Modulation of Gaze-Evoked Blinks Depends Primarily on Extraretinal Factors

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INTRODUCTION

In humans, rapid, reorienting movements of the eyes and head—gaze shifts—are frequently accompanied by contraction of the orbicularis oculi (OO), the lid-closing muscle. These contractions have been referred to as gaze-evoked blinks (Evinger et al. 1994). Generally, gaze-evoked blinks occur with changes in gaze larger than about 20° in amplitude. This phenomenon does not seem to be a result of a reflex evoked during shifts of gaze are often suppressed when the gaze shift is made to an important visual stimulus, suggesting that the visual system can modulate the occurrence of these blinks. In head-stabilized, human subjects, we tested the hypothesis that the presence of a visual stimulus was sufficient, but not necessary, to modulate OO EMG (OOemg) activity during saccadic eye movements. Rapid, reorienting movements of the eyes (saccades) were made to visual targets that remained illuminated (visually guided trials) or were briefly flashed (memory-guided trials) at different amplitudes along the horizontal meridian. We measured OOemg activity and found that the magnitude and probability of OOemg activity occurrence was reduced when a saccade was made to the memory of the spatial location as well as to the actual visual stimulus. The reduced OOemg activity occurred only when the location of the target was previously cued. OOemg activity occurred reliably with spontaneous saccades that were made to locations with no explicit visual stimulus, generally, back to the fixation location. Thus the modulation of gaze-evoked OOemg activity does not depend on the presence of visual information per se, but rather, results from an extraretinal signal.

METHODS

Subjects

Six male and two female subjects (ages, 29–40 yr) participated in the experiments. All had uncorrected, normal vision. One subject (MAB) knew the goals of the experiment; the other seven were naïve. Similar results were observed in all subjects, so the data were pooled across subjects. Each subject participated in at least one recording session lasting 30–40 min, and they sat in a 4° magnetic field frame with their head supported on a chin rest to minimize movements of the head. We used the scleral search coil technique to monitor eye movements (CNC Engineering) (Collewijn 1999; Fuchs and Robinson 1966; Robinson 1963). We measured OOemg by differential recording across a pair of silver ball electrodes (≈1.5 mm diam) that were briefly flashed (memory-guided trials) at different amplitudes along the horizontal meridian. We measured OOemg activity and found that the magnitude and probability of OOemg activity occurrence was reduced when a saccade was made to the memory of the spatial location as well as to the actual visual stimulus. The reduced OOemg activity occurred only when the location of the target was previously cued. OOemg activity occurred reliably with spontaneous saccades that were made to locations with no explicit visual stimulus, generally, back to the fixation location. Thus the modulation of gaze-evoked OOemg activity does not depend on the presence of visual information per se, but rather, results from an extraretinal signal.

Why blinks are associated with shifts of gaze is unknown. One hypothesis proposed is that the mechanisms for saccadic suppression and blinking are shared (Volkmann et al. 1980). In this scheme, the corollary discharge responsible for the decreased visual sensitivity that occurs during saccades also drives contraction of OO motoneurons. The common drive ensures that a blink occurs during a saccade. This motor hypothesis has two advantages. First, it can explain why, despite the frequency of blinking (20/min; Leigh and Zee 1999), resulting in large changes in the image on the retina, the visual world remains stable. Second, corneal lubrication can occur when any disruptive effects on visual processing that would result from blinking are minimized. Whereas this scheme assumes that blinks have a negative role from the visual system perspective, others have suggested that blinking during saccades has a useful role for the visual system. Spurious visual information such as retinal blur that might occur during saccades is minimized if a blink occurs along with a saccade (Watanabe et al. 1980). Whether both or neither of these schemes is correct is unknown. What is clear is that there is a linkage between the visual, saccadic, and blink systems. Previous experiments have shown that the linkage of saccadic gaze shifts and blinking is not obligatory. For example, when humans make saccadic eye movements to a continuously visible target in a single plane, gaze-evoked blinks are smaller than those made during similar amplitude, re-centering saccades (Evinger et al. 1994). What is responsible for this modulation is unknown. As a first step toward understanding this, we consider here whether the visual stimulus is responsible for the reduction in gaze-evoked blinking or whether some other, extraretinal factor, produces the suppression. We tested the hypothesis that visual information is sufficient but not necessary to produce the suppression of gaze-evoked oo emg OOemg activity during certain saccades. To do this, we compared gaze-evoked OOemg activity during head-stabilized saccadic eye movements made to visible and previously visible target locations. We found that the occurrence of gaze-evoked OOemg activity was dramatically reduced within the context of saccadic tasks regardless of whether a visual target was present. These results support the hypothesis that the visual stimulus, per se, is not solely responsible for the reduction in OOemg activity during saccades.
Fig. 1 In the memory task, this spot was illuminated only briefly (200 ms, ms. Then, a second spot was illuminated at varying amplitudes (20, Subjects fixated this spot for a random delay between 500 and 1,500 illuminated at the center of the screen or at 20 or 30° in the periphery. In both tasks, a spot was illuminated at the center of the screen or at 20 or 30° in the periphery. Subjects fixated this spot for a random delay between 500 and 1,500 ms. Then, a second spot was illuminated at varying amplitudes (20, 30, 40, and 60°) from the fixation spot along the horizontal meridian. In the memory task, this spot was illuminated only briefly (200 ms, Fig. 1B), whereas in the visually guided task, the spot remained illuminated for 800–1,200 ms (Fig. 1A). Removal of the fixation point was the cue to make a saccade to the location of the target. Lid movements that occur with vertical saccades (lid saccades) are associated with changes in the activity of the levator palpebrae muscle and not the OO (Evinger et al. 1991). In some cases, large vertical saccades (>40°) can be accompanied by OOemg activity despite the fact that contraction of the OO would counteract the lid saccade at least for upward saccades (Evinger et al. 1991). To eliminate these possibilities, we presented targets only along the horizontal meridian. Placing the fixation point either at the center or at a peripheral location allowed us to present large amplitude saccade targets. For the 20 and 30° targets, the fixation point was located at 0°. For the 40 and 60° targets, the fixation point was located at 20 and 30°, respectively. Interleaved with delayed-saccade tasks was the gap saccade task (Saslow 1967). These saccades are also visually guided, so for the analysis, we included these with the visual-guided delayed trials. In the gap task (Fig. 1C), the fixation stimulus appeared for a random delay (500–1,500 ms) and then was removed. After a delay of 200 ms, during which the subject was required to remain fixating in the dark, a peripheral target was illuminated. The appearance of the peripheral target was the cue for the subject to make a saccade to the location of the visual stimulus. The removal of the fixation point serves to disengage visual attention, allowing more rapid processing of subsequent, incoming visual stimuli (Fischer and Weber 1993), although other hypotheses have been proposed (Paré and Munoz 1996). All saccade conditions were randomly interleaved, and the color of the fixation point identified the trial type. Generally, after subjects completed the saccade to the cued target location, they made a saccade back to the location of the center of the tangent screen or to the fixation location. We termed this saccade, the “refixational saccade” (Fig. 1). This saccade was not cued but was made in anticipation of the upcoming trial. Subjects were required to maintain an accuracy of 5° square around the fixation point and 12.5° square around the target. This was monitored using an electronic window. If subjects failed to maintain this level of accuracy, the trial was aborted. A time out period was imposed (1,500 ms) after which a new trial commenced. Subjects received instructions to maintain eye position on the target and to make eye movements, without head movements, to track the target as accurately as possible.

Data acquisition and analysis

Voltage signals proportional to horizontal and vertical components of eye position were filtered (8-pole Bessel, 3 dB, 180 Hz), digitized at 16-bit resolution, and sampled at 2 kHz. The signals from the OOemg electrodes were filtered (300 Hz–5 kHz) and amplified (100 times). These data were digitized at 16-bit resolution and sampled at 2 kHz.

All analog data were saved for off-line analysis using an interactive computer program designed to display and measure eye position, velocity, and OOemg activity. Measurements of the data were made on eye position traces, and saccadic eye movements were identified using velocity and acceleration criteria (10–25°/s and 500–800°/s2). Each trial was inspected by the experimenter to ensure the accuracy of the algorithm. If saccades were missed, the criterion was adjusted to catch all saccades. OOemg data analysis was performed in Matlab using a custom designed program. For each trial, the OOemg trace was rectified and displayed. An algorithm computed the baseline OOemg activity and determined the point on the OOemg trace that exceeded 2 SD of the baseline. This point determined the onset of a
blink. The algorithm defined the region of the OOmeg where the amplitude was maintained at the level of 2 SD above baseline to define the duration of the blink. The end of the blink was defined as the point on the OOmeg trace where the activity dropped below 2 SD from baseline. The area under the curve defined by the beginning and end of the blink was computed to determine the OOmeg magnitude. The occurrence of OOmeg activity was computed for all saccades within a trial. This was performed for each trial of each saccade task. The experimenter verified the beginning and end of OOmeg activity. Statistical analyses were performed in Matlab, Excel, or Sigma Stat. Parametric descriptive and inferential statistics, such as ANOVA and t-test, were performed. If the distributions failed normality tests, the nonparametric equivalents such as the Kruskal-Wallis or the Mann-Whitney rank sum and Dunn’s tests were used.

RESULTS

When subjects made saccades to a visible target, the OOmeg was very small (Fig. 2A, visually guided saccade). However, when a similar, refixational, saccade was made back to the center of the screen, the OOmeg was large (Fig. 2A, refixational saccade). Indeed, the refixational saccadic eye movement in this example was slightly (~2°) smaller than the initial, targeting saccade, but the OOmeg activity was more than twice the magnitude of that occurring during the initial saccade. In a second subject, the effect was so profound that this person rarely showed OOmeg activity for the initial targeting saccade (Fig. 2B) but showed robust OOmeg activity for the return saccade.

Figure 2, C and D, compares OOmeg activity during visually guided and memory-guided saccades. During the visually guided saccade, the initial targeting saccade was unaccompanied by OOmeg activity, whereas the return saccade was associated with a robust drive to the OO motoneurons (Fig. 2C). This occurred despite the fact that the initial saccade was larger than the return saccade. In memory-guided saccade trials (Fig. 2D), a similar pattern was observed. The initial saccade to the location of the now invisible target was not associated with OOmeg activity, whereas the return saccade was associated with robust OOmeg activity.

Across our sample of eight subjects, this pattern was very consistent. We normalized the magnitude of the OOmeg activity in all conditions by the OOmeg magnitude measured during targeting, visually guided saccades (Fig. 2E). Thus, the visual to target condition magnitude is one. The magnitude of the OOmeg measured during the memory-guided trials was statistically indistinguishable from that measured during the visually guided trials (P > 0.05) for all subjects. Similarly, the
OOeemg activity associated with the refixational saccade in both trial types was different from the OOeemg measured during the targeting saccades (P < 0.05). One-way ANOVA (Kruskal-Wallis) and Dunn’s pairwise comparison tests revealed significant differences (P < 0.05) in OOeemg magnitude between the visual to target and refixational conditions as well as the memory to target and refixational conditions. There were no significant differences between visual to target and memory to target or between the refixational saccade conditions. These results support the hypothesis that the presence of a visual stimulus is not necessary to reduce the OOeemg activity during a saccade. Therefore, the modulation must arise from an extraretinal source.

Thus far, we have examined the modulation of OOeemg magnitude. Previous work has shown that, in head-unrestrained subjects, the probability of OOeemg activity associated with a gaze shift is modulated by the amplitude of the head movement (Evinger et al. 1994). To determine whether OOeemg probability was modulated during head-stabilized saccadic eye movements, we asked subjects to perform a delayed-saccade task while varying the amplitude of the required saccade. There were two notable results. First, as the amplitude of the saccadic eye movement increased, the probability of measuring OOeemg activity during the saccade also increased as was described for head-free gaze shifts. Second, and similar to the OOeemg activity during the saccade to the target location compared with those made back to the fixation location, in either the visually guided (2.9 vs. 74%) or the memory-guided saccade task (3.4 vs. 67%). Thus it seems that the presence of the visual stimulus can exert a small amount of inhibition on the occurrence of OOeemg activity during saccades, but does not override the effects of targeting a spatial location regardless of the presence of the visual stimulus. Thus the presence of a visual stimulus is sufficient, but not necessary, to reduce OOeemg activity concomitant with a saccade.

Across our eight subjects, we computed the mean probability of OOeemg occurrence during the saccade to the target location in the visually guided and memory-guided tasks (Fig. 3A). We then plotted these probabilities against the saccade amplitude. As the saccade amplitude increased, the probability of measuring OOeemg activity increased. We performed an ANOVA comparing the probability of measuring OOeemg activity across target eccentricity (4 levels, 20, 30, 40, and 60°). We found an effect of target eccentricity indicating that the differences in the probability of OOeemg occurrence we measured with varying saccade amplitudes were statistically significant [ANOVA F(3,1617) = 1,220.00, P < 0.001]. The mean probability of OOeemg occurrence for the visually guided condition was 2.9% (Fig. 3A, ⊖), whereas the mean for the memory-guided was 3.4% (Fig. 3A, □). Thus there was a small, but significant (P < 0.001), difference in the probability of OOeemg occurrence depending on whether the visual target was present as the saccade amplitude increased. However, this difference was small and did not exceed the difference in OOeemg probability measured during saccades made to the target location compared with those made back to the fixation location, either the visually guided (2.9 vs. 74%) or the memory-guided saccade task (3.4 vs. 67%). Thus it seems that the presence of the visual stimulus can exert a small amount of inhibition on the occurrence of OOeemg activity during saccades, but does not override the effects of targeting a spatial location regardless of the presence of the visual stimulus. Thus the presence of a visual stimulus is sufficient, but not necessary, to reduce OOeemg activity concomitant with a saccade.

Interestingly, the difference in OOeemg probability occurring during saccades made to the visible target location and those made to the invisible target location was evident even in the execution of the return saccade (cf., 74 vs. 67%). This difference was also significant (P < 0.001) and suggests that there is more modulating OOeemg occurrence than simply the presence or absence of a visual stimulus. Because of the difference between OOeemg occurrence during memory-guided saccades and refixational saccades, this indicates that the modulatory influence may reflect a factor related to the attention to spatial location rather than a simple nonvisual phenomenon. In the case of the refixational saccade, attention is not required since accuracy is not demanded. Future experiments will test this hypothesis.

Finally, for the refixational saccades, a similar trend was evident (Fig. 3B). As the saccade amplitude increased, the probability of measuring OOeemg activity also increased. However, the trend appeared primarily as a reduced variability (note the decrease in scatter; solid line is the mean). This difference was not because the refixational saccades were smaller than...
SUPPRESSING BLINKS

The gaze-evoked blink is thought to originate from a drive that is common to the eye, neck, and lid motoneurons (Evinger et al. 1994; Rottach et al. 1998). The superior colliculus (SC), a brainstem region critically involved in the generation of saccadic gaze shifts (Sparks 2004), may be the site of overlap. Indeed, a role of the SC in reflex blinking (Ooemg activity evoked by trigeminal activation) has been shown (Basso et al. 1996). However, if the command to initiate a saccadic gaze shift is also responsible for a drive to the OO motoneurons causing a blink to occur, why does the probability of Ooemg activity increase as the saccade amplitude is increased? In other words, why are small saccades less likely to be accompanied by a blink if the origin of the drive is the same?

We propose that the extraretinal signal described here—in the form of an attentional signal—may reconcile this. This signal may provide a constant drive, either directly or indirectly, to inhibit the omnipause neurons (OPNs) (Baloh et al. 1982; Horn et al. 1984; Langer and Kaneko 1984), the brainstem neurons considered to gate saccadic eye movements (Fuchs et al. 1985; Keller 1974). Small saccades would drive a population of OPNs to pause, but it would take a larger or longer OPN pause to also release Ooemg activity. The generation of larger saccades would release more inhibition on the OPNs or release it for a longer time, allowing a blink to occur along with the saccade. This hypothesis is dependent on the premise that evoking blinks along with saccades requires a larger or longer cessation of OPN activity than that required for a saccade, and that larger saccades are associated with greater pauses in OPNs.

There is support for this. The distribution of activity within the SC is invariant for saccades of different amplitudes; however, a faster decline in the activity of SC neurons is associated with smaller saccades (Anderson et al. 1998; Keller 1974; Sparks et al. 1976). This causes the OPNs to resume their discharge faster, perhaps precluding the occurrence of concomitant Ooemg activity. Moreover, there is some suggestion that the rostral SC has a stronger, excitatory input to the OPNs (Paré and Guitton 1994) making a pause in OPNs less likely when the rostral SC is active. The latter idea, that a larger (e.g., recruitment of more OPNs or longer duration) pause in OPNs is required to produce a blink along with a saccade, is supported by the observation that the velocity of abnormally slow saccades can be normalized if a voluntary blink is initiated at the time of the saccade (Leigh et al. 1983; Zee et al. 1983).

Finally, we propose that exploring the linkage between blinking and saccadic eye movements in clinical populations will help determine where the linkage is and where the extraretinal modulation is. For example, a hallmark symptom of Parkinson’s disease is a loss of habituation and a hyperexcitable blink reflex (Dengler et al. 1982; Kimura 1973). It is possible that these patients may also have disturbances in gaze-evoked blinks. If the loss of blink suppression during gaze shifts occurs in these patients, it would implicate the basal ganglia as an important component of the interaction between extraretinal factors and motor control.

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