Effect of Vergence on Human Ocular Following Response (OFR)

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Joshi AC, Thurtell MJ, Walker MF, Serra A, Leigh RJ. Effect of vergence on human ocular following response (OFR). J Neurophysiol 102: 513–522, 2009. First published May 20, 2009; doi:10.1152/jn.00045.2009. The human ocular following response (OFR) is a preattentive, short-latency visual-field–holding mechanism, which is enhanced if the moving stimulus is applied in the wake of a saccade. Since most natural gaze shifts incorporate both saccadic and vergence components, we asked whether the OFR was also enhanced during vergence. Ten subjects viewed vertically moving sine-wave gratings on a video monitor at 45 cm that had a temporal frequency of 16.7 Hz, contrast of 32%, and spatial frequency of 0.17, 0.27, or 0.44 cycle/deg. In Fixation/OFR experiments, subjects fixed on a white central dot on the video monitor, which disappeared at the beginning of each trial, just as the sinusoidal grating started moving up or down. We measured the change in eye position in the 70- to 150-ms open-loop interval following stimulus onset. Group mean downward responses were larger (0.14°) and made at shorter latency (85 ms) than upward responses (0.10° and 96 ms). The direction of eye drifts during control trials, when gratings remained stationary, was unrelated to the prior response. During vergence/OFR experiments, subjects switched their fixation point between the white dot at 45 cm and a red spot at 15 cm, cued by the disappearance of one target and appearance of the other. When horizontal vergence velocity exceeded 15°/s, motion of sinusoidal gratings commenced and elicited the vertical OFR. Subjects showed significantly (P < 0.001) larger OFR when the moving stimulus was presented during convergence (group mean increase of 46%) or divergence (group mean increase of 36%) compared with following fixation. Since gaze shifts between near and far are common during natural activities, we postulate that the increase of OFR during vergence movements reflects enhancement of early cortical motion processing, which serves to stabilize the visual field as the eyes approach their new fixation point.

INTRODUCTION

The human fovea corresponds to the area of retina with greatest visual acuity for objects with high spatial frequencies, such as conventional text. Thus the foveal line of sight of each eye must be pointed at a feature of interest in the visual environment to see it best (Carpenter 1991). Many elements of the visual world lie in different directions and at different distances (depths). Consequently, most natural shifts of the binocular point of fixation are achieved using a combination of saccades and vergence movements (Collewijn et al. 1995). During locomotion, shifts of the binocular point of fixation between a handheld object and the distant visual environment may occur frequently, such as when a hunter moves the point of visual fixation from a near, handheld weapon to a distant prey. During such gaze shifts, the visual background is moving due to the optic flow caused by locomotion. Thus it appears that some short-latency mechanism is required to hold the eye steady at its new point of fixation, whether near or far.

The human ocular following response (OFR) is a preattentive, short-latency visual tracking mechanism, which seems suited to act as a visual-field–holding response (Miles 1998; Sheliga et al. 2005, 2008). Thus the OFR is enhanced by as much as 100% in the wake of a saccade, when ocular drifts occur and could constitute a threat to clear vision, if not promptly terminated (Gellman et al. 1990). The OFR has been extensively studied in response to horizontal stimulus motion (Sheliga et al. 2005, 2008), but during fixation of a near object in the lower visual field, the background optic flow induced by locomotion is predominantly downward. Thus the first goal of this study was to examine the vertical OFR in a group of 10 normal human subjects, define their range of responses, and relate them to other forms of visual tracking during locomotion, such as optokinetic responses. A second goal was to determine whether the vertical OFR would be enhanced as subjects shifted their point of fixation between targets lying at different depths in the horizontal plane. We found that the vertical OFR was enhanced during ongoing smooth vergence eye movements compared with responses when there was no need to shift the point of visual fixation. Preliminary results have appeared as an abstract (Joshi et al. 2008).

METHODS

Subjects

We studied 10 healthy human subjects (8 male; median age 38 yr, range 27–61 yr); 5 were naive to the goals of the study. None was taking any medicine with effects on the CNS. All gave informed written consent in accordance with the Declaration of Helsinki and our Human Subjects Institutional Review Board. Binocular eye movements were measured using the magnetic search coil technique (Robinson 1963); the SD of the noise of our system was ±0.016°.

Visual stimuli

Subjects sat in a dark room with their head stabilized by supports attached to a chair, with a distance of 45 cm from the corneal vertex to a Viewsonic G225F computer monitor; any small head movements that occurred were detected using a search coil attached to their forehead. Visual images presented on the computer monitor were viewed binocularly and consisted of one-dimensional horizontal sine-wave grating patterns shifted at a temporal frequency of 16.7 Hz, which has been shown to evoke optimal responses (Gellman et al. 1990). These stimuli had a contrast of 32% and a spatial frequency (Fs) of 0.17, 0.27, or 0.44 cycle/deg, so that corresponding speeds were 100, 62.5, and 37.5°/s. Each image extended 400 mm horizontally (1,600 pixels, subtending 50°) and 300 mm vertically (1,200 pixels, subtending 37.5°); mean luminance was 42.6 cd/m² and frame rate was 100 Hz (Sheliga et al. 2005).
grating was randomized from trial to trial at intervals of 1/6 wavelength. Prior to each OFR-fixation trial, subjects viewed a white central spot (diameter 0.25°) centered on stationary gratings on the computer monitor. For experiments in which OFR was tested during vergence movements, subjects viewed a “near stimulus,” consisting of a red laser spot (diameter 0.4°), which was projected onto a transparent sheet of plastic at a viewing distance of 15 cm. Before testing, a nine-point calibration procedure was run as subjects fixed on a small white dot that moved from the center to four horizontal and four vertical eccentric positions on the computer monitor. Subjects who were not emmetropes wore their spectacles during testing and we were able to make an adjustment for the rotational magnification due to their refractive correction during this nine-point calibration procedure. Three test paradigms, each with a control, were applied; these are summarized in Fig. 1. In addition, four further control experiments were conducted to take account of differences in visual stimuli during each of the test paradigms.

**FIXATION/OFR EXPERIMENTS.** Subjects were instructed to fix on a white spot centered on a grating pattern on the video monitor, which was presented for a random period of 200–300 ms, before it disappeared, just as the sinusoidal grating started moving up or down (Fig. 1). During Fixation/OFR trials (A), the subject was instructed to fix on a white spot at the center of the gratings on the video monitor. After 200–300 ms, the white spot was turned off and the sinusoidal grating started to move up or down. After 200 ms, the screen was switched to uniform gray (trial end). During Fixation/OFR control trials (B), the gratings did not move when the white spot was turned off. During Divergence/OFR trials (C), the subject started by fixing on a near red stimulus; after a randomized period of 2.5–3 s, the near red stimulus was turned off and the white spot and gratings appeared on the monitor, which was the cue to diverge; when divergence velocity exceeded 15°/s, the white spot was turned off and the grating began to move. During Divergence/OFR control trials (D), the gratings did not move when the white spot was turned off. During Convergence/OFR trials (E), the subject started by fixing on the white spot on the monitor. After a randomized period of 2.5–3 s, the white spot was turned off and the near red spot appeared; this was the cue to converge; when convergence velocity exceeded a threshold of 15°/s, the red light was turned off and the gratings started to move. During Convergence/OFR control trials (F), the gratings did not move when the red light was turned off.

**FIG. 1.** Schematic summary of visual stimuli. Upward or downward motion of 3 sinusoidal gratings were applied under each experimental condition. During Fixation/ocular following response (OFR) trials (A), the subject was instructed to fix on a white spot at the center of the gratings on the video monitor. After 200–300 ms, the white spot was turned off and the sinusoidal grating started to move up or down. After 200 ms, the screen was switched to uniform gray (trial end). During Fixation/OFR control trials (B), the gratings did not move when the white spot was turned off. During Divergence/OFR trials (C), the subject started by fixing on a near red stimulus; after a randomized period of 2.5–3 s, the near red stimulus was turned off and the white spot and gratings appeared on the monitor, which was the cue to diverge; when divergence velocity exceeded 15°/s, the white spot was turned off and the grating began to move. During Divergence/OFR control trials (D), the gratings did not move when the white spot was turned off. During Convergence/OFR trials (E), the subject started by fixing on the white spot on the monitor. After a randomized period of 2.5–3 s, the white spot was turned off and the near red spot appeared; this was the cue to converge; when convergence velocity exceeded a threshold of 15°/s, the red light was turned off and the gratings started to move. During Convergence/OFR control trials (F), the gratings did not move when the red light was turned off.
1A). The motion lasted for 200 ms, at which point the screen became a uniform gray (luminance, 42.6 cd/m²), marking the end of the trial. After an inter-trial interval of 1,500 ms a new grating pattern together with a fixation point appeared, commencing a new trial. During 20% of trials, the sinusoidal grating remained stationary during the trial, instead of moving up or down (Fixation/OFR control trials, Fig. 1B).

DIVERGENCE/OFR EXPERIMENTS. Subjects were instructed to fix on the near red stimulus, with the monitor screen set at an isoluminance gray; after a randomized period of 2.5–3 s, the near red stimulus was turned off and the white spot and gratings appeared on the monitor, which was the cue to diverge. The OFR stimulus (and offset of the white spot) was triggered when divergence velocity exceeded a threshold of 15°/s (Fig. 1C). In practice, the time period from when divergence velocity exceeded this threshold until the onset of vertical motion of the sinusoidal grating was about 30 ms. During 20% of trials, the sinusoidal grating remained stationary during the divergence movement (Divergence/OFR control trials, Fig. 1D).

CONVERGENCE/OFR EXPERIMENTS. Subjects were instructed to fix on the white spot centered on stationary gratings on the computer monitor; after a randomized period of 2.5–3 s, the white spot was turned off and the near red spot appeared, which was the cue to converge. The OFR stimulus was triggered (and the red spot was turned off) when convergence velocity exceeded a threshold of 15°/s; the actual onset of vertical motion of the sinusoidal grating occurred about 30 ms later (Fig. 1E). During 20% of trials, the sinusoidal grating remained stationary during the convergence movement (Convergence/OFR control trials, Fig. 1F).

Each Fixation/OFR and Vergence/OFR session lasted for 150 s, comprising six different stimulus conditions (three spatial frequencies × two directions of motion). Stimulus conditions, including control trials, were randomized in order and timing of presentation. Subjects completed at least three sessions for each of the three test paradigms, with rest breaks in between (total test time: about 20 min).

CONTROL EXPERIMENTS. Four sets of control experiments were conducted on four subjects. Control experiments 1 and 2 induced a “gap” between offset of the fixation target and onset of grating motion; Control experiments 3 and 4 had “no gap” between the offset of the fixation target and onset of grating motion. Thus for Control experiment 1, the fixation target was turned off and vertical grating motion started after a controlled delay, which was the average time that each subject took to reach the convergence threshold (15°/s) during Convergence/OFR experiments. For Control experiment 2, the fixation target was turned off and vertical grating motion started after a controlled delay, which was the average time that each subject took to reach the divergence velocity threshold (15°/s) during Divergence/OFR experiments. For Control experiment 3, subjects fixated on the white spot, with no gratings pattern, on the monitor for 2.5–3 s, and the moving grating stimulus was presented for the last 200–300 ms (similar to stimulus presentation during the Divergence/OFR experiments). For Control experiment 4, subjects fixated on the white spot, centered on stationary gratings pattern, on the monitor for 2.5–3 s, and the moving grating stimulus was presented for the last 200–300 ms (similar to stimulus presentation during the Convergence/OFR experiments). Responses from each of these control experiments were compared with responses from the standard Fixation/OFR experiment.

RESULTS

OFR following fixation of a stationary target

Figure 2 displays mean, representative upward responses from Subject 7 and downward responses from Subject 5 for each of the three spatial frequencies for the three paradigms (black traces). Vertical dashed lines indicate the times at which eye position was sampled (70 and 150 ms) to calculate the amplitude of the OFR.

Figure 3 is a boxplot summarizing mean amplitude values of OFR from all 10 subjects. Group mean OFR ± SE of upward responses was 0.10 ± 0.01° and of downward responses was 0.14 ± 0.02°, similar to values previously reported (Gellman et al. 1990). Substantial intersubject variability was evident, but a paired t-test showed that downward mean responses were significantly greater in amplitude than upward mean responses (P < 0.001). Using a pairwise multiple comparison procedure (three-way ANOVA, Holm–Šidák method), we found that the Fixation/OFR response magnitude showed dependence on the spatial frequency of the stimulus (P < 0.001). The group means ± SE response amplitude for each spatial frequency were: Fs of 0.17 cycle/deg: mean amplitude = 0.16 ± 0.02°; Fs of 0.27 cycle/deg: mean amplitude = 0.12 ± 0.02°; Fs of 0.44 cycle/deg: mean amplitude = 0.08 ± 0.02°. Thus despite the intersubject variability, there was an inverse relationship between
between OFR amplitude and the spatial frequency of our stimuli; this is evident in Fig. 3.

We found that the latency (mean ± SD) to onset of downward OFR (85 ± 15 ms) was significantly shorter ($P < 0.001$) than that of upward OFR (96 ± 17 ms). Using a three-way ANOVA, we found that latency showed dependence on the spatial frequency ($P = 0.005$), being significantly shorter (84 ± 14 ms) for the lowest spatial frequency (Fs of 0.17 cycle/deg, $P < 0.023$). However, latency was not statistically different between the two higher spatial frequencies (91 ± 18 ms for 0.27 cycle/deg and 95 ± 17 ms for 0.44 cycle/deg).

We investigated whether eye drifts occurring during each Fixation/OFR control trial was influenced by the moving stimulus of the prior trial. We found that eye drifts during control trials were small, idiosyncratic and stereotyped for each subject, and uncorrelated with the direction of grating motion in the preceding trial ($r = -0.05$).

**Comparison of OFR with predictable visual tracking**

Since different subjects showed a broad range of OFR values (Fig. 3), we asked whether this variability was related to smooth ocular following of predictable target motion (Kawano 1999; Leigh and Zee 2006). Accordingly, we compared OFR and “optokinetic responses” (OKRs) to a 0.27 cycle/deg grating that moved sinusoidally through several cycles at frequencies between 0.1 and 2.5 Hz. Note that this visual stimulus was predictable, not open-loop, and that subjects attempted to track an individual grating (“look” optokinetic responses). Inspection of Bode plots of OKR (Fig. 4, top) indicated that the gain (eye velocity/target velocity) declined sharply for frequencies $>1$ Hz, and so we conducted a paired comparison of OKR gain at 1.0 Hz and mean OFR amplitude in response to the 0.27 cycle/deg stimulus. The OKR gain and mean OFR amplitudes were separately normalized by assigning a value of 1.0 for the response of the individual with the best tracking and scaling values for other subjects proportionally. Figure 4 (bottom) shows that there was no correlation between OFR and OKR for up or down movements for our group of 10 subjects. Thus these two tracking behaviors appear to differ, as previously suggested (Gellman et al. 1990).

**OFR during vergence movements**

Figure 5A displays mean (total number of trials = 133) upward and downward OFR during divergence movements from Subject 2; note that the downward response to the 0.44 cycle/deg stimulus is small and does not move the eye below zero vertical position. Figure 5B shows the mean ($n = 33$) vertical eye movement occurring during divergence when the visual background was stationary (divergence control trials). Note that the upward drift in Fig. 5B persists throughout the 200-ms epoch. Such vertical eye drifts associated with the vergence response occurred even after careful attempts to align the near and far targets and, when they persisted beyond 70 ms after the onset of grating motion, we assumed that they would be superimposed on the OFR. Such an effect could be cor-

![FIG. 3. Box-plot summary of mean Fixation/OFR amplitudes for all 10 subjects; percentile values for each data set are labeled at left (50% is the median). Note that response magnitude is inversely related to the spatial frequency of the stimulus and that responses are generally greater for downward than for upward stimuli.](http://jn.physiology.org/)

![FIG. 2. Summary of representative mean responses from subjects S5 (downward responses) and S7 (upward responses), corrected for offset by setting eye position for each curve to zero at 70 ms, for each stimulus condition and spatial frequency. Vertical dashed lines indicate times at which eye position was sampled (70 and 150 ms) to calculate OFR amplitude. Fixation/OFR responses (black) are greatest in response to the 0.17 cycle/deg stimulus (the lowest spatial frequency) and smallest for the 0.44 cycle/deg stimulus; for each spatial frequency. Divergence/OFR responses are shown in red and Convergence/OFR responses in blue; both are generally greater than responses to Fixation/OFR. In this and following figures, positive values indicate upward eye movements.](http://jn.physiology.org/)
corrected as shown in Fig. 5C, which shows the results of subtracting the waveform in Fig. 5B from the OFR responses in Fig. 5A, and offsetting the curves to zero at 70 ms. We confirmed that the direction of eye drifts occurring during vergence control trials, when gratings were stationary, was not correlated ($r = 0.04$) with the stimulus direction in the prior trial. Furthermore, we carried out a paired comparison of mean change of vertical eye position during the period 0–60 ms after the onset of grating motion for upward versus downward stimuli for each subject at each spatial frequency and found no significant difference for either convergence ($P = 0.052$) or divergence ($P = 0.13$).

Figure 2 compares representative upward and downward Fixation/OFR raw responses (in black) versus Divergence/OFR responses (in red) and Convergence/OFR responses (in blue), from two subjects, S5 (downward responses) and S7 (upward responses), for each of the three spatial frequencies. The responses made during vergence/OFR are greater than responses during Fixation/OFR. Of the group of subjects, three were unable to reliably generate divergence responses and two were unable to generate convergence during our test conditions. The remaining subjects, as for Fixation/OFR, showed substantial variability of the amplitude of responses between individuals.

Group means ± SE was $0.19 ± 0.02°$ for Divergence/OFR, and...
0.22 ± 0.02° for Convergence/OFR. A paired t-test of Convergence/OFR versus Divergence/OFR responses for each subject, stimulus direction and spatial frequency showed no significant differences (P = 0.06). Paired t-test showed no significant differences between the amplitude of upward and downward responses during either divergence (P = 0.62) or convergence (P = 0.24) movements. Thus group mean ± SE OFR amplitude for upward/divergence was 0.18 ± 0.02° and for downward/divergence was 0.19 ± 0.02°; group mean OFR amplitude for upward/convergence was 0.21 ± 0.02° and for downward/convergence was 0.24 ± 0.02°. Using a pairwise multiple comparison procedure, we found that the Divergence/OFR response magnitude showed no dependence on the spatial frequency of the stimulus (P = 0.623). For Convergence/OFR responses, the magnitude showed a significant (P = 0.002) dependence on the spatial frequency of the stimulus, except between the higher two frequencies. Thus for Fs of 0.17 cycle/deg, mean ± SE amplitude was 0.30 ± 0.03°; for Fs of 0.27 cycle/deg, mean amplitude was 0.19 ± 0.02°; and for Fs of 0.44 cycle/deg, mean amplitude was 0.18 ± 0.03°.

Using a paired t-test, we found no significant difference between the latency of upward (mean ± SD: 83 ± 15 ms) versus downward (82 ± 9 ms) responses during Divergence/OFR (P = 0.697). However, during Convergence/OFR, we observed significantly greater (P = 0.01) latency for upward (89 ± 14 ms) versus downward (80 ± 11 ms) responses. The latency was not dependent on the spatial frequency for either Divergence/OFR or Convergence/OFR. There was no significant difference in latency between Convergence/OFR versus Divergence/OFR.

Comparison of Fixation/OFR and Vergence/OFR

Figure 6 displays a paired comparison of the amplitude of responses for each subject at each spatial frequency for OFR following fixation (abscissa scale) versus OFR either during divergence (A and C) or convergence (B and D) (ordinate scale). Subjects showed significantly larger OFR during convergence (absolute group mean increase of 46%) or divergence (absolute group mean increase of 36%) compared with following fixation.

Note that the Vergence/OFR data in Fig. 6 have been calculated using the drift correction exemplified in Fig. 5. Since some convergence responses showed a persistent drift even after this correction, we carried out a further analysis after eliminating such responses. To select responses to eliminate, we used a criterion of change in eye position exceeding 2SDs for the corresponding vergence control during the period 0–60 ms following stimulus onset. Using this reduced data set (mean number of trial per subject = 46), paired comparison of mean amplitudes still demonstrated a significantly greater response (P < 0.001) for Convergence/OFR versus Fixation/OFR.

We also considered a second way in which persistent vertical drifts associated with vergence responses could influence OFR: they could subtract from retinal image slip due to grating motion. Prior studies have suggested that retinal image slip due

![FIG. 6. Paired comparison of mean amplitudes of responses during Fixation/OFR (abscissa scale) vs. either Divergence/OFR or OFR/convergences (ordinate scale). In each case, OFR amplitude was greater when it was accompanied by a vergence eye movement. Note that 7 subjects could diverge during Divergence/OFR and 8 subjects could converge during Convergence/OFR testing (see text). Significance levels shown are from paired comparisons using the Wilcoxon rank-sum test.](http://jn.physiology.org/)

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to saccades have <30% effect on OFR (Gellman et al. 1990), but vertical slip due to vergence movements is more prolonged and might directly affect OFR. Thus to estimate the magnitude by which retinal image slip due to the vertical component of vergence may have affected OFR, we applied a simple model in which retinal image velocity was due to both vertical eye drifts and the motion of the visual stimulus (Fig. 7). Note that our goal was to address two issues: 1) whether vertical eye drifts influenced the stimulus for OFR; 2) whether there was an increase of internal gain (G) during Vergence/OFR. First, we calculated optimal values of the internal parameters, gain G, and time constant T, for the mean Fixation/OFR response of individual subjects at one spatial frequency (see the Appendix for details). We took into account any small drifts that occurred during control trials when the gratings were stationary. Thus EVcontrol is mean eye drift during Fixation/OFR control trials, and EVOFR is the model’s output. The value of the Delay was set as measured for that subject and stimulus. The model gave a good fit, defined here as a residual sum-of-squares error of <20% and $R^2$ values >0.9, for >80% of subjects upward or downward mean Fixation/OFR responses at each frequency; a representative example is shown in Fig. 7B. We then asked whether the model with the parameter values estimated for Fixation/OFR could also simulate mean Divergence/OFR or Convergence/OFR responses to the same visual stimulus; in all cases it failed. Finally, we reestimated parameter values as the model was applied to simulate Vergence/OFR responses, taking account of the effects of vertical eye drifts on retinal image slip; thus in addition to G and T, we estimated the optimal value of K (see pathway in gray in Fig. 7A, in which the summing junction represents the retina). For Vergence/OFR trials, the model was less successful in obtaining a good fit, especially for Convergence/OFR, when vertical drifts were more commonly affected by saccades. Nonetheless, we were able to identify 18 trials (21% of total) when the model gave a good fit for Vergence/OFR responses; an example is shown in Fig. 7C. Paired comparisons of Vergence/OFR versus Fixation/OFR made with the Wilcoxon rank-sum test (Fig. 7D) showed a statistically significant increase ($P = 0.004$) of G from a median of 0.10 to 0.17 but no significant change in T (median of 0.03 s for both conditions). The median value of K was 0.13, indicating a relatively small effect of vertical eye drifts on retinal image slip, and being smaller than the estimate of 0.3 for the effects of image motion due to saccades on the OFR (Gellman et al. 1990).

When we compared the latency of Vergence/OFR versus Fixation/OFR, using a paired t-test, we found that for downward responses, there was no significant difference between the latency for Fixation/OFR (mean ± SD: 82 ± 14 ms), Divergence/OFR (82 ± 9 ms), or Convergence/OFR (80 ± 11 ms). For upward responses, Fixation/OFR latency (94 ± 13 ms) was significantly greater ($P < 0.05$) than Divergence/OFR (83 ± 15 ms) but not Convergence/OFR (89 ± 14 ms).

**Results of control experiments**

A pairwise multiple comparison procedure (ANOVA) showed no significant difference ($P = 0.98$) for each of the four control experiments versus responses during the standard Fixation/OFR experiment. Thus the increased amplitude of

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**FIG. 7.** Summary of an application of a simple model (A) to compare Fixation/OFR responses with Vergence/OFR responses. Grating Vel is the velocity-step stimulus that sums at the retina (summing junction) with the velocity of vertical drifts of the eyes (EVcontrol, estimated from control trials); s is the Laplace complex frequency. The difference is retinal error velocity (REVel) that, after a Delay (mean value measured for each stimulus), is the input to a first-order lag element of gain G and time constant T. EVOFRvel is the model’s velocity command to move the eyes, which sums with vertical eye drifts and is integrated to give EVsum, which was compared with the subject’s measured OFR. First, optimal values of internal parameters, gain G and time constant T, were calculated for the mean Fixation/OFR response for individual subjects at one spatial frequency (see text and the Appendix). Since mean eye drift (EVcontrol) during Fixation/OFR control trials was small, K was set to zero for this part of the estimation. B: a representative mean response (Subject 4, upward 0.27 cycle/deg stimulus) and the model's simulation of it after optimal parameter values were estimated; in this case the value of K (gray pathway) was estimated to determine the effect of mean eye drift. Note how G and T increase from Fixation/OFR to Divergence/OFR, but K is zero. A paired comparison of the values of gain G estimated for Fixation/OFR vs. Vergence/OFR is shown in D; the Wilcoxon rank-sum test showed a significant difference, as indicated (see text).
OFR that occurred during vergence movements could not be ascribed to differences in stimulus presentation during Fixation/OFR versus Convergence/OFR or Divergence/OFR experiments.

**Discussion**

We set out to determine whether the magnitude of the vertical OFR in normal humans is increased if it is generated as subjects shift their point of fixation between near and far visual targets. First, we established the range of the vertical OFR in ten normal human subjects following visual fixation of a stationary target (Fixation/OFR), and found responses similar to those previously reported (Gellman et al. 1990). We then compared each subject’s Fixation/OFR responses with those occurring if the stimulus was presented during the course of a vergence eye movement, and found that these Vergence/OFR responses were consistently increased in amplitude. This section addresses four issues raised by our results. First, what are the characteristics of the vertical OFR? Second, what relationship does OFR bear to other smooth ocular tracking responses? Third, what factors could account for the increase of OFR that occurs if it is made during a vergence movement? Finally, how could the OFR contribute to gaze stabilization during combined vergence–saccade gaze shifts?

**Properties of vertical OFR following fixation**

There was substantial variability of OFR between different subjects (Fig. 3), similar to a prior report (Gellman et al. 1990). Nonetheless, subjects tended to show the same overall pattern (e.g., Fig. 2), with downward responses being larger and made at shorter latencies than upward responses. This is the opposite of the asymmetry of latency reported for vertical saccades (Zhou and King 2002), which may reflect a shorter response time for shifts of attention to targets presented in the upper visual field. Since the OFR is preattentive, the up–down asymmetry might thus be attributable to different mechanisms. The largest responses were also evoked with the stimulus with the lowest spatial frequency (0.17 cycle/deg). These consistent properties of the vertical OFR are discussed further in the final section.

We wondered whether the variability of responses for each subject was influenced by anticipatory drifts based on prior experience. Such a possibility has been suggested during studies of the initial, presaccadic component of smooth pursuit (Barnes and Collins 2008), which might be related to the OFR. Accordingly, we compared vertical eye movements during control trials, during which the grating stimulus was stationary, with stimulus direction during the prior OFR. We found no correlation between the direction of eye drifts occurring during control trials, which were idiosyncratic and stereotyped for each subject, and the prior trial. This result supports the view that, at least under our experimental conditions, the OFR is not noticeably influenced by anticipatory or memory-driven eye drifts.

**Relationship between OFR and other forms of visual tracking**

It has been suggested that OFR may act as a visual-field–holding reflex that is most influential in the wake of a gaze shift (Gellman et al. 1990). During locomotion, which induces an optic flow of images on the retina, other visual tracking systems act to stabilize gaze, such as smooth pursuit and optokinetic responses. (Vestibular mechanisms make an important contribution for high-frequency disturbances.) Although the OFR appears to have unique properties (Gellman et al. 1990; Sheliga et al. 2005), we took the opportunity to compare our subjects’ OFR with other visual tracking responses. Accordingly, we tested each subject’s responses to the 0.27 cycle/deg visual stimulus when it was moved sinusoidally through frequencies ranging from 0.1 to 2.5 Hz. The ability of individual subjects to track this predictable “optokinetic” stimulus—during which they were instructed to follow an individual grating (“look” optokinetic behavior, without induced circular vection)—bore no relationship with their OFR responses (Fig. 4). Thus it appears that OFR and tracking responses to our sinusoidal stimulus motion are due to different tracking mechanisms. However, it remains possible that OFR is related to other forms of visual tracking. Recent studies demonstrated that the amplitude of the OFR was maximized when the moving gratings occupied 50% of a screen subtending 45° horizontally and 30° vertically; responses decreased with larger stimuli that possibly favored local inhibitory surround over central excitatory mechanisms (Miles et al. 1986; Sheliga et al. 2008). Thus a large-field visual display may not be the optimal stimulus to evoke the OFR, whereas it is for optokinetic responses.

Other studies have indicated that the smooth-tracking response to onset of motion of a small visual stimulus has two main components: an initial response that is variable and does not match target velocity and a second component following the first saccade that more accurately tracks the target (Barnes 2008; Priebe et al. 2001; Wilmer and Nakayama 2007). Although the latency to onset of OFR is smaller than that for smooth pursuit, it would seem of interest to determine whether OFR has other differences from the initial component of smooth-pursuit tracking. Differences of OFR from optokinetic and smooth-pursuit responses would support the view that OFR is driven by a low-level system that senses first-order motion energy (Sheliga et al. 2005).

**Mechanisms by which OFR is increased during vergence**

Our subjects showed consistent increases in the magnitude of the OFR made during vergence movements compared with following steady fixation. The OFR is known to be enhanced in the wake of a saccade (Gellman et al. 1990), but most natural shifts of the point of fixation are between targets located at different distances and in different directions. Our study differed from that of Gellman and colleagues (1990) in that we tested the OFR in the direction orthogonal to the (vergence) eye movements; also our stimuli lay in different depth planes. Furthermore, Gellman and colleagues were able to study post-saccadic enhancement only ≈600 ms, yet vergence movements last longer.

One question we addressed was how much our measurements during Vergence/OFR were affected by vertical eye drifts that accompanied horizontal vergence movements, even if the near and far targets were carefully aligned. Our initial approach was to subtract vertical drifts occurring during vergence control trials, when no movement of the visual grating
stimulus occurred (Fig. 5). However, since some vertical drifts persisted throughout the OFR, we needed to take into account not only the superimposed eye drift itself, but also its potential effect on retinal image slip during the period of grating motion. For this additional analysis, we used a simple model of the OFR, which did not seek to represent details of the underlying neural mechanism (Yamamoto et al. 1997), but which did take account of retinal image slip due to vertical eye drifts (Fig. 7). This analysis of a subset of our data indicated that vertical eye drifts had only a small impact on retinal image motion. Estimation of optimal parameter values demonstrated a substantial increase of the internal gain of the OFR when responses occurred during vergence, compared with OFR following fixation (Fig. 7D). Such an enhancement is consistent with the notion that OFR is a visual-field–holding reflex, which is called into action after each gaze shift, and it is also consistent with prior studies showing increased responsiveness of one eye movement response when combined with another (Das et al. 1999; Kumar et al. 2005; Lisberger 1998). In preliminary, unpublished studies, we have found no increase in OFR if stimuli are presented during sinusoidal vergence versus the OFR following fixation. Thus it may be that the sudden shift of the point of fixation and center of visual attention constitute the cue to increase the OFR.

Possible function of human OFR

One may ask what visual role these small, variable eye movements serve during natural behavior. One possibility is that they contribute to gaze stabilization during head perturbations. However, when the vestibular sense is lost, visually mediated eye movements fail to provide a clear stable view of the world (Crawford 1952). Another possible purpose, for which they evolved, might be to compensate for eye drifts immediately following gaze shifts (Gellman et al. 1990). Following saccades, transient eye drifts—glissades—may impair vision. During combined saccade–vergence movements, larger eye drifts are more likely and so it seems possible that OFR may help to stabilize the field of view after such gaze shifts. In accord with this view, the OFR is increased in the wake of both saccades and saccade–vergence movements, although their amplitude may not be adequate to compensate for some eye drifts occurring during such gaze shifts (e.g., Fig. 5).

Although the amplitude of the OFR shows intersubject variability, up–down asymmetries and its dependence on contrast and spatial frequency are consistent properties across subjects, leading to the suggestion that the OFR reflects the activity of low-level motion detectors (Sheliga et al. 2005). Given the small, variable size of responses, it remains possible that the OFR does not actually contribute to clear vision but rather represents the initial processing of motion signals that later lead to eye movements that can help to stabilize gaze. If this were correct, the OFR could be regarded as a probe of early cortical motion processing (Kodaka et al. 2007), even though the responses have little protective effect (“survival value”) for vision during gaze shifts. As an experimental probe, the OFR holds potential value for studying a range of clinical disorders affecting either the afferent (Rucker et al. 2006) or efferent components of visual tracking mechanisms.

### APPENDIX

The simple model shown in Fig. 7A was coded in SIMULINK (The MathWorks). Parameter estimation techniques provide a rigorous mathematical procedure to simultaneously estimate the value of several parameters with precision and have been previously applied to studies of eye movements (Das et al. 1999; Huebner et al. 1992; Kumar et al. 2006; Seidman et al. 1995). In our analysis, we took advantage of the seamless integration of SIMULINK with MATLAB (The MathWorks) to execute the model at each iterative step of the parameter estimation procedure. Parameter estimation was performed using the “lsqcurvefit” function of the MATLAB Optimization Toolbox (Coleman et al. 1999), which uses the method of conjugate gradients to minimize the objective function ($\Phi$)

$$\Phi(B) = \sum (y_i - f_i(B))^2$$

where $y_i$ represents the measured data values, $f_i(B)$ represents the calculated model output values, and $B$ is the optimal parameter vector. The goal of the optimization algorithm is to minimize this objective function. The difference ($y_i - f_i$) is called the residual at time point $t_i$.

We selected individual cases for simulation, consisting of one subject’s mean response, upward or downward, to one stimulus spatial frequency. Initially, Fixation/OFR responses were selected for simulation and parameter estimation. Subsets of the recorded vertical eye position data from the mean response and the control trial were selected, corresponding to the epoch 0–150 ms after stimulus onset.

The stimulus to the model was a velocity step of 200-ms duration, corresponding to the speed of the actual stimulus (see METHODS). Velocity input signals were used for model simulation and these were integrated to provide positional displays that were compared with subjects’ data. The value of the Delay was set to the measured value for that subject and stimulus. Initially, the model simulation was run with parameters set to initial guess values, consistent with published values of smooth-tracking models (Robinson et al. 1986). We did not incorporate the pathway by which EVcontrol influenced retinal image slip (gray pathway in Fig. 7A) for Fixation/OFR because control eye drifts were very small; we confirmed this impression in some simulations using the gray pathway: there was no detectable effect. After the first simulation (preestimation), we applied constraints on the range of parameter values, so that G could range 0–5 and T could range 0.03–0.2 s. Then the formal parameter estimation process was started, from different initial guess values (to avoid convergence on local minima) using the recursive least-squares algorithm (lsqcurvefit), until the objective function was minimized and was not changing. Then the residual sum-of-squares (RSS) and $R^2$ (coefficient of determination) were obtained, along with optimal values for G and T. Only simulations with RSS <20% and $R^2$ values >0.9 were considered good fits and were included in our analysis. A representative comparison of a subject’s mean Fixation/OFR response and the model’s simulation of it following parameter estimation is shown in Fig. 7B.

We then tested whether the model, with the parameter values estimated for Fixation/OFR, could also simulate mean Divergence/OFR or Convergence/OFR responses to the same visual stimulus. The value of Delay was set to that measured for the corresponding Vergence/OFR trial. In all cases, the model failed to simulate the recorded data. Finally, parameters were reset to initial guess values and the effects of vertical eye drifts on retinal image slip (differentiated EVcontrol signal) were studied by estimating the optimal value of K (see pathway in gray in Fig. 7A); K was allowed to vary in the range 0–1.0. Parameter estimation then was rerun. Although >80% of cases of Fixation/OFR satisfied goodness-of-fit criteria, only 35% of Divergence/OFR and 7% of Convergence/OFR did so (due to large, vertical eye drifts, which were especially common during convergence). A representative comparison of a subject’s Divergence/OFR mean response and the model’s simulation with a good fit is shown in Fig. 7C. Paired comparisons for G are shown in

[Refs](http://jn.physiology.org/doi/10.1152/jn.00614.2008)
Fig. 7D; there is a significant increase when OFR is performed during vergence. No significant changes in the values of T or K occurred.

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