Enhancement of the Vestibulo-Ocular Reflex by Prior Eye Movements

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Das, Vallabh E., Louis F. Dell'Osso, and R. John Leigh. Enhancement of the vestibulo-ocular reflex by prior eye movements. *J. Neurophysiol.* 81: 2884–2892, 1999. We investigated the effect of visually mediated eye movements made before velocity-step horizontal head rotations in eleven normal human subjects. When subjects viewed a stationary target before and during head rotation, gaze velocity was initially perturbed by ~20% of head velocity; gaze velocity subsequently declined to zero within ~300 ms of the stimulus onset. We used a curve-fitting procedure to estimate the dynamic course of the gain throughout the compensatory response to head rotation. This ar.alysis indicated that the median initial gain of compensatory eye movements (mainly because of the vestibulo-ocular reflex, VOR) was 0.8 and subsequently increased to 1.0 after a median interval of 320 ms. When subjects attempted to fixate the remembered location of the target in darkness, the initial perturbation of gaze was similar to during fixation of a visible target (median initial VOR gain 0.8); however, the period during which the gain increased toward 1.0 was >10 times longer than that during visual fixation. When subjects performed horizontal smooth-pursuit eye movements that ended (i.e., 0 gaze velocity) just before the head rotation, the gaze velocity perturbation at the onset of head rotation was absent or small. The initial gain of the VOR had been significantly increased by the prior pursuit movements for all subjects ($P < 0.05$; mean increase of 11%). In four subjects, we determined that horizontal saccades and smooth tracking of a head-fixed target (VOR cancellation with eye stationary in the orbit) also increased the initial VOR gain (by a mean of 13%) during subsequent head rotations. However, after vertical saccades or smooth pursuit, the initial gaze perturbation caused by a horizontal head rotation was similar to that which occurred after fixation of a stationary target. We conclude that the initial gain of the VOR during a sudden horizontal head rotation is increased by prior horizontal, but not vertical, visually mediated gaze shifts. We postulate that this "priming" effect of a prior gaze shift on the gain of the VOR occurs at the level of the velocity inputs to the neural integrator subserving horizontal eye movements, where gaze-shifting commands and vestibular signals converge.

INTRODUCTION

For clear vision of objects within the environment, their images must be held fairly still on the retina (Carpenter 1991). Head perturbations occurring during natural activities, especially locomotion, pose a threat to clear vision (Das et al. 1995). The vestibulo-ocular reflex (VOR) and visually mediated eye movements act in conjunction to generate eye movements that compensate for head perturbations. The VOR acts at much shorter latency (<15 ms) (Crane and Demer 1998; Maas et al. 1989) than visually mediated eye movements (~130 ms) (Carl and Gellman 1987). Therefore, if vestibular function is lost, visually mediated eye movements alone cannot compensate for the high-frequency head perturbations that occur during locomotion (J. C. 1952; Das et al. 1995; Leigh and Brandt 1993). Nonetheless, vision does appear to aid the VOR, even at high frequencies, because the gain of compensatory eye movements is less if subjects attempt to fix on the remembered location of a target in darkness rather than if they actually view it (Barr et al. 1976; Collewijn et al. 1981, 1983; Correia et al. 1985; Das 1998b; Demer 1992; Keller 1978; Paige 1994).

Current evidence indicates that the interaction between the VOR and visually mediated eye movements during responses to compensate for head rotations is nonlinear (Das et al. 1998b). One factor that may influence the compensatory response to head rotations is the prior occurrence of an eye movement. Huebner and colleagues (1992a) reported that, if subjects fix on a stationary target, gaze is perturbed at the onset of a velocity-step head rotation but not its offset (cessation of rotation) 1 s later. They found that, starting at ~70 ms after the onset of a head rotation, gaze velocity started to decline toward zero. Thus the gain of the compensatory response at the onset of head rotation was ~0.75 but was subsequently dynamically modulated up toward a steady-state value of 1.0 at the time of stimulus offset.

We investigated how a range of prior eye movements influences the gain of the ocular motor response that compensates for a sudden horizontal head rotation. We found that, when visually mediated eye movements were made just before head rotation, gaze was hardly perturbed, but only if the prior movements were in the same plane as the head rotation. Some preliminary results have been previously reported (Das et al. 1998a). The work reported in this paper constitutes research performed by V. E. Das as part of the requirements for his doctoral dissertation.

METHODS

Subjects and experimental equipment

We studied 11 normal human subjects (8 male, 3 female) whose ages ranged from 25 to 50 yr; all gave informed consent in compliance with our institutional guidelines and the tenets of the Declaration of Helsinki. Five of the subjects were experienced in ocular motor studies (subjects 1, 2, 3, 4, and 11), three were aware of the purpose of the experiments (subjects 1, 3, and 11), and the other subjects were naive as to the goals of the study. Subjects 3, 7, 9, and 10 were myopic; they did not wear glasses during the experiment but were

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easily able to see the visual target. Head and gaze rotations were measured with the magnetic search coil technique, with 6-ft field coils (CNC Engineering; Seattle, WA) that used a rotating magnetic field in the horizontal plane and an alternating magnetic field in the vertical plane. The system was 98.5% linear over an operating range of ±20° in both planes, cross talk between horizontal and vertical channels was <2.5%, and the SD of system noise was <0.02°. Search coils were initially calibrated before each experimental session with a protractor device; this calibration was then normalized to take account of each subject's head geometry (see EXPERIMENTAL PARADIGMS and DATA ACQUISITION AND ANALYSIS). Each subject wore a scleral search coil (Skalar; Delft, Netherlands) on one eye and another firmly attached to the forehead to measure angular head position. Subjects sat in a 30-ft-lb vestibular chair (Templin Engineering; Laytonville, CA) during all the experimental paradigms. The subjects' heads were clamped to the headrest of the chair throughout all experiments, and we confirmed that head and the chair movements were tightly coupled.

Experimental stimuli

The visual stimulus ("target") was a small laser spot (subtending an angle of 0.2°) on a white, translucent tangent screen, located at a distance of 1.2 m from the subject; the room was otherwise not illuminated. The position of the moving target was controlled by an X-Y mirror galvanometer (model CCX-660, General Scanning; Watertown, MA) that was driven by a computer-generated signal. Vestibular stimuli were also computer generated and consisted of velocity-step horizontal chair rotations at 15, 25, or 30°/s. To reduce oscillations of the chair headrest at the onset of the head rotation, the acceleration of the chair was minimized to ~200°/s^2. The actual acceleration of the chair varied slightly, depending on the weights of the subjects. This reduced acceleration stimulus improved the reproducibility of the head rotation from trial to trial. Data acquisition and stimulus generation were performed by a Pentium computer with programs developed in LABVIEW software with National Instruments boards.

Experimental paradigms

Before each session, a calibration file was collected in which subjects fixed on the stationary visual target while being rotated sinusoidally at 0.2 Hz and a peak velocity of 20°/s. All the subjects were able to fixate the visual target continuously throughout this trial and thereby maintain the gain of compensatory eye movements close to 1.0 (appropriate for the viewing distance). Thus the gain estimated during this trial was used to normalize all the eye movement responses in the following experiments. We applied eight experimental paradigms, which are listed subsequently; the abbreviations denote the condition before/after the onset of head rotation. All 11 subjects were tested with experimental paradigms 1–3; 4 subjects were tested with all paradigms. For those paradigms that involved presentation of moving visual stimuli before head rotation, we chose a fixed interval of 335 ms between the cessation of visual target motion and commencement of head rotation (based on preliminary experiments, we determined that this interval was long enough to allow gaze to become stationary before the chair started to move).

1) Fixation of a stationary visual target before and during horizontal head rotation (VisFix/VisFix). Subjects attempted to maintain fixation on the visual target before and during horizontal rotation in the chair. The rotational stimuli for this and all of the following paradigms were velocity steps of 15, 25, or 30°/s. The direction of chair rotation (leftward or rightward) and the magnitude of the velocity step were randomized.

2) Attempted fixation of the remembered location of a stationary target before and during horizontal head rotation (MemFix/MemFix). Subjects attempted to fixate the remembered location of the stationary target, in complete darkness, before and during chair rotations as used in paradigm 1. The central stationary target was extinguished 335 ms before onset of chair rotation.

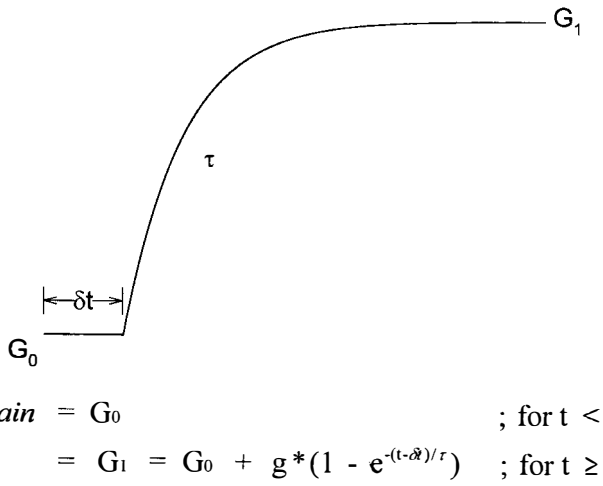

FIG. 1. Variable gain function used to fit the eye movement response during transient steps in head velocity. G_o was the gain of the open-loop response until time δt. Modulation of the compensatory eye movement response began at $t = \delta t$. The gain of the compensatory eye movement response subsequently increased from G_o to the steady-state value of G_1 with a time constant of τ. The equations describing the gain function are shown below the figure.

3) Horizontal smooth pursuit before horizontal head rotation while fixating a stationary visual target (HSP/VisFix). Each trial began as subjects smoothly pursued the visual target moving horizontally with their eyes (head stationary). The visual target moved at constant velocity of 15°/s for a period of 1 s before coming to a stop. The target motion started at an eccentric location and moved toward the center, but the exact starting and stopping position of the target was randomized. Then, 335 ms after the target came to a stop, the chair commenced a velocity-step rotation. During the head rotation, the subject attempted to maintain fixation on the stationary visual target.

4) Horizontal saccades before horizontal head rotation while fixating a stationary visual target (HSac/VisFix). Subjects first tracked horizontal step movements of the target at 1 Hz with saccades (head stationary). The starting and stopping position and the direction of target movements were randomized. Then, 335 ms after the target came to a stop, the chair commenced a velocity-step rotation. During the head rotation, the subject attempted to maintain fixation on the stationary visual target.

5) Horizontal passive tracking of a head-fixed target (VOR cancellation) before head rotation while fixating a stationary visual target (VORC/VisFix). In this paradigm, the visual target first moved in synchrony with the chair (and the subject's head, VOR cancellation or suppression) at a constant velocity of 10°/s for a period of 1 s before coming to a stop. Then, 335 ms later, the chair started moving again in either direction at 15, 25, or 30°/s, but this time the visual target was stationary and the subject attempted to maintain fixation of it.

6) Horizontal smooth pursuit before horizontal head rotation while attempting fixation of the remembered location of a stationary visual target (HSP/MemFix). This paradigm was similar to paradigm 3 except that 335 ms after the target came to a stop it was turned off, and when chair rotation commenced the subject attempted to maintain fixation on the remembered location of the stationary target.

7) Vertical smooth pursuit before horizontal head rotation while fixating a stationary visual target (VSP/VisFix). This paradigm was similar to paradigm 3 except that the subject pursued the target moving vertically at a constant velocity of 15°/s for a period of 1 s before coming to a stop. Then, 335 ms after the target came to a stop, the chair commenced a horizontal velocity-step rotation. During the

head rotation, the subject attempted to maintain fixation on the stationary visual target.

8) Vertical saccades before horizontal head rotation while fixating a stationary visual target (VSac/VisFix). This paradigm was similar to paradigm 4 except that the subject attempted to track, with saccades, vertical step movements of the visual target at 1 Hz. Then, 335 ms after the target came to a stop, the chair commenced a horizontal velocity-step rotation. During the head rotation, the subject attempted to maintain fixation on the stationary visual target.

Data acquisition and analysis

Head- and gaze-position signals were filtered with analogue Butterworth filters (Krohn-Hite; Avon, MA) set at a bandwidth of 0–150 Hz before digitization at 500 Hz with 16-bit resolution. Gaze and head positions were recorded in trials that lasted for 30 s each. The analysis was performed with programs written with MATLAB (Math Works; Natick, MA).

The first step in the analysis was to correct the eye and gaze signals for the eccentricity of eye position and the target distance (Huebner et al. 1992b). The parameters of head geometry were measured for each subject, and a correction to the eye movement records was made that corresponded to moving the eye to the axis of rotation of the head. In this way, data from different subjects could be compared. Eye position (in the orbit) was obtained by subtracting head position from gaze (eye position in space). Data were then digitally differentiated with a two-point central difference algorithm to obtain velocity signals. Data were software filtered with a notch filter set at 60 Hz to remove power line interference.

Measurement of gaze perturbation and determination of VOR parameters

We measured the ratio of eye velocity/head velocity at the time of peak gaze velocity, which was identified by examining each individual response. We then measured the dynamic change of the gain of compensatory eye movements during each response with a nonlinear curve-fitting method to determine the variable gain parameters (Das et al. 1998b; Huebner et al. 1992a). Figure 1 shows the function that we used for the curve fit. We estimated the values of G_0, δt, τ, and g, where G_0 is the initial gain of the response at the onset of the head stimulus, δt is the time delay before a modulation of the gain occurs, τ is the time constant of the gain modulation, and g is a scaling factor to determine the steady-state gain of compensatory eye movements. To prevent convergence of parameters on local minima and therefore improve the reliability of the curve fit, the initial guess for G_0 was set to the value obtained from the measurements of eye velocity/head velocity from individual responses. We then compared the initial gain at the onset of head rotation, G_0, under the different experimental conditions with ANOVA. All comparisons were performed with a P value of 0.05.

RESULTS

Gaze perturbations induced by head rotations during attempted fixation of a stationary target

All subjects showed a perturbation of gaze during the 250 ms after the onset of head rotation if they fixed on the stationary target before and during the head rotation (VisFix/VisFix condition); a representative record is shown in Fig. 2*A*. This

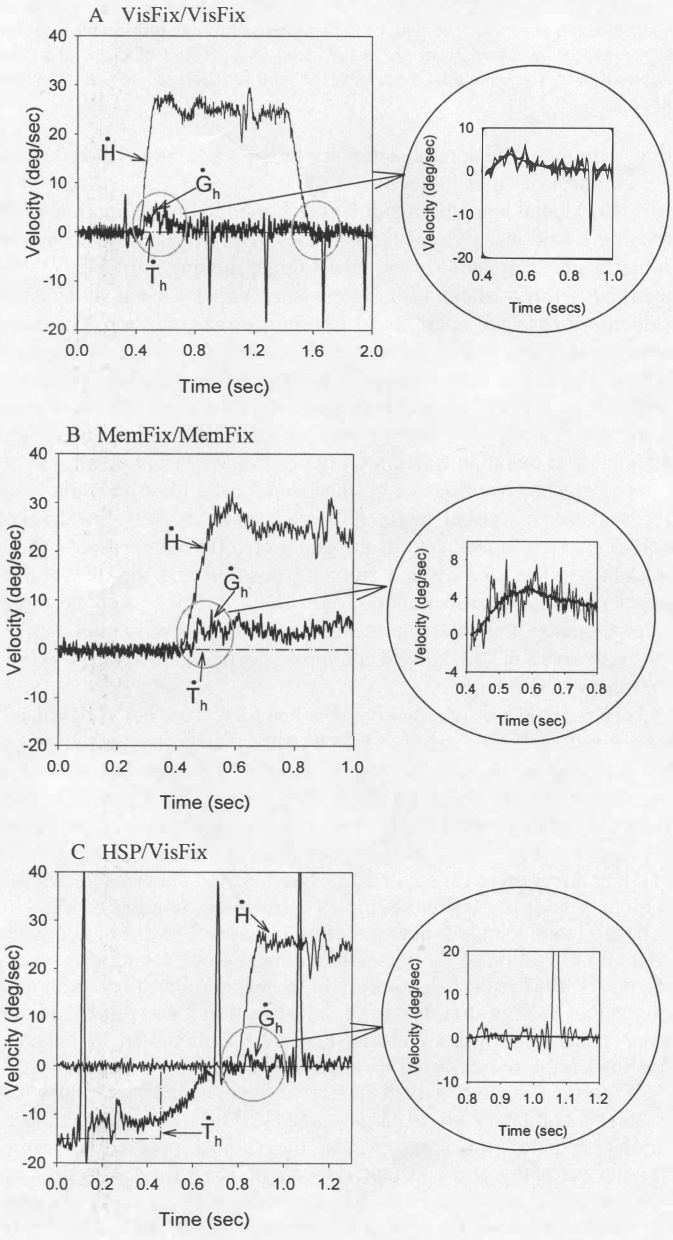

FIG. 2. Representative data from subject S3 shows gaze-movement response to head rotation in 3 test conditions. Positive values in all raw data plots indicate rightward/upward movements, and negative indicate leftward/downward movements. *Inset plots*: fits (smooth curves) for each gaze velocity perturbation based on the function shown in Fig. 1. A: response when subject was fixating the stationary target (target velocity, $\dot{T}_h = 0$) before and during the horizontal velocity-step head movement (VisFix/VisFix). There was an initial gaze perturbation (shown inside the shaded circle) that lasted ~250 ms. Gaze (eye-in-space) velocity, $\dot{G}_h$, subsequently fell close to 0°/s, indicating that a dynamic modulation of gain toward a value close to 1.0 occurred after the head movement started. The residuals between model fit and experimental data were normally distributed with a mean of 0.01°/s ± 1.4°/s. There was no gaze perturbation at the offset of head rotation, indicating that the gain at offset was still close to 1.0. *B*: response when the subject attempted to fixate remembered location of the stationary target in darkness before and during head rotation (MemFix/MemFix). The stimulus produced a similar initial gaze perturbation as in *A*, but it persisted and gaze velocity did not decline to 0°/s indicating that the gain of the compensatory eye-movement response remained at <1.0. The residuals between model fit and experimental data were normally distributed with a mean of 0.05°/s ± 1.4°/s. *C*: response to a head rotation after horizontal smooth pursuit of a laser target (HSP/VisFix). The gaze perturbation at the onset of the head rotation was minimal, indicating that the onset gain of the compensatory response had been increased by prior pursuit, before head rotation started. The amplitude of the saccade just before head rotation was 0.4°. The residuals between model fit and experimental data were normally distributed with a mean of −0.05°/s ± 1.3°/s.

TABLE 1. *Comparison of initial gain G_0 of compensatory eye movements at onset of head perturbation*

Subject	VisFix/VisFix	MemFix/MemFix	HSP/VisFix
S1	0.73 (0.11)	0.79 (0.11)	0.83* (0.13)
S2	0.82 (0.11)	0.90 (0.07)	0.93* (0.08)
S3	0.87 (0.05)	0.81 (0.08)	0.93* (0.06)
S4	0.74 (0.11)	0.79 (0.09)	0.86* (0.08)
S5	0.75 (0.05)	0.74 (0.12)	0.82* (0.08)
S6	0.79 (0.09)	0.83 (0.16)	0.90* (0.13)
S7	0.79 (0.05)	0.83 (0.07)	0.84* (0.05)
S8	0.80 (0.07)	0.84 (0.09)	0.87* (0.10)
S9	0.80 (0.09)	0.83 (0.10)	0.87* (0.07)
S10	0.79 (0.09)	0.81 (0.10)	0.86 (0.07)
S11	0.76 (0.06)	0.79 (0.14)	0.88* (0.08)
Median	0.79	0.81	0.87

Values in parentheses indicate SDs. VisFix/VisFix, fixation of stationary target before and during horizontal head rotation; MemFix/MemFix, attempted fixation of remembered location of stationary target before and during horizontal head rotation; HSP/VisFix, horizontal smooth-pursuit before horizontal head rotation while fixating a stationary visual target. * Significant difference ($P < 0.05$) compared with the VisFix/VisFix condition.

confirms a prior report (Huebner et al. 1992a). The median ratio of eye velocity/head velocity measured interactively at the time of peak gaze velocity for all subjects was 0.84 (range of means 0.79–0.89). If subjects attempted to fixate the remembered location of the stationary target while in darkness (MemFix/MemFix), the initial perturbation of gaze was similar but persisted much longer (Fig. 2*B*). The median ratio of eye velocity/head velocity at the time of peak gaze velocity for all subjects was 0.84 (range of means 0.75–0.90).

The curve-fitting procedure indicated in Fig. 1 enabled us to estimate the dynamic course of the gain throughout the response to head rotation. When the stationary target was visible throughout the trial (VisFix/VisFix), the median initial gain, G_0, for all the subjects was 0.79. When subjects attempted to fixate the remembered location of the target in darkness (MemFix/MemFix), the median initial gain, G_0, for all the subjects was 0.81. Values for individual subjects for both conditions are summarized in Table 1. Thus vision of the target before or during head rotation did not increase the initial gain of the response compared with attempted fixation in darkness.

The results in Table 1 are based on responses to stimuli at three head velocities. We separately analyzed the data to determine if G_0 was different at the higher (25 or 30°/s) head velocity compared with 15°/s. Six subjects showed a higher mean gain for the higher head velocities compared with 15°/s stimulus, although these differences reached statistical significance in only three of the subjects. These three subjects were not used for any of the control experiments described later (paradigms 4–8). Data for all stimulus head velocities were pooled for further analysis.

Although values of G_0 were similar for VisFix/VisFix and MemFix/MemFix, the subsequent course of the gain of compensatory eye movements differed between the two conditions. Thus, when the target was visible (VisFix/VisFix), modulation of gain started at a median latency (δt) of 100 ms (range of means 76–130 ms). All subjects showed a subsequent significant increase ($P < 0.001$), with group median steady-state gain (G_1) of 1.00 (range of means 0.96–1.02). The median time constant of the modulation (τ) was 72 ms (range of means 30–600 ms). In contrast, when subjects attempted to fixate the remembered location of the target in darkness (MemFix/MemFix), modulation of gain started at a median latency (δt) of 131 ms (range of means 82–303 ms), and the group median steady-state gain (G_1) was 0.94 (range of means 0.82–0.99). The steady-state gain was significantly increased in 7 of 11 subjects. The median time constant of the modulation (τ) was 1.18 s (range of means 181–2,451 ms). In summary, the initial gain at the onset of the head rotation was similar for the VisFix/VisFix and MemFix/MemFix conditions, but the increase of gain of compensatory eye movements occurred >15 times slower if subjects were not able to view the visual stimulus.

Gaze perturbations induced by head rotations that were preceded by smooth pursuit

When subjects performed horizontal smooth pursuit before chair rotation (HSP/VisFix), the perturbation of gaze after the onset of head rotation was reduced or absent; Fig. 2*C* shows a representative record. This was the case, although the eye was stationary (0 gaze velocity) before the head rotation, similar to the VisFix/VisFix condition. The median ratio of eye velocity/head velocity measured interactively at the time of peak gaze velocity for all subjects was 0.89 (range of means 0.85–0.92).

When we determined G_0 with the parameter estimation method shown in Fig. 1, the median value for all subjects was 0.87. Statistical comparison of the initial gain, G_0, for the three main experimental conditions (Table 1) with ANOVA showed that 10 of 11 subjects had significantly greater values of initial gain for the HSP/VisFix condition compared with the VisFix/VisFix condition. A comparison of the mean value of the initial gain of compensatory eye movements for each subject under each condition is displayed in Fig. 3; note that initial gain is always greater when the head rotation follows smooth pursuit.

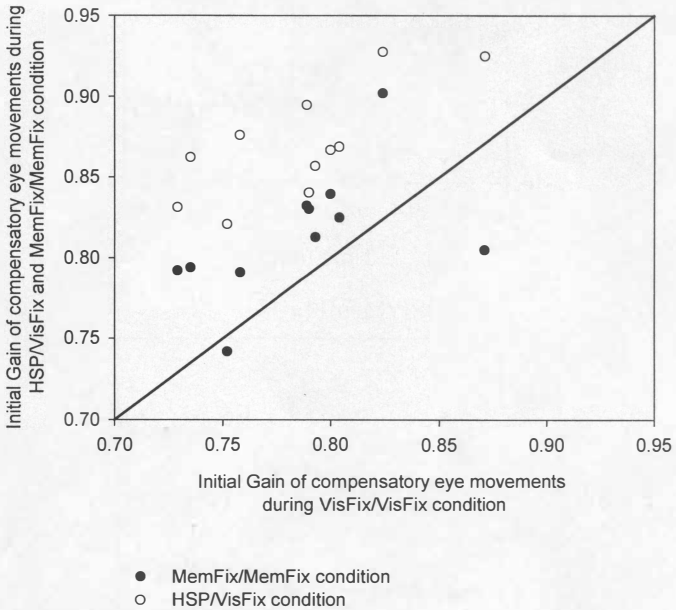

FIG. 3. Graphic comparison of mean values of the initial gain of compensatory eye movements, G_0, after the onset of head rotation during VisFix/VisFix, MemFix/MemFix, and HSP/VisFix tasks for all subjects. Open circles above the 45° line indicate that the initial gain value was greater during HSP/VisFix than VisFix/VisFix; in 10/11 subjects this difference was significant. Closed circles indicate that gain values during MemFix/MemFix were also generally greater than during VisFix/VisFix, but no subject showed a significant difference.

Thus, although vision of the stationary target did not consistently affect the initial gain of compensatory eye movements after a head rotation, a prior smooth-pursuit eye movement significantly increased it. Although initial gain values during MemFix/MemFix were also generally greater than during VisFix/VisFix, no subject showed a significant difference.

We carried out further analyses to determine if the direction of smooth-pursuit movement affected the magnitude of the initial gain of the response during the subsequent head rotation. We separated the HSP/VisFix data into two parts, one in which the smooth pursuit was in the same direction as the subsequent head rotation (HSPsame/VisFix) and the other in which smooth pursuit was in the opposite direction as the subsequent head rotation (HSPopp/Fix). When we compared the onset gains between these two conditions, 9 of 11 subjects showed no difference in the initial gain of compensatory eye movements for the subsequent head rotation. The other two subjects showed increased gain when the previous tracking task was opposite in direction to the later head rotation.

We also compared HSPsame/VisFix and HSPopp/VisFix with the VisFix/VisFix condition and found only idiosyncratic differences. Thus 7 of 11 subjects showed increased onset gain following both directions of prior smooth pursuit. Two subjects showed an increased onset gain only in the HSPsame/VisFix condition, whereas two other subjects showed an increased onset gain only in the HSPopp/VisFix condition. In a typical example, subject 1 showed a mean gain of 0.83 for HSPsame/VisFix and a mean gain of 0.83 for HSPopp/VisFix. These gains were not significantly different from each other (*t*-test; $P = 0.98$) and were both significantly different from the onset gain of 0.73 during VisFix/VisFix ($P < 0.05$).

Effects of other horizontal visual tracking tasks on gaze perturbations induced by head rotations

These further experiments were carried out on four subjects. First, when subjects performed a series of visually guided, horizontal saccades before the onset of head rotation (HSac/VisFix), all four showed a small or absent gaze perturbation (Fig. 4*A*), and this was reflected in the values of initial gain, which were increased in all four subjects compared with VisFix/VisFix, significantly so in three (Table 2).

Second, when subjects performed VOR cancellation before head rotation (VORC/VisFix), all four showed a small or absent gaze perturbation at the onset of head rotation (Fig. 4*B*), and the values of initial gain were increased in either direction in all four compared with VisFix/VisFix, significantly so in three (Table 2). In this condition, eye movements in the orbit

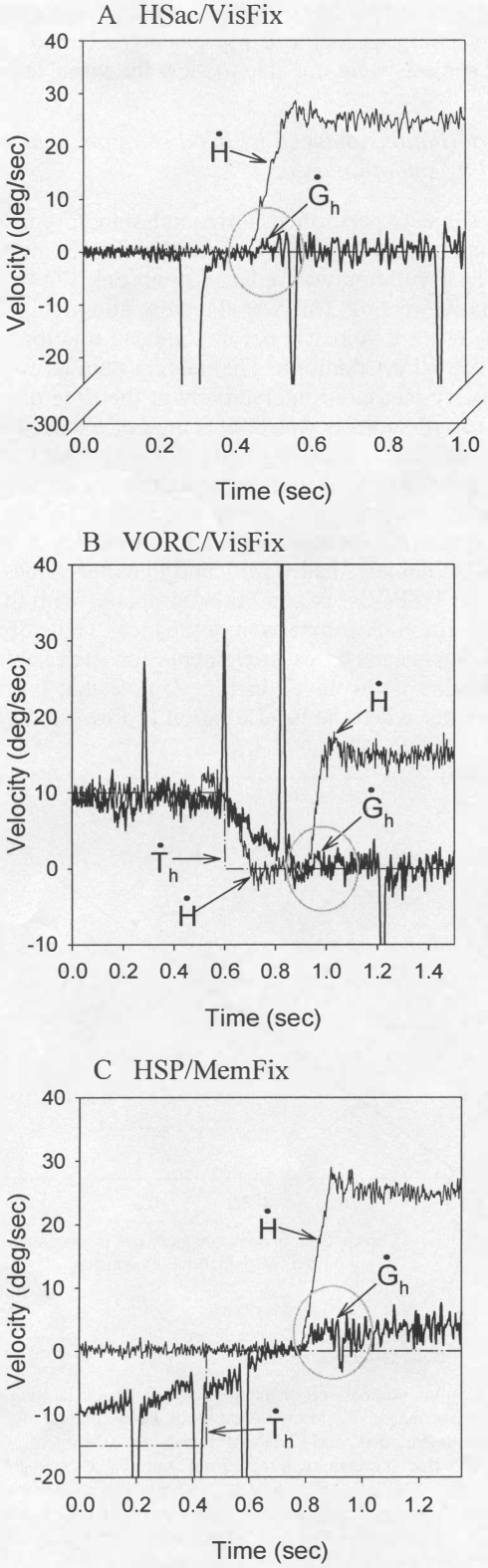

FIG. 4. Representative data from subject S2 showing the response to head rotation subsequent to performing visually guided gaze shifts in the horizontal plane. *A*: initially the subject tracked stepping movements of the visual target with saccades; after the target stopped moving, it remained visible and a head rotation commenced (HSac/VisFix). There was no gaze perturbation after the horizontal saccadic task, indicating that the gain of compensatory eye movements was increased before the onset of the head rotation. *B*: initially the subject smoothly tracked a head-fixed target [vestibulo-ocular reflex (VOR) cancellation]; the target and chair stopped; the chair commenced rotation again (VORC/VisFix) during which the subject viewed an earth-stationary target. There was no gaze perturbation at the onset of the second head rotation, indicating an increase in the initial gain of the compensatory response. Amplitude of the saccade just before head rotation was 0.6°. *C*: initially the subject tracked a smoothly moving target; the target stopped and was extinguished, and a head rotation commenced as the subject attempted to fix on the remembered location of the target (HSP/MemFix). The gaze perturbation at the onset of the head rotation was smaller compared with that during VisFix/VisFix but was larger compared with that during HSP/VisFix.

TABLE 2. *Comparison of initial gain G_0 at onset of head perturbations in further control experiments*

Subject	VisFix/VisFix	HSac/VisFix	VORC/VisFix	HSP/MemFix	VSP/VisFix	VSac/VisFix
S1	0.73 (0.11)	0.88* (0.13)	0.88* (0.12)	0.83 (0.06)	0.73 (0.11)	0.73 (0.07)
S2	0.82 (0.11)	0.93* (0.07)	0.94* (0.05)	0.87 (0.13)	0.84 (0.09)	0.79 (0.10)
S3	0.87 (0.05)	0.88 (0.08)	0.89 (0.08)	0.78 (0.12)	0.78 (0.08)	0.78 (0.09)
S11	0.76 (0.06)	0.88* (0.06)	0.88* (0.10)	0.85* (0.06)	0.72 (0.04)	0.74 (0.13)

Values in parentheses indicate SDs. HSac/VisFix, horizontal saccades before horizontal head rotation while fixating a stationary visual target; VORC/VisFix, horizontal passive tracking of a head-fixed target (VOR cancellation) before head rotation while fixating a stationary visual target; HSP/MemFix, horizontal smooth pursuit before horizontal head rotation while attempting fixation of remembered location of a stationary visual target; VSP/VisFix, vertical smooth pursuit before horizontal head rotation while fixating a stationary visual target; VSac/VisFix, vertical saccades before horizontal head rotation while fixating a stationary visual target. * Significant difference ($P < 0.05$) compared with the VisFix/VisFix condition.

were minimal during the VOR cancellation because motion of the chair and visual target were synchronized during the initial part of the trial. It should be noted that, although small saccades were also present during VORC/VisFix and HSP/VisFix paradigms and might have contributed to the increased initial gain, we observed individual responses in which saccades were absent but gain was increased.

Third, when horizontal smooth pursuit was conducted before head rotation in darkness during which subjects attempted to fixate the remembered location of a perceived earth-stationary target (HSP/MemFix), a gaze perturbation occurred, although this was generally less than for the condition in which subjects viewed a stationary target before and after head rotation (compare Figs. 4*C* and 2*A*). Estimated values of the initial gain of compensatory eye movements during the HSP/MemFix condition were greater than during the VisFix/VisFix condition in three subjects (significantly so in 1); the opposite was the case in one subject (Table 2).

Effects of vertical visual tracking tasks on horizontal gaze perturbations induced by head rotations

The same four subjects also performed visually guided tasks in the vertical plane before fixating the stationary target during horizontal head rotation. When subjects performed vertical smooth pursuit before horizontal head rotation (VSP/VisFix), perturbations of gaze were similar to during visual fixation of the stationary target before and during head rotation (VisFix/VisFix); this is evident if Fig. 5*A* is compared with Fig. 2*A*. Estimation of the values of initial gain during these two conditions showed no differences (Table 2). Similarly, when subjects performed visually guided vertical saccades before horizontal head rotation (VSac/VisFix), perturbations of gaze were similar to during visual fixation of the stationary target before and during head rotation (VisFix/VisFix) (Fig. 5*B*). Estimation of the values of initial gain during these two conditions showed gains to be generally lower following vertical saccades (Table 2).

DISCUSSION

We examined the effect of prior visually guided tasks on the eye movements that occur at the onset of a sudden horizontal head rotation. We first established that the initial gain of eye movements made to compensate for head rotations (mainly because of the VOR) are not affected by whether subjects view a target or attempt to view the remembered location of the target in darkness. The gain at the onset of head rotation in these two tasks was ~0.80, and the initial gaze perturbation was similar for both conditions. Second, we demonstrated that horizontal smooth pursuit, saccades, or VOR cancellation movements made before the head rotation increase the initial gain of compensatory eye movements and so reduce the initial gaze perturbation. Third, we found that smooth-pursuit and saccadic eye movements did not increase the initial gain of compensatory eye movements if they were made orthogonal to the plane of subsequent head rotation. Data for all paradigms for a typical subject are summarized in Fig. 6. To offer possible explanations for our findings, we will discuss each in turn.

Effects of target visibility on eye movements induced by sudden head rotation

We confirmed prior studies (Crane and Demer 1998; Huebner et al. 1992a) showing that the initial gain of eye movements induced by a velocity-step head rotation is less than that required to keep gaze (the line of sight) aimed at the object of regard (Fig. 2*A*). We further showed that this initial gain of ~0.80 is not influenced by whether the object of regard is visible or its location is remembered in darkness. Thus the initial gain of compensatory eye movements is probably the "default" gain value of the VOR, being similar with or without visual input.

Starting ~70 ms after the onset of head rotation, the gain of compensatory eye movements increases and by 300 ms it is ~1.0, provided the target is visible. The dynamics of gain modulation are much slower if the subjects attempted to fix on the remembered location of the target in darkness. There are several reasons the improved performance of compensatory eye movements that occurs if the target is visible cannot be due to a simple superposition of visually mediated eye movements, such as smooth pursuit, and the VOR with a gain of ~0.8. First, the gain of compensatory eye movements at the time of sudden cessation (off-step) of rotation is ~1.0, with a minimal gaze perturbation (Fig. 2*A*) (Huebner et al. 1992a). Second, studies employing high-frequency head rotations that are above the operating range of visually mediated eye movements have demonstrated that VOR gain rises to levels required to guarantee clear vision (Das et al. 1998b). Thus it appears that either the visual stimulus or the eye movements influence the magnitude of the compensatory response, possibly the VOR gain itself. It was this observation that served as an impetus for this study to determine whether other types of eye movements could increase the initial gain of the response to a sudden head turn.

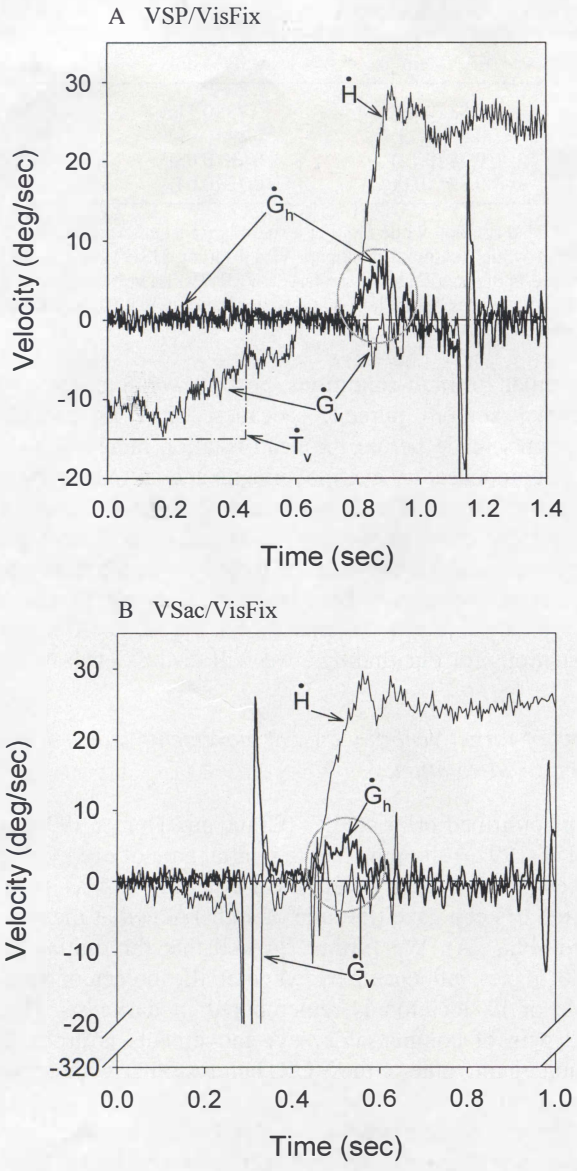

FIG. 5. Representative data from subject S1 showing gaze movement response after visually guided eye movements in vertical plane. *A*: initially, the subject pursued the visual target, which was moving at a constant velocity in the vertical plane ($\dot{T}_V$); after the target stopped moving, it remained visible, and a horizontal head rotation commenced (VSP/VisFix). The head rotation caused a gaze perturbation similar in magnitude to that caused when the target did not move before head rotation (VisFix/VisFix). This gaze perturbation indicated that there had been no increase of the initial gain of horizontal compensatory eye movements associated with the prior vertical pursuit eye movement. *B*: initially, the subject tracked the visual target, which was stepping in the vertical plane, with saccades; after the target stopped moving, it remained visible, and then a horizontal head rotation commenced. The head rotation caused a gaze perturbation of similar magnitude to when the target did not move before head rotation. This gaze perturbation indicated that there had been no increase of the initial gain of horizontal compensatory eye movements associated with the prior vertical saccades.

Visually mediated eye movements improve the initial response to sudden head rotation

The ability to improve the performance of one type of ongoing eye movement by generating another is now a well-established phenomenon. Thus saccades are reported to speed up a variety of types of eye movements: disparity or radial-flow induced vergence movements (Busettini et al. 1996, 1997; Zee et al. 1992), ocular following of large-field moving stimuli (Gellman et al. 1990; Kawano and Miles 1986), and the onset of smooth pursuit (Lisberger 1998). In experiments investigating mechanisms for cancellation of the VOR, Cullen et al. (1991) found that, if the monkey was already canceling its VOR during an eye-head tracking movement, then the response to a sudden change in head acceleration occurred at a short latency. They therefore conclude that this "priming" effect of the previous cancellation task is due to a vestibular signal that is gated by a desire to fixate a visual target.

Our new finding was that prior smooth pursuit, saccades, or VOR cancellation all may improve the initial compensatory response (VOR) to a sudden head rotation, when the eye is initially stationary. It seems unlikely that the vestibular input is primarily responsible for adjusting the gain of the VOR because a range of visually mediated eye movements induced the effect before head rotation. The phenomenon that we report is also somewhat different from the cases of saccade–vergence or saccade–pursuit interaction, when gaze was continuously changing; in our experiments, gaze velocity was 0°/s at the onset of head rotation. Furthermore, in our paradigm of prior VOR cancellation, little motion of the eye occurred in the orbit because the subject's head and the visual target moved together. This leaves the possibility that the priming effect that we observed was somehow due to a prior gaze-tracking command (smooth or saccadic).

Although the presence of a visual target (as opposed to its remembered location in darkness) did not influence the gain of the initial response to head rotation, vision was important for modulation of the subsequent compensatory eye movements. Thus the gain modulation occurred much more rapidly in the presence of the target (comparing VisFix/VisFix and MemFix/

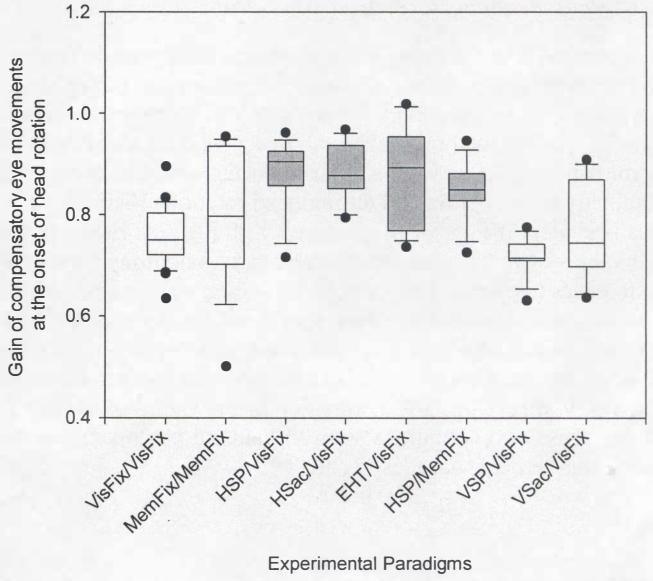

FIG. 6. Comparison of the initial gain of compensatory eye movements during head rotation for all test paradigms for subject 11. Paradigms that show significant differences compared with the VisFix/VisFix condition are shown in shaded areas. The initial gain of the response was significantly increased after horizontal smooth pursuit (HSP/VisFix), horizontal visually guided saccades (HSac/VisFix), and horizontal VOR cancellation (VORC/VisFix). This subject also showed increased gain when he attempted to view the remembered location of the stationary target after the horizontal smooth-pursuit task (HSP/MemFix). There was no increase in the initial gain for all other test paradigms.

MemFix), and the effects of a prior smooth-pursuit eye movement were less if the target light was not visible (i.e., was remembered) at the onset of head rotation (compare HSP/VisFix and HSP/MemFix). This pervasive role played by vision in facilitating responses is supported by the results of VOR cancellation paradigms reported by Cullen et al. (1991).

Visually mediated eye movements made orthogonal to the direction of head rotation do not improve the initial response to sudden head rotation

Further clues to the relative contributions of visual, oculomotor, and other factors may be derived from the finding that vertical saccades and vertical smooth pursuit did not increase the initial gain of the response to sudden horizontal head rotation. This is different from other cases of interactions of eye movements; thus vertical saccades may improve horizontal vergence (Zee et al. 1992) or smooth pursuit onset (Lisberger 1998). The lack of effect of vertical eye movements on subsequent responses to horizontal head rotation militates against an effect of light itself on luminance detectors (Miles et al.1986), the effects of attention or anticipation (Kowler et al. 1984), or the switching off of a visual fixation system (Luebke and Robinson 1988). Lisberger (1998) has suggested that the improved smooth pursuit that follows a saccade may be due to a switch that activates visuomotor processing, and he martials other evidence to support this view, such as demonstrations of improved pursuit responses to visual stimuli if the eye is already moving rather than stationary. Furthermore, Lisberger suggests that the direction of target motion (centripetal motion toward the fovea) is more effective than the converse (centrifugal motion away from the fovea) in activating the "pursuit switch." We looked for, but failed to find, any consistent relationship between the prior direction of smooth pursuit and the direction in which the gain of the initial response to head rotation was increased. Thus, although prior eye movements needed to be in the same plane as the head rotation to produce their priming effect, the direction did not seem to matter.

A possible mechanism by which prior eye movements could improve the responses to head rotation

What could account for the ability of smooth pursuit, saccades, VOR cancellation, and even vestibular eye movements (Huebner et al. 1992a) to improve the initial response to a subsequent head rotation? Previously we have suggested that visual, vestibular, and attentional factors such as readiness or expectations are unlikely to be the main mechanism that initiate the gain modulation, although all may contribute toward the dynamics of subsequent response.

We propose that the gaze-tracking command for the saccadic or pursuit eye movement influences the vestibular pathway to cause the increase in gain. These gaze movement signals, whether saccadic or pursuit, have access to the "common neural integrators" for eye movements. Certain anatomic structures and pathways make relatively more contributions to horizontal or vertical gaze. The nucleus prepositus-medial vestibular nucleus region appears more important for horizontal than vertical movements (Cannon and Robinson 1987; Mettens et al. 1994), whereas the converse is the case for the interstitial nucleus of Cajal (Helmchen et al. 1998). Thus we propose that the phenomenon that we describe here is due to a priming effect of the prior gaze shift on the velocity inputs to the network of cells that contributes to the ocular motor neural integrator so that, when a head rotation follows, the initial gain of compensatory eye movements (mainly VOR) is increased. Investigators have proposed a similar priming mechanism for the generation of express saccades by the superior colliculus whereby superposition of visual activity on a preexisting state of increased excitability facilitates saccade generation (Dorris et al. 1997; Sommer 1997; Sparks et al. 1998).

If there is indeed interaction between the VOR and a visually mediated eye movement command at the velocity inputs to the neural integrator, then the question is how could visual inputs produce such a short latency response that initiates gain modulation? Cortical pathways for SP and saccades are probably not involved because such responses are generally of longer latency (Carl and Gellman 1987). Recent evidence suggests that the accessory optic system (AOS) and the nucleus of the optic tract (NOT) may play a role in generating short-latency visual following eye movements (Büttner-Ennever et al. 1996; Ilg and Hoffmann 1996; Mustari and Fuchs 1989). First, AOS/NOT receives inputs from retina and lateral geniculate nucleus and projects to the vestibular nuclei and nucleus prepositus hypoglossi, which are important components of the neural integrator mechanism. Second, neurons in AOS/NOT are visually driven at short latency because they receive direct input from the retina (Ilg and Hoffman 1996; Mustari and Fuchs 1989); they have been shown to be sensitive to retinal slip during tracking of a small spot (Ilg and Hoffman 1996) in a particular plane. Third, Mustari and colleagues (1997) have shown that a certain subgroup of cells (the "following omnipause neurons" or FOPNs) in the NOT cease firing immediately after a saccade. Thus one hypothesis is that short-latency visual signals via AOS/NOT interact with gaze-tracking commands (smooth or saccadic) in the nucleus prepositus-vestibular nucleus region (which is important for the neural integration of horizontal gaze signals), thereby changing the internal gain of the VOR response. Further studies are required to determine the time course of the phenomenon and whether it has an electrophysiological counterpart. Finally, there is need to determine the functional significance of the priming effect of eye movements on the VOR. For example, the increased VOR seems appropriate as the subject's behavior switches from one of steady fixation while stationary to tracking components in the environment that will subsequently require locomotion.

We are grateful to Drs. Gerald M. Saidel and David L. Wilson for critical comments.

This work was supported by the Office of Research and Development of the Department of Veterans Affairs, by National Eye Institute Grant EY-06717 to R. J. Leigh, and by the Evenor Armington Fund.

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Received 10 December 1998; accepted in final form February 1999.

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