cullen and McCrea 1993; May and McCrea 1985; McCrea et al. 1996; Roy and Cullen 1998, 2002).

One feature initially suggested by Robinson (1982) was that some form of prediction during periodic stimulation might play a part in nonvisual VOR suppression (VORS). Prediction plays a large part in human SP as evidenced by the persistence of responses after targets unexpectedly disappear during pursuit (Becker and Fuchs 1985; Carl and Gellman 1987; von Noorden and Mackensen 1962). Prediction also helps SP to overcome inherent time delays in visual feedback. These delays underlie the latency (~100 ms) of SP in response to sudden target motion (Rashbass 1961). One manifestation of prediction, common to both VORS and SP, is that the phase error of SP at modest stimulus frequencies (e.g., 0.25–0.5 Hz) is much less than would be expected on the basis of known visual feedback delays (Bahlil et al. 1980).

A particularly fascinating predictive phenomenon is that of anticipatory smooth eye movements (Boman and Hotson 1988; Kowler and Steinman 1979). These are often difficult to demonstrate because smooth eye movements cannot normally be evoked in the absence of a moving target (von Noorden and Mackensen 1962) and in early experiments, the paradigm used to evoke anticipatory eye movements produced low velocities (<2°/s) of doubtful value for SP (Kowler and Steinman 1979). However, more robust anticipatory eye movements have subsequently been described during repeated presentations of transient target motion in a predictable sequence (Barnes and Sharpe 1988).
Asselman 1991). Moreover, such anticipatory movements can even be generated when the target does not appear at regular intervals as long as each presentation is preceded by a regularly timed warning cue (Barnes and Donelan 1999). The eye velocities attained prior to target onset in this procedure can be much higher (≤20°/s) than those demonstrated in early experiments and are therefore more meaningful in relation to normal ocular pursuit.

In the current experiments, we exploited the cued pursuit task to examine responses to head movement alone (the VOR) as well as during VOR suppression using both HFTs and IHFTs. One objective was to assess whether anticipatory eye movements would arise prior to head motion and in particular whether such movements would be apparent in the IHFT condition despite the absence of any concrete visual stimulus. Given that such anticipatory movements were indeed observed, our second objective was to assess what contribution such a predictive process might make to nonvisual VOR suppression.

The evidence suggests that it does indeed play a part, primarily in the IHFT condition. Studies have shown that anticipatory movements over repeated SP trials could be readily generated under a similar paradigm. Results are presented from a total of 15 runs conducted in two sessions lasting 30–40 min each.

In the SP task, the sinusoidal target trajectory had a frequency of 0.5 or 1.0 Hz with a peak velocity of 25 or 50°/s, respectively. Subjects were instructed to follow the target as accurately as possible during the stimulus presentation. In the VOR, HFT, and IHFT conditions, trials of turntable motion at 0.5 and 1.0 Hz were performed at a peak velocity of 50°/s. However, in an experiment to specifically address the effect of stimulus amplitude, peak velocities of 20, 40, and 60°/s were studied, all at a stimulus frequency of 1.0 Hz. In the VOR condition, subjects were instructed to simply stare straight ahead in the dark. In the HFT condition, subjects were instructed to fixate and track a real HFT (the same as for the SP condition) as accurately as possible. In the IHFT condition, subjects were instructed to suppress the VOR during rotation by fixating an imagined HFT in darkness.

In most conditions, “catch” trials were interjected after a random number (4, 5, or 6) of identical sequences of cue trials. Three types of catch trial were employed: the warning cue was omitted so that target and/or head motion began unpredictably, the target failed to appear as expected (SP and HFT conditions), and the motion stimulus was not delivered after the tone cue.

**Data analysis**

The analogue signals representing eye, turntable, and target movement were low-pass filtered at 50 Hz, sampled at 100 Hz, and stored on disc for subsequent off-line analysis. Eye velocity was obtained by a two-point digital differentiation, and saccades were removed using a technique similar to that described previously (Bennett and Barnes 2003), based on a combination of acceleration (750°/s²) and velocity (60°/s) threshold criteria. A linear interpolation routine was used to bridge the gaps produced by removal of saccades from the eye velocity trajectory. Measures referred to as steady state (SS) were derived from each sequence of repeated trials by averaging the velocity trajectories of all trials between the third iteration and the subsequent catch trial and across several such sequences of matching condition. Signals were always time-locked to target onset. This yielded one SS trajectory per subject per experimental condition. Where mean values across subjects are quoted, the mean ± SE is also given. Catch trials were averaged separately for each of their three forms (see preceding text).

The following specific measures of eye movement were derived from each response:

- **V0, V100**—eye velocity at, or 100 ms after, onset of the stimulus, respectively. Values at 100 ms were examined because they correspond to the last time at which the response is uninfluenced by visual feedback (e.g., Carl and Gellman 1987). **T0**—The time of onset of each individual response. T0 was determined by first estimating the time at which the velocity exceeded a threshold of 5% of the SS peak velocity.
velocity for each series. A linear regression was then carried out on data points for the subsequent 100 ms and extrapolated backward to its intersection with zero velocity. Gain was calculated for each half cycle of the ocular response by determining the slope of the relationship between eye velocity and stimulus velocity.

Analysis focused on the difference between the velocity trajectories for the cued (predictive) and noncued (nonpredictive) versions of each stimulus condition. This difference signal rose to a peak \( V_{pk} \) and the time \( T_{pk} \) of its occurrence in relation to expected stimulus onset.

ANOVA was used throughout to assess differences between conditions (SPSS, Chicago, IL).

**RESULTS**

**SP—cued versus noncued**

Repetitions of single-cycle SP stimuli preceded by warning cues resulted in anticipatory smooth eye movements that grew to a SS over two to three presentations as noted previously (Barnes and Asselman 1991). Anticipatory eye movements at SS (Fig. 1) climbed over the 300 ms after the audio cue to reach mean (with SE) velocities at target onset \( (V0) \) of 4.18 ± 0.38°/s for 0.5-Hz trials and 5.34 ± 0.84°/s for 1.0-Hz trials. In contrast, when unexpected presentations were given without cues (catch trials), smooth eye movements were initiated after a characteristic visual feedback delay averaging 168.3 ± 10.8 ms (see Fig. 1). \( V0 \) was significantly greater \( \bar{F}(1,5) = 30.11; P = 0.003 \) in the cued than the noncued condition for which mean \( V0 \) was negligible \( (0.12 ± 0.54°/s) \). Eye velocity 100 ms after target onset \( (V100) \) was still negligible in the noncued condition \( (0.22 ± 0.13°/s) \) but increased in the cued condition to 5.78 ± 0.45°/s for 0.5-Hz and 7.97 ± 1.82°/s for 1.0-Hz trials. Although eye velocity subsequently increased during noncued tracking and ultimately caught up with cued-trial counterparts, the difference between cued and noncued responses (Fig. 1B) remained greater than zero for 400–500 ms, reaching mean \( V_{pk} \) values of 9.63°/s (1.39) for 0.5Hz and 14.34°/s (2.97) for 1.0Hz trials. Corresponding mean \( T_{pk} \) values were 236.7 ± 33.6 and 218.3 ± 18.5 ms, respectively. Mean cued SP gains were 0.79 ± 0.06 at 0.5 Hz and 0.63 ± 0.05 at 1.0 Hz. Corresponding noncued SP gains were 0.82 ± 0.06 and 0.75 ± 0.07.

**Head rotation in darkness (VOR)—cued versus noncued**

Head rotation in darkness (Fig. 2) during noncued trials evoked a slow-phase compensatory VOR response of short latency (effectively instantaneous given our modest sample rate), with a mean gain of 0.73 ± 0.04 at 0.5 Hz and 0.79 ± 0.04 at 1.0 Hz. Mean gains for cued trials measured 0.77 ± 0.04 and 0.86 ± 0.05, respectively. In contrast to SP responses, there were no eye-movement responses prior to cued head movements (Fig. 2) and no significant difference in \( V0 \) between cued and noncued responses.

**Head rotation in the presence of a HFT—cued versus noncued**

Head rotations were performed in the presence of real HFTs (Fig. 3). In the noncued HFT condition, the VOR initially drove eye movements in the opposite direction to head motion. However, after a latency of ≥100 ms, suppression of the VOR was initiated, and eye velocity was reduced to a low level throughout the remainder of the cycle. By contrast, in the cued condition, anticipatory smooth eye movements developed over the first two presentations. They were always in the same direction as head movement and anticipated VOR suppression. Mean \( T0 \) values were slightly less than for SP \( (−241.7 ± 26.9 \text{ ms at 0.5 Hz}; −198.0 ± 17.2 \text{ ms at 1.0 Hz}) \). Mean \( V0 \) was also slightly less than for SP \( (4.28 ± 0.48 \text{ and } 3.67 ± 1.27°/s, \text{ respectively}) \). \( V0 \) for the cued condition was significantly

![FIG. 1. Steady-state smooth pursuit (SP) responses to repeated target motion stimuli (single cycles at 0.5 Hz) with and without audio warning cues (labeled). The target was illuminated only during target motion, as indicated in lower traces. A: mean response of 6 subjects. B: detail of initial eye velocity from mean response, ... indicating clear separation of cued and noncued eye velocity; mean of 16 trials in 1 subject ± SD.](http://jn.physiology.org/Downloadedfrom/hntn/jn/889/1020333600008.png)
greater \( F(1,5) = 30.11; P = 0.003 \) than for the noncued condition, for which mean \( V_0 \) was negligible (0.13 ± 0.04°/s). Analysis of the difference between cued and noncued responses (Fig. 3B) showed that eye velocity remained less in the cued than in the noncued condition for \( \approx 400 \) ms. Mean \( T_{pk} \) for the difference signal was somewhat less than that for SP (158.3 ± 13.0 ms at 0.5 Hz; 163.3 ± 38.8 ms at 1.0 Hz), and mean \( V_{pk} \) was also less than for SP (9.47 ± 0.68 and 6.86 ± 1.27°/s, respectively).

Compared with the VOR in darkness, HFT responses revealed a clear reduction in steady-state eye velocity over the entire cycle (Fig. 3A), although the VOR was never completely suppressed. The level of suppression (VORS gain) was obtained by calculating the ratio of HFT gain to VOR gain. Suppression of the VOR for cued HFT trials was more effective at 0.5 Hz (Fig. 3A; mean VORS gain = 0.12 ± 0.03) than at 1.0 Hz (mean VORS gain = 0.27 ± 0.05). Corresponding noncued VORS gains were 0.12 ± 0.02 and 0.28 ± 0.06. Comparison with SP gains shown in the preceding text confirms that as frequency increases there is deterioration in both SP (reduced gain) and VOR suppression (VORS gain increase). For the noncued HFT condition (Fig. 3B), VOR suppression was not initiated until \( \approx 120 \) ms after stimulus onset at both stimulus frequencies.

Clearly, the pattern of eye movement in the first few hundred milliseconds of HFT trials is very different from that of SP. However, this difference can be resolved if the HFT response is considered in terms of gaze velocity (i.e., eye velocity in

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**FIG. 2.** A: steady-state vestibuloocular reflect (VOR) recorded in darkness in response to repeated whole-body motion stimuli (single cycle at 0.5 Hz) with and without warning cues. Mean of 6 subjects. B: detail of difference (diff.) between cued and noncued VOR shown in A, • • • , onset of head motion and 100 ms later. C: initial part of response, indicating clear separation of cued and noncued eye velocity; mean of 16 trials in 1 subject ± SD.

**FIG. 3.** Eye-velocity response during suppression of the VOR with a real head-fixed target (HFT). The head-velocity stimulus was a repeated single-cycle sinusoidal motion at 0.5 Hz, with or without audio warning cues. A: mean response of 6 subjects. B: detail of initial HFT and VOR responses recorded in the dark (from Fig. 2) derived from mean response. Diff. is defined in Fig. 1. Broken vertical line, onset of head movement and 100 ms later. C: initial part of response, indicating clear separation of cued and noncued eye velocity; mean of 16 trials in 1 subject ± SD.
space) in relation to target velocity in space (same as head velocity for HFT). Re-plotting the data of Fig. 3 in this way, it is evident that anticipatory gaze velocity for HFT (Fig. 4) acts in the same direction and in the same manner as for SP (Fig. 1).

**Head rotation in the presence of an IHFT—cued versus noncued**

For trials in which subjects imagined a HFT during rotation (IHFT), the characteristics of initial responses were remarkably similar to those with a real target (HFT). Thus in the cued condition, anticipatory eye movements appeared as in SP and HFT trials (Fig. 5). Mean T0 values measured $-268.3 \pm 26.1$ ms at 0.5 Hz and $-202.0 \pm 28.9$ ms at 1.0 Hz, values comparable to those of cued HFT trials. In contrast, in the noncued condition VOR suppression did not begin until well after the start of head motion. As such, mean V0 values for the cued IHFT condition ($3.77 \pm 0.56^\circ$/s at 0.5 Hz; $3.21 \pm 0.67^\circ$/s at 1.0 Hz) were significantly greater than for noncued IHFT trials (mean $V0 = 0.39 \pm 0.64^\circ$/s at 0.5 Hz; $0.48 \pm 0.57^\circ$/s at 1.0 Hz). The peak in the difference signal occurred slightly earlier (mean $Tpk = 145.3 \pm 15.2$ ms; $120.0 \pm 22.8$ ms) and with lower peak velocity ($5.69 \pm 2.34^\circ$/s; $4.45 \pm 1.27^\circ$/s) than in the HFT condition. Further, V0 for cued IHFT trials proved smaller than the HFT equivalent, indicating less anticipatory "visual suppression" for the imagined than the real visual target.

True suppression of the VOR during IHFT trials (imagined targets) was also less effective than in HFT trials (real targets). Mean VORS gain for cued IHFT trials across the entire cycle was $0.50 \pm 0.05$ at 0.5 Hz and $0.63 \pm 0.07$ at 1.0 Hz; both greater (less suppressed) than values presented above for HFT trials. Corresponding VORS gains for noncued IHFT were

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**FIG. 4.** Data presented in Fig. 3, A and B, represented in terms of gaze velocity, rather than eye velocity with respect to the head, by summatting head and eye signals.

**FIG. 5.** Eye-velocity response during suppression of the VOR with an imagined HFT in darkness (IHFT). The head-motion stimulus was a repeated single-cycle sinusoidal motion stimulus at 0.5 Hz with and without warning cues. A: mean response from 6 subjects. B: detail of initial responses in the IHFT condition compared with the VOR in the dark from mean response. Diff. is defined in Fig. 1. Broken vertical line indicates head motion onset and 100 ms later. Note that VOR suppression does not start until well after this 100-ms marker. C: initial part of response, indicating clear separation of cued and noncued eye velocity; mean of 16 trials in 1 subject ± SD.
very similar (0.42 ± 0.04 and 0.61 ± 0.07). There was thus little difference between cued and noncued HFT conditions in the level of suppression achieved particularly in the second half cycle. In other words, the major suppressive effect could not be attributed to anticipatory activity, the effect of which died away within the first half cycle as revealed by the difference signal (Fig. 5B). Notably, in the noncued condition, there was a latency of ≥100 ms before any difference appeared between the IHFT and VOR responses. It thus took a latency comparable to that associated with visual feedback (or SP initiation) for suppression of the VOR to appear during IHFT trials (Fig. 5B).

Effects of head velocity on HFT and IHFT responses

STEADY STATE RESPONSE. To assess the effectiveness of VOR suppression as a function of head velocity, we calculated VORS gains (ratio of HFT or IHFT gains to VOR gain) at peak head velocities of 20, 40, and 60°/s (frequency, 1.0 Hz). For the HFT condition (Fig. 6A), VORS gain climbed (i.e., suppression declined) significantly as peak head velocity increased for both cue conditions and during both half-cycles of head rotation [$F(2,10) = 4.28; P = 0.045$]. Gains in the second half were significantly lower [$F(1,5) = 134.51; P < 0.001$] than in the first half, indicating an increase in VOR suppression from the first to the second half-cycle. In the first half-cycle, VORS gains were significantly less for cued than for noncued trials ($P = 0.015$), but by the second half cycle, there was no difference between them. In contrast to HFT trials, VORS gain during IHFT trials (Fig. 6B) displayed no significant effects of cue condition or half-cycle. Separate analyses for the two half-cycles indicated a significant effect of head velocity in the first half-cycle [$F(2,10) = 7.41; P = 0.011$] that arose from the high levels of suppression achieved at the lowest head velocity (20°/s). There was no significant effect of head velocity for the second half-cycle. Overall, mean gain was 0.63. Findings in the IHFT condition thus contrasted with those in the HFT condition both qualitatively and quantitatively. There was no enhancement of VOR suppression across the cycle for IHFT, as observed for HFT. In fact, at the lowest head velocity, VOR suppression during IHFT trials (unlike HFT) deteriorated between the first and second half-cycles.

VELOCITY SCALING OF THE ANTICIPATORY RESPONSES. There was a significant increase [$F(2,10) = 4.37; P = 0.043$] in V0 with increasing head velocity in the HFT condition (Fig. 7), in line with previous findings during SP (Barnes and Donelan 1999). However, this same trend proved statistically insignificant for the IHFT condition, although the levels of V0 were comparable to those in the HFT condition. Only three of the six subjects showed clear evidence of scaling, and greater inter-subject variance was apparent for larger stimulus amplitudes.

RESPONSES TO CATCH TRIALS DURING SP, HFT, AND IHFT CONDITIONS. Catch trials without warning cues. For all cued conditions resulting in anticipatory responses (SP, HFT, and IHFT), we examined responses to trials in which the audio cue was omitted at random after at least four cued trials. In all cases, eye velocity at onset (V0) was negligible (<0.2°/s) and not significantly different from equivalent noncued V0 values.

Catch trials without expected target appearance (HFT condition). During sequences of cued HFT trials at 0.5 Hz, sporadic trials were interjected in which the cue was given but the expected target did not appear. This allowed us to explore the transition from cued HFT to cued IHFT conditions. In response to the cue, anticipatory eye movements arose that clearly resembled those during normal cued HFT trials (Fig. 8A). These two responses continued in tandem for >200 ms after...
the onset of head rotation, but then eye velocity in catch trials slowly increased (and diverged from their HFT counterparts) as the cycle progressed (and VOR suppression declined). Mean gain in the first half cycle increased from 0.10 ± 0.04 in the SS HFT condition to 0.20 ± 0.03 in the IHFT catch condition. However, VOR suppression over the first half cycle of the IHFT catch condition proved more effective than for the normal cued IHFT condition (where SS gain = 0.31 ± 0.05; Fig. 8B). In the second half cycle, gain in the IHFT catch condition increased to 0.45 ± 0.04. This proved no different from gain in the SS IHFT condition (0.46 ± 0.04; Fig. 8B) but was much greater than the gain in the normal SS HFT condition (0.08 ± 0.01; Fig. 8A). In other words, during the catch trial, the initial suppression resembled the HFT condition, but gradually deteriorated during the first half cycle and was no different from that of normal IHFT trials by the second half of the head rotation.

Catch trials without head movement (HFT condition). Finally, during a series of HFT runs, we examined the response to sporadic trials in which an audio cue was given but no head movement ensued. There were two variants, one with the expected target appearance intact and the other without. In both cases, smooth anticipatory eye movements arose prior to the expected head movement, closely resembling typical SS HFT responses (Fig. 9). But, whereas in SS HFT responses the eye reversed direction shortly after the onset of head movement (driven by the VOR; Fig. 9A), in catch trials (absent VOR), the eye continued to accelerate in the same direction for 100 ms before reaching a peak and then gradually declining to zero. The decline in eye velocity was more rapid in trials containing a target than in those remaining in darkness.

Because these catch trials were devoid of actual head movement, the continuation of anticipatory responses allowed us to assess velocity scaling of anticipatory eye movements over a longer period than in normal SS-HFT trials. An ANOVA applied to catch trials revealed that eye velocity 100 ms after the head would have moved (V100) rose significantly \[F(2,10) = 8.25; P = 0.007\] with peak head velocity of the

![Figure 8](http://jn.physiology.org/)

**FIG. 8.** Eye velocity during suppression of the VOR. In A, the target was on for 4–6 presentations (SS HFT) but then unexpectedly failed to appear even though the cue was given (IHFT–catch trial). In B, the IHFT catch trial from A is compared with the response to the SS IHFT condition. Cues were presented in all conditions; frequency 0.5 Hz. Mean of 6 subjects. Target on traces refer only to HFT trials.

![Figure 9](http://jn.physiology.org/)

**FIG. 9.** A: detail of eye-velocity responses during catch trials in which the expected head motion (solid line) was not delivered and in which the target appeared or remained off. These responses are compared with a SS-cued HFT response. B: the relationship between anticipatory eye velocity (V100) and expected head velocity for the catch trials shown in A. Values reflect means ± SE of pooled target-on and -off trials in 6 subjects.
trials just prior to the “catch.” Findings resembled those from previous SP trials (Barnes et al. 2000).

**Discussion**

**Overview**

We have compared SP with suppression of the VOR in two visual contexts; with HFTs and IHFTs. The comparison has been made using single-cycle sinusoids under two stimulus conditions, with or without an advance auditory warning cue. The results from SP trials show that anticipatory smooth eye movements reliably arise prior to the appearance of a moving visual target in the cued condition in accord with prior observations (Barnes and Donelan 1999; Becker and Fuchs 1985; Kowler and Steinman 1979). In contrast, noncued trials show no such anticipatory response; rather, there is a latency of 168 ms before initiation of a response. This latency is slightly longer than for step-ramp stimuli (Carl and Gellman 1987; Rashbass 1961; Robinson 1965) but close to values reported during sudden onset sinusoidal stimuli (Paige 1994).

The results from repeated rotation trials with HFTs show that anticipatory smooth eye movements, similar to those during SP trials, also arise when there is an expectation (auditory cue) of head movement combined with a visual target moving with the head, a condition that demands suppression of the VOR. Results are in accord with previous studies that have shown the presence of predictive activity in visual suppression of the VOR (Barnes and Grealy 1992; Barnes and Lawson 1989; Collins and Barnes 1999; McKinley and Peterson 1985). However, earlier studies employed continuous periodic waveforms. The results presented here show that such responses are not dependent on a persistent periodic stimulus; subjects can use elapsed time from a sound cue to elicit the response even though time between presentations is randomized. The common factor in the SP and HFT conditions is an expectation of target motion in space at a particular moment in time. For SP, this results from target motion with respect to the fixed head, whereas in HFT conditions, it is a consequence of rotation of the head and target together. The key common element is the generation of anticipatory smooth gaze movements in both conditions (cf. Figs. 1 and 4). As in previous studies, our findings of declining SP and VOR suppression as stimulus frequency or velocity increases suggest a common relationship between SP and suppression of the VOR (Barnes et al. 1997; Paige 1983, 1994; Paige et al. 1998) and reinforce the notion of a common underlying process of prediction in these two conditions.

An important new finding is the demonstration that anticipatory smooth eye movements can also occur prior to head movement when subjects simply imagine a HFT (IHFT condition). This anticipatory response only occurs in the cued condition when subjects can predict the time of occurrence of head and target motion. In the noncued condition, there is a latency of ~150 ms before the initiation of VOR suppression just as with real targets (HFT condition). Note also that anticipatory movements only occur when subjects expect that VOR suppression will be required and not when rotated in darkness with the simple instruction to stare straight ahead even though a timing cue may be given (VOR, Fig. 2). In other words, the VOR itself cannot produce anticipatory eye movements even when cued. Interestingly, the response to cued IHFT trials shows that anticipatory smooth eye movements do not require prior visual motion information (as in SP) but can be evoked simply by imagining targets in association with head motion.

**Role of SP in VOR suppression**

The role of visual and nonvisual mechanisms in modulating the VOR has been debated for many years. Visual suppression of the VOR shares many characteristics with SP, such as its low-pass response characteristics and the role of prediction (see Barnes 1993 for review). However, there is also evidence, for which our results now show further support, that the VOR can be suppressed in the absence of a visual target simply by imagining a HFT (Barr et al. 1976; Furst et al. 1987; Gauthier and Robinson 1975). Generally, it has been argued that this phenomenon could not result from activity of the SP system (Robinson 1982) because it is widely accepted that SP cannot normally be generated in the absence of a visible moving target. The original evidence for this conclusion came from a number of early sources (Heywood and Churcher 1971; von Noorden and Mackensen 1962). However, it is now evident that this is not correct and that it is possible to initiate and sustain SP in the absence of a visual target. A clear example is the ocular tracking of a moving sound (Hashiba et al. 1996; Kukowski and Stone 2002; Paige et al. 2000). Further, SP of auditory targets, as well as the influence of imagined targets, on the VOR follows similar dynamic properties to visual SP although with reduced gain (Paige et al. 1998; Paige et al. 2000).

The factor that appears to be most important for the initiation of anticipatory SP is the expectation of a future moving target (Barnes et al. 1997; Kowler and Steinman 1981) and knowledge of the time at which it will be appear. The ability to scale the velocity of the anticipatory movement in proportion to expected target velocity is also an important requirement if the anticipatory movement is to form a useful predictive estimate. In general, it has been found that the scaling of the anticipatory SP response is based on previously stored information derived from the prior visual stimulus (Barnes and Asselman 1991; Barnes et al. 2000). The current experiments are consistent with, and extend, this inference.

In the HFT condition of the current experiments, there is evidence for the release of previously stored activity in the catch trials without head movement (Fig. 9A) and in the scaling of anticipatory responses (V0, Fig. 7; V100, Fig. 9B). However, the input for this cannot arise from eye velocity itself (as it could in SP) because this is virtually eliminated by the fixation of the HFT. In fact, as we have argued previously (Barnes and Grealy 1992), it is probable that stored information is derived from a premotor source, upstream of the stage at which visual and vestibular signals interact. In SP, this premotor drive is responsible for directly controlling eye velocity, whereas in the HFT condition, it is responsible for interacting with the vestibular afferent drive and thus suppressing the VOR. Support for this concept has been provided by recent experiments in the monkey (Dubrovsky and Cullen (2002)). Further evidence that the source is not eye velocity itself is given by the finding that subjects can derive appropriately scaled velocity information even when required to fixate during...
presentation of a moving visual target (Barnes et al. 1997, 2000).

The fact that we have now observed anticipatory smooth movements in the IHFT condition, where there is no visual target, suggests that nonvisual mechanisms, including vestibular signals, may also have access to the SP system and its predictive capabilities, as suggested previously (Paige et al. 1998). However, our results provide limited evidence for scaling of the anticipatory response under IHFT conditions, in contrast to HFT trials (real targets). This may simply reflect the weaker influence of imagined than real targets in influencing the VOR.

Although it is possible to initiate smooth eye movements in the absence of a moving target, it is more difficult to sustain them. If the eye tracks a target that unexpectedly disappears, eye velocity can normally be maintained for only a short period (von Noorden and Mackenson 1962; Whittaker and Eaholtz 1982). Eye velocity tends to start decaying ~100 ms after target offset (Pola and Wyatt 1997; Robinson et al. 1986), and the time constant of decay is usually ~90–150 ms. However, smooth eye movements proportional to prior target velocity can be sustained for longer periods if target reappearance is expected (Becker and Fuchs 1985; Bennett and Barnes 2003).

Could the interaction of this sustained nonvisual SP component with the VOR account for the suppression of the VOR under IHFT conditions? The difference between the peak VOR response and the peak IHFT response for the highest head velocity (60°/s) had a mean value of 13.5°/s. This is within the range of sustained SP velocity recorded by Becker and Fuchs (~8°/s) and Bennett and Barnes (mean of 14°/s for 9 subjects). On this basis, it is feasible that the level of suppression in the IHFT condition could be accounted for by a centrally generated nonvisual signal that normally participates as part of the SP system (Paige et al. 1998). It is notable that the latency of the IHFT response in the noncued condition is very similar to that of the HFT condition, as though it is being accomplished through similar circuitry to visual feedback. If the expectation of target reappearance was an important factor in sustaining SP, it would have to be assumed that the continuation of the motion stimulus in the IHFT condition provides the expectancy that allows the response to be sustained in this way, but this is a factor that remains to be demonstrated.

Current evidence suggests that a likely source of a centrally generated signal responsible for anticipatory gaze control is the frontal eye field (FEF). The slowly increasing velocity profile of the anticipatory smooth movement has been observed by Gottlieb et al. (1993) and Tian and Lynch (1995) during microstimulation of FEF. In particular, Gottlieb et al. found that when the image was stabilized on the retina, the eye continued to accelerate for as long as stimulation continued and that the velocity increased with stimulus intensity. These are characteristics that would be required to control the timing and amplitude of anticipatory eye movements (Fig. 3). More recent experiments (Fukushima et al. 2000) have further shown that FEF processes information related to predictive activity during both pursuit and VOR suppression. FEF is known to be in bidirectional communication with the site responsible for visual motion processing in the tempo-occipital junction (V5/V5A), and both areas exhibit activity related to extraretinal activity as well as retinal slip as revealed by target blanking during pursuit (Fukushima et al. 2002; Komatsu and Wurtz 1988). Timing of the release of activity from the FEF may be mediated by the supplementary eye field (SEF) in dorsomedial frontal cortex (Heinen and Liu 1997).

**Evidence of other VOR suppression mechanisms**

It is clear that SP and nonvisual but SP-related mechanisms interact with the VOR in tangible ways. However, additional mechanisms of VOR suppression have been proposed. One alternative is a direct effect on the VOR independent of any relationship to SP. Most of the evidence for this type of VOR suppression has come from studies of gaze shifts or transient perturbations of the head (Guitton and Volle 1987; Heubner et al. 1992; Lauritius and Robinson 1986; Pelisson and Prablanc 1986; Tomlinson and Bahra 1986). Other support, derived from the clinical literature, relies on rare examples of dissociation between SP and VOR suppression as exemplified by Takeichi et al. (2000) in patients with spinocerebellar atrophy (SCA-6). However, the possibility of specialized or relative adaptation remains, and it is far more common to observe a clear association between deficits in SP and VOR suppression (Leigh et al. 1987).

Evidence for a direct form of VOR suppression in normal subjects remains mixed. Lisberger (1990) showed that when there is a sudden change in head velocity during VOR suppression, corrective action can occur with a latency as short as 36 ms in the monkey. This is considerably less than the latency of SP. The effect was found to be dependent on prior visual suppression, and it is thus conceivable that it might reflect a predictive velocity estimation process. Notably, the earliest part of the VOR response was not modified, so that there was no evidence for a parametric modification of the VOR prior to the change in head velocity, just as in our experiments (e.g., Fig. 5C, noncued response). Similarly, Gauthier and Vercher (1990) reported (in humans) that the early response (~150 ms) to a transient head rotation was similar whether the subject viewed a head- or earth-fixed target or remained in darkness.

More compelling evidence derives from experiments on monkeys by Cullen et al. (1991), who monitored suppression of the VOR induced by whole-body rotation on a turntable after sudden changes in head or target motion. They showed clear differences in VOR gain in the early part of the transient response as a function of the velocity of head motion. These differences were present when there was a sudden change in head acceleration but not target acceleration. Visual feedback mechanisms, including prediction, would be expected to operate equally in both cases, but the observation of a reduced VOR response after a change in head acceleration alone clearly indicates that a modification of the VOR had taken place during the prior fixation period. This form of VOR suppression is identifiable in recordings from VOR-related neurons in the vestibular nuclei (Cullen and McCrea 1993; McCrea et al. 1996). Of particular relevance is the recent finding of Roy and Cullen (2002) that the suppression of activity in these VOR-related neurons is present only when there is an expectation of gaze redirection, as in our HFT and IHFT conditions rather than gaze stabilization, which is equivalent to our VOR condition.
Conclusions

Our experiments illustrate the ability of human subjects to generate anticipatory smooth eye movements in advance of either expected head movements or expected target motion so long as head movement is linked with a real or imagined moving target. Such anticipatory responses likely represent the predictive control of gaze in response to the expected motion of a target in space. Results are compatible with other evidence favoring eye movements within the context of gaze control (Freedman 2001; Guitton 1992). The manner in which this process is carried out has been the subject of many attempts to model the behavior. The uncertain issues that surround such attempts include the role played by the VOR and the true nature of SP as well as their interaction. VOR suppression close to its input source and the potential for SP to exist without the actual presence of a visual target are also confounding. The evidence presented here and in other experiments (Jarrett and Barnes 2002) shows that smooth eye movements can be generated in the absence of a target when there is sufficient expectation of future target motion, regardless of the presence or absence of head movement (and therefore the VOR). We suggest that a central SP mechanism could be used in a very versatile way; not only in the context of the conditions examined here, but also, for example, in the modification of responses to linear VOR stimulation that accompany changes in viewing distance (Paige and Tomko 1991b; Paige et al. 1998). Elucidation of these phenomena will enable development of more representative and expansive models of visual-vestibular interaction.

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