Properties of Memory-Guided Saccades Toward Targets Flashed During Smooth Pursuit in Human Subjects

Kenji Ohtsuka

Purpose. This study in human subjects investigated whether or not the saccade system can monitor smooth changes of the eye position in total darkness.

Methods. The authors studied the properties of memory-guided saccades toward targets flashed during pursuit eye movements (target velocities of 15°/s, 30°/s, and 45°/s) in four normal human subjects. Subjects were instructed to execute memory-guided saccades toward the position of the flashed target in total darkness when the pursuit target was extinguished.

Results. The vector of the saccade was more highly correlated with the vector of "spatial error" (the vector from the position of the eye at the time of the saccade to the position of the flashed target in space) than with the vector of "retinal error" (the vector from the position of the eye at the time of the presentation of the flashed target to the position of the flashed target). The amplitude and direction errors of memory-guided saccades were correlated with the amplitude of the retinal error but not with amplitude of eye deviation after the presentation of the flashed target. Pursuit velocity did not affect the error of the saccade.

Conclusions. These findings suggest that the saccade system can monitor smooth changes of the eye position in total darkness, regardless of the velocity of pursuit, and that the accuracy of memory-guided saccades is dependent only on the amplitude of the retinal error. Invest Ophthal Vis Sci. 1994;35:509-514.

Becker and Fuchs demonstrated the ability of human subjects to execute saccades toward a remembered position where a visual target had previously appeared in the dark. Sparks and Mays indicated that the monkey can maintain the spatial accuracy of memory-guided saccades in total darkness, even if the eye movement is induced by electrical stimulation after the target disappears. Several cerebral processes are required to perform such a memory-guided saccade. First, the position of the visual target in the visual field (the vector of the retinal error) has to be organized in space with respect to the cranioptical coordination. For this purpose, the current eye position in the orbit should be monitored and integrated with the retinal error (visuomotor integration). Second, this encoded position is memorized. Finally, a memory-guided saccade is triggered in relation to the spatial error (the vector from the position of the eye at the time of the saccade to the position of the remembered target in space). Although the evaluation of the properties of the visuomotor integration is important for elucidating properties of the saccade system, we currently have only limited knowledge on this. We previously reported accuracy of memory-guided saccades. If a saccade made in darkness brings the eye to a position more than 5° away from the location of the previously seen target, an accurate corrective saccade is made. These findings suggest that the eye position in the orbit can be monitored within an error of 5°.

In this study, we investigated the properties and accuracy of memory-guided saccades toward targets flashed during pursuit eye movements in total darkness in four normal human subjects. In this way, we tried to elucidate whether or not the saccade system can monitor smooth changes of the eye position, and what parameters affect accuracy of memory-guided saccades.
METHODS

The experiment was conducted in four healthy volunteers. Their ages ranged from 26 to 42 years, with a mean of 35 years. All had a corrected Snellen visual acuity of at least 20/20 in the tested eye. Informed consent was obtained from all subjects after the nature of the procedure had been explained. Tenets of the World Medical Association Declaration of Helsinki were followed, and institutional human experimentation committee approval was obtained. Horizontal and vertical positions of one eye were recorded by infrared reflection devices (Takei [Tokyo, Japan], model TKK 928). In this system, the linear range was 20° to either horizontal side and 15° to either vertical side of the primary position. This system has a resolution of 0.3°. Characteristics of this system were reported previously. The measurements were calibrated with the use of 10° horizontal and vertical target displacements. Throughout the experiment, the subject was seated on a chair in total darkness, and the chin, brow and head were tightly fixed on a frame. Head immobilization was adequate to prevent drifts generated by head movements.

The experimental paradigm is illustrated in Figure 1. The subject was instructed to pursue a moving target until the target was extinguished. The pursuit target was moved from “E1” (10° left of the primary position) to “E2” (10° right of the primary position) along the horizontal meridian with constant velocity (15°/s, 30°/s, or 45°/s). The velocity of the pursuit target was randomly chosen in each trial. The flashed target “T” appeared off the horizontal meridian at unspecified times during pursuit (E’ in Fig. 1). The timing for flashing the target “T” was randomly determined by computer. The flashed target was extinguished 50 milliseconds later. The subject was instructed to execute memory-guided saccades toward the position of the flashed target in total darkness when the pursuit target was extinguished. The stimulus used for smooth pursuit was a laser spot projected onto a tangent screen positioned 1.5 m in front of the subject. Five light-emitting diodes embedded in the tangent screen were used as the flashed targets. The size of the light-emitting diode was about 6 minutes of arc. These light-emitting diodes were located 10° up the horizontal meridian, and spaced 10° apart in the horizontal direction (Fig. 1). The subjects did not know the location of the light-emitting diodes before the experiment. We defined “retinal error” (A in Fig. 1) as the vector from the position of the eye at the time of the flash to the position of the target. We defined “spatial error” (B in Fig. 1) as the vector from the position of the eye at the time of the saccade to the position of the flashed target in space according to a previous paper. “D1” and “D2” in Figure 1 represent the angle of the direction of the retinal error and that of the spatial error, respectively. In this system, amplitude of the retinal error and the spatial error ranged from 10° to 31.6°, and the direction of spatial error (D2) was always larger than that of the retinal error (D1). We defined saccade error as differences in amplitude and direction between the spatial error and the first memory-guided saccade, excluding corrective saccades after a initial saccade. To elucidate learning effects on accuracy of memory-guided saccades, we compared the mean saccade error of the initial 20 saccades with the mean saccade error of the last 20 saccades in one experimental session. To compare the latency of memory-guided saccades with that of visually guided saccades, subjects 3 and 4 made visually guided saccades from “E2” to one of “T1” to “T5.” Target and eye position signals were recorded on magnetically tape for later analysis and displayed on a thermal rectilinear polygraph. After being filtered through a low-pass filter (50 Hz), data were digitized by a com-

![Figure 1](https://iovs.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/933179/)
puter with a sampling rate of 500 Hz. This filtering does not affect peak velocity of saccades. For calculating the amplitude and the latency of saccades, we considered the moment when the saccadic velocity reached 20°/s as the onset and offset of saccades.

RESULTS

Each subject performed over 40 trials for each target velocity. The four subjects exhibited essentially the same responses in this paradigm. They made memory-guided saccades according to the spatial error and were able to bring their eyes near the position of the flashed target by a saccade. Figure 2 illustrates data from Subject 1. The amplitude (top panels) and direction (bottom panels) of memory-guided saccades are plotted against the values of retinal and spatial errors. Comparison of the two upper panels shows that saccade amplitude was better correlated with the amplitude of the spatial error (r = 0.903) than with the amplitude of the retinal error (r = 0.334). Comparison of the lower panels shows that saccade direction was better correlated with the direction of the spatial error (r = 0.981) than with the direction of the retinal error (r = 0.864). The correlation between the direction of saccades and the retinal error resulted from the correlation between the direction of the retinal error and the spatial error (r = 0.889). The variability of the direction of saccades decreased as the retinal error approaches the maximum value, because the difference between the direction of the retinal error and the spatial error is 0° at the maximum value in this paradigm. Table 1 indicates results in the four subjects. The slopes of regression lines between the spatial error and saccades (ARE versus AS and DRE versus DS in Table 1) were almost 1.0 in all four subjects (Table 1).

### Table 1. Properties of Memory-Guided Saccades

<table>
<thead>
<tr>
<th></th>
<th>Subject 1</th>
<th>Subject 2</th>
<th>Subject 3</th>
<th>Subject 4</th>
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<tr>
<td>ARE vs. AS</td>
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<tr>
<td>r</td>
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<td>S</td>
<td>0.146</td>
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<tr>
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<tr>
<td>r</td>
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<td>0.921</td>
<td>0.972</td>
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<tr>
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<tr>
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<td>DRE vs. DS</td>
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<tr>
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<td>DSE vs. DS</td>
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<tr>
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<td>Amplitude error</td>
<td>2.1 ± 2.8°</td>
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<td>0.8 ± 1.6°</td>
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<td>Direction error</td>
<td>4.5 ± 7.3°</td>
<td>3.2 ± 4.5°</td>
<td>8.4 ± 17.9°</td>
<td>1.9 ± 3.1°</td>
</tr>
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</table>

ARE = amplitude of retinal error; ASE = amplitude of spatial error; DRE = direction of retinal error; DSE = direction of spatial error; AS = amplitude of saccade; DS = direction of saccade; IC = intercept; S = slope.
Accuracy of memory-guided saccades was almost consistent among the subjects. Table 1 shows the mean absolute values of the amplitude and direction errors in each subject. The amplitude and the direction errors were less than 5° and 15° in 95% of saccades in all four subjects, respectively. Figure 3 shows distributions of amplitude and direction errors of memory-guided saccades in all subjects. The rates of hypermetria and hypometria were not significantly different from each other. In addition, there was no direction bias, indicating that directions of memory-guided saccades were dependent only upon the direction of the spatial error. The accuracy of the initial 20 saccades was not significantly different from that of the last 20 saccades in all four subjects (two-tailed t test, \( P > 0.05 \)), indicating no learning effects on this task. The saccade error was independent of the pursuit velocity. Values of the mean amplitude error and SD for each pursuit velocity of all subjects were 1.5 ± 1.2° (for 15°/s), 1.7 ± 1.8° (for 30°/s) and 1.4 ± 2.2° (for 45°/s). These values did not differ significantly (Mann-Whitney U test, \( P > 0.05 \)). Figure 3 indicates relations of the amplitude and direction errors of saccades to the eye deviation from the time of the flashed target.

\[ \text{FIGURE 3.} \text{ Distributions of the amplitude and the direction errors of memory-guided saccades (A, D) in all four subjects and relations of the absolute values of amplitude and direction errors to the eye deviation (B, E) and the amplitude of retinal error (C, F). Plots in B, C, E, and F were fit to a second-order polynomial regression curve. (G) Three-dimensional plot of the amplitude of the retinal error against the amplitude error and the direction error of saccades and a smooth surface through points in the three-dimensional plot made by the negative exponential interpolation.} \]
Properties of Memory-Guided Saccades

mean = 210.3 ms
sd = 31.8 ms
n = 73

FIGURE 4. Distributions of the latency of visually guided saccades (A) and memory-guided saccades (B) in subjects 3 and 4.

presentation to the time of the saccade and the amplitude of retinal error. Both the amplitude and the direction errors were slightly correlated with the amplitude of the retinal error, but not with the eye deviation. The increase in the amplitude of the retinal error resulted in the increase of both the amplitude and the direction errors of saccades (Fig. 3G). Figure 4 shows distributions of latencies of visually guided and memory-guided saccades in subjects 3 and 4. The mean latencies were 210.3 milliseconds (SD = 31.8, n = 73) in visually guided saccades and 375.0 milliseconds (SD = 95.7, n = 70) in memory-guided saccades. The latency of memory-guided saccades was significantly longer than that of visually guided saccades (two-tailed t test, P < 0.01).

DISCUSSION

In previous experiments using monkeys, it is still unknown whether or not memory-guided saccades correspond with the spatial error. Schlag et al. indicated that monkeys were able to execute memory-guided saccades corresponding with the spatial error in the same paradigm, although McKenzie and Lisberger suggested that monkeys did not execute saccades corresponding with the spatial error but did so with the retinal error. The differences in results between these two experiments were explained by differences in duration of target flash. In this experiment we used relatively longer duration of target flash reported by Schlag et al. The subjects executed memory-guided saccades corresponding with the spatial error rather than the retinal error. There was no direction bias of memory-guided saccades toward the direction of the retinal error. In addition, there were no learning effects on the accuracy of memory-guided saccades. These findings suggest that the subjects had to estimate the spatial error from the retinal error and the eye deviation for each memory-guided saccade in total darkness.

There are two hypotheses concerning the mechanism for obtaining the spatial error. Goldberg and Bruce suggested that in the double-step paradigm, the vector of the second saccade is obtained by vector subtraction of the vector of the first saccade from the vector described by the retinal location of the target. In the double-step paradigm, the first saccades is visually guided. Therefore, the vector of the first saccades is equivalent to the retinal error signal and obtained without the eye position information. This subtraction obviates the necessity for the explicit calculation of target position in head-centered coordinates. In the second hypothesis, the spatial error is obtained by encoding the target location in space with respect to the head-centered coordinates, which are secured by the integration of the retinal information with the eye position signal. In contrast to the double-step paradigm, the first movement of the eye is a smooth pursuit in the paradigm used in this study. There is no retinal error signals for the vector of the smooth pursuit. Therefore, the integration of the visual information with smooth changes of the eye position is needed for obtaining the spatial error in this paradigm. It is thought that there are two mechanisms for monitoring the eye position signal. The most popular explanation is that the central nervous system monitors the effort of will (efference copy information). In addition, afferent information from the orbit could also be used. In this way, the sensory system maintains the spatial accuracy, regardless of the eye position.

Previous studies using monkeys have indicated that the inferior parietal cortex, especially area 7a, is involved in such visuomotor integration. For many neurons in area 7a, visual excitability changes as a function of the angle of gaze. This gating of visual signals by eye position produces a tuning for location in head-centered space. In patients with damage to area 7a, both accuracy and latency of memory-guided saccades were impaired. Area 7a receives extensive input from the medial superior temporal (MST) area, which provides information on smooth changes of the eye position. We indicated that accuracy of memory-guided saccades was not affected by the increase in amplitude of smooth changes of the eye position and pursuit velocity. In addition, the maximal
value of the amplitude error was 5°. This value was compatible with the error in the task of simple memory-guided saccades without smooth pursuit. This means that performance of visuomotor integration is not affected by the metrics of smooth pursuit. The saccade error was correlated with the amplitude of the retinal error but not with the amplitude of the eye deviation. These findings suggest that the process of retinal error signals in the central nervous system, but not of eye position signals, is critical for execution of accurate memory-guided saccades. The mechanism of this phenomenon is not known. However, it could be due to poorer spatial resolution in the peripheral retina. Area 7a projects mainly to the prefrontal cortex in and around the principal sulcus (area 46 of Brodmann) but is only weakly connected to the frontal eye fields in the monkey. The result of the visuomotor integration is probably sent to the prefrontal cortex, where it is stored using short-term memory. The prefrontal cortex is also involved in the control of memory-guided saccades in humans. After lesions in the prefrontal cortex, latency of memory-guided saccades was significantly increased and accuracy was impaired. The prefrontal cortex projects mainly to the frontal eye field. The spatial information stored in the prefrontal cortex could then be used in directing an imminent saccadic eye movement. Latencies of memory-guided saccades in this paradigm were significantly longer than those of visually guided saccades.

Acknowledgment

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References