Initiation and Stability of Pursuit Eye Movements in Simulated Retinal Prosthesis at Different Implant Locations

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PURPOSE. To assess the possible effects of retinal prosthesis implant location on the initiation and stability of pursuit eye movements.

METHODS. Six normally sighted subjects visually tracked a horizontally moving target in natural vision and in simulated prosthetic vision. Subjects were instructed to press a key when the target jumped. Prosthetic vision was simulated with a 10 x 10 array of 1° diameter phosphenes. Three implant locations in the retina were simulated: macular, 8° superior, and 8° nasal. Target motion had two speeds: 4°/s and 8°/s. Eye movement latency, horizontal stability, and vertical stability were assessed. Key-press behaviors responding to target jump were analyzed to evaluate functional eye movements.

RESULTS. Compared with natural vision, horizontal eye position with respect to target position was less stable in simulated prosthetic vision at macular, superior, and nasal implant locations, in ascending order of the degree of instability. Vertical eye position with respect to target position in simulated prosthetic vision with the superior implant location was less stable in tracking slow target motion than fast. Eye movement latency in simulated prosthetic vision was longer than in natural vision. Key-press performance was impaired in simulated prosthetic vision.

CONCLUSIONS. Pursuit eye movements in prosthetic vision, compared to natural vision, are significantly slower in initiation and less smooth in motion. They seem, however, still functional, even if the prosthesis is implanted in the peripheral retina. A superior implant location may help the prosthesis wearer better control horizontal eye movements, which are more frequently used in the activities of daily living. (Invest Ophthalmol Vis Sci. 2008;49:3933–3939) DOI:10.1167/iovs.07-1346

A retinal prosthesis is an electronic device composed of an electrode array attached over the inner limiting membrane (epiretinal implant) or inserted between the retina and the retinal pigment epithelium in place of degenerated photoreceptors (subretinal implant) and an image processing unit that transforms the incoming light pattern captured by a sensor into electrical charges that stimulate the remaining inner retinal neurons through the electrode array. Neural responses to the stimulation elicit a sensation of patterned light or phosphenes, called prosthetic vision.1-3 Such phosphenes have been developed to restore some functional vision in those with outer retinal blindness. Although most prototype prostheses under testing use an image sensor in fixed relation to the head (head-centric), research on prostheses with the image sensor placed inside the eye (eye-centric) is under way. With eye-centric technology, prosthesis wearers may direct sight using eye movements, as is the case in natural vision. However, retinal prostheses have far lower spatial resolution than the resolution of the normal retina4,5 (Wilke R, et al. IOVS 2006; 47:ARVO E-Abstract 3202) and may have to be implanted outside the fovea because of anatomic and pathologic conditions, such as the eccentric displacement of second- and third-order neurons around the foveola. A two-fold question thus arises: How will eye movements be affected by a low-resolution retinal prosthesis and by the implant location on the retina?

Eye movements are a basic visual function and play an important role in acquiring visual information.6,7 Prosthetic vision with an implant location outside the fovea resembles eccentric viewing in patients with a central scotoma, caused by conditions in which foveal vision is damaged but some peripheral vision remains functional. These patients often develop a retinal area outside the scotoma, called preferred retinal locus (PRL), to be used for fixation.8-10 A PRL usually resides next to the scotoma and can be thought of as a “high-end” retinal prosthesis that is placed eccentrically and has spatial resolution lower than foveal vision but higher than the prosthetic vision made possible by current technology. Studies have shown that, through practice, patients with central scotoma and normally sighted subjects with a simulated central scotoma could direct their PRL using eye movements.11-13 PRLs have the following characteristics. First, fixation with the PRL is less stable than foveal fixation, and it decreases with increasing eccentricity, resulting in jerky saccades for refixation.14 Second, visually guided saccades with a PRL, compared with normal saccades, have longer latency, longer duration, slower velocity, and poorer accuracy.12 Those saccades are usually undershot in proportion to target eccentricity.12 For pursuit eye movements, one study on simulated central scotoma showed that spatial accuracy decreased with the increase of scotoma size or PRL eccentricity.11 Those findings suggest that extrafoveal viewing with a retinal prosthesis affect oculomotor dynamics temporally and spatially. It has been reported that PRL above or below the fovea might offer better control of horizontal eye movements.15 Studies of simulated prosthetic vision, though few, have shown effects of implant location on functional vision. For example, Sommerhalder et al.16,17 studied the effects of implant location on text reading and found that, in simulated prosthetic vision subtending a 10° x 3.5° visual field with 286 phosphenes, subjects’ reading accuracy was approximately 90% when the visual field was 5° below foveal fixation but was reduced to approximately 25% to 30% when the visual field was 15° below foveal fixation.

Horizontal pursuit eye movements are often used in the activities of daily living, such as in preparing food and monitoring a passing vehicle or moving object,10,19 and are thus...
functionally important for future retinal prosthesis wearers. Pursuit eye movements can be characterized by two variables, latency (the time between the onset of the moving target and the onset of eye movement) and accuracy (the spatial difference between the target position and the fixation position during pursuit). Latency and accuracy reflect the function of oculomotor control. The present study was undertaken to assess the possible effects of implant location on latency and stability of horizontal pursuit eye movement. Stability refers to the spatial relationship between the target position and fixation position. The information to be attained from the present research can be used as a basis for future studies of eye movements in nonhorizontal directions. The investigation was carried out in normally sighted subjects in natural vision and in simulated prosthetic vision, allowing manipulation of implant location and within-subject comparisons across experimental conditions. To assess functional usefulness of such eye movements, we designed an experimental paradigm—a signal detection task—commonly used in behavioral research. The task required the subject to visually track a horizontally moving target and to press a key whenever the target briefly jumps. By measuring how quickly the subject detects a jump and reacts and how accurate the detection is, we can assess behavioral performance as a function of different viewing conditions.

METHODS

Subjects

Six normally sighted subjects (three men, three women) participated in the study. All subjects had 20/30 or better visual acuity with no or best correction and were between 20 and 50 years of age. The study was designed in accordance with the tenets of the Declaration of Helsinki and was approved by the Institutional Review Board of the Johns Hopkins University School of Medicine. Informed consent was obtained from each subject after explanation of the nature and possible consequences of the study. Subjects received a lunch coupon and $10 (US) for each 1-hour experimental session.

Retinal Prosthesis Simulation

Prosthetic vision was simulated monocularly as a grid of 10 × 10 white dots against a dark background (Fig. 1). The dot grid spanned a visual field of 9.4° × 9.4° at the viewing distance of 0.66 m. Each dot subtended a visual angle of 0.94° in diameter and simulated a phosphene with a circular Gaussian luminance profile with a SD of 0.33°. Phosphene luminance ranged from 0 (darkest) to 255 (brightest). Peak luminance of any phosphene was obtained as Peak luminance = (LSL/MSL) × PLR + PBL, where LSL is the local mean luminance across the scene area subtended by the phosphene, MSL is the maximum luminance anywhere in the scene, PLR is the phosphene luminance range, and PBL is the phosphene background luminance. Rayleigh luminance contrast was defined as PLR/(PLR + PBL). Based on the observations of brightness resolution in a clinical study, we chose a phosphene luminance scale of 8 gray levels and luminance contrast of 68%. Unlike other studies in our laboratory, no dynamic noise (sparks) or dropouts (missing dots) were simulated in the present study. The dot grid was presented on a 17-inch monitor and viewed by the left eye only; the right eye was occluded. The center of the grid on the monitor was positioned in reference to the subject’s foveal fixation. An infrared eye tracking system (ViewPoint Eye Tracker; Arrington Research Inc., Scottsdale, AZ) was used to track left eye foveal fixation at 60 Hz (Fig. 2). The video display on the monitor was refreshed at 30 Hz (frame rate) because of a limitation in the video-processing software. The lower frame rate might cause a discrepancy between eye position and dot grid position. In this study, the target could move as fast as 8°/s or 0.27°/frame. If the subject was tracking the target smoothly, the lag of the dot grid would not exceed 0.27° or approximately 30% of the phosphene diameter. This amount of discrepancy was below the spatial resolution of 0.5° in the eye-tracking system and, therefore, was tolerable. However, a large saccade could result in intolerable discrepancy. We took two measures to work around this problem. First, subjects engaged in sufficient practice to minimize the incidences of large saccades. Second, image delay caused by large saccades would result in erratic eye movements. When such eye movements occurred, the experiment would be repeated to ensure adequate data quality.

Experimental Paradigm and Procedure

The experimental paradigm was a visual signal detection task. The signal was a brief upward or downward jump of a visual target, a white dot of 0.94° in diameter. The paradigm started with a fixation cross presented at the center of a computer monitor for 3000 ms. The cross was then replaced with the target for a stationary period between 500 and 1500 ms. After that period, the target began to move at a constant speed horizontally either leftward or rightward, determined by a randomization sequence, and then back to the central position. Such a round-trip of target movement constituted one experimental trial. Target motion spanned between 6° and 9°. The moving target might briefly jump at a random point of time for 0 to 4 times during a trial (Fig. 3). A jump displaced the center of the dot either above or below its current position by 1.41° for 120 ms. During this interval, the dot
continued moving at the same speed and in the same direction. The subject was instructed to keep the target centered in the dot grid during target movement and to press the space bar on a computer keyboard as soon as the target jumped.

An experimental session began with the subject seated in an examination chair with the head steadied against the headrest. The seat was adjusted so that the subject’s eye was at the level of the display center and 0.66 m away from the display. Instructions were then given to the subject. If needed, the subject practiced the signal detection task under certain experimental conditions (see Experiment 1 and Experiment 2) until the subject felt comfortable with the task and task performance became stable. After practice, a calibration procedure was performed to map foveal fixations on the display to the magnitude of eye movements, and the calibration data were saved for offline data analysis. Immediately after calibration, the subject performed the formal experiment in a block of 40 trials without breaks.

Measurements of Eye Movement and Task Performance

Eye movements were recorded at 60 Hz. Manual responses (spacebar press) to target jumps were recorded at 30 Hz. All recordings were synchronized online and saved for offline analysis. Pursuit eye movements were characterized by three variables: latency, defined as the time between the onset of target movement and the onset of eye movement; horizontal variability (HV), defined as the SD of the distance between horizontal foveal fixation and horizontal target position across all sampling points during a trial; and vertical variability (VV), defined as the SD of the distance between vertical foveal fixation and vertical target position across all sampling points during a trial. Foveal fixation was determined by pupil center. The reciprocals of HV and VV reflected fixation stability with respect to the target. In conditions of simulated prosthetic vision, some subjects might not have tracked the moving target at the center of the dot grid but at another location within the grid. Such behavior was acceptable because the subject was still tracking the target with the retinal prosthesis. Therefore, the appropriate measures of eye movement stability would be those concerning eye movement fluctuation across a trial instead of the distance between the target and the center of the dot grid.

Task performance was assessed with the visuomotor response time (RT), defined as the time between a target jump and the first spacebar press after the jump. Hit rate (HR) was defined as the number of correct spacebar presses over the number of target jumps, and false alarm rate (FA) was defined as the number of incorrect spacebar presses over the total number of spacebar presses. A correct spacebar press was defined as the first spacebar press occurring any time between 100 ms after the onset of a target jump and before the onset of the next target jump, and an incorrect spacebar press was a spacebar press that did not meet the definition of a correct spacebar press.

Software developed in-house was used offline to identify target movement onset, eye movement onset, target jump onset, and spacebar press onset. A saccade, which often occurred at the beginning of a pursuit eye movement to catch up with the target, was defined as an eye movement whose velocity was no less than 50°/s and whose duration was no less than 10 ms.25 Saccade onset was defined as the first data point whose position exceeded twice the standard deviation of the noise level of data recording. A segment of eye position data was identified as a pursuit eye movement if its position exceeded noise level, velocity was below saccade speed, and direction was consistent with target motion.

Statistical Analysis

Of 40 trials under each combination of experimental conditions, the first 10 were used for warm-up and, therefore, were not included in the analysis. Trials with eye movement latency less than 100 ms, no eye movements, or incomplete recording were discarded. This proved necessary for 1 to 29 trials of 160 trials recorded per subject in experiment 1 and for 2 to 25 trials of 240 trials per subject in experiment 2. Statistical analyses were carried out using repeated-measures analysis of variance in the general linear model of SAS (SAS Institute Inc, Cary, NC), with an α value of $P = 0.05$ considered significant. Post hoc pairwise comparisons were carried out using analysis of variance of contrast variables.25

RESULTS

Experiment 1

The purpose of experiment 1 was to assess how spatial resolution affects pursuit eye movements at two different target speeds. The experiment called for a two-factor within-subjects design ($2 	imes 2$) with the two factors (mode and speed). Mode had two levels: natural vision (NV), which was the foveal vision of the normally sighted, and simulated prosthetic vision (SPV, as described in Methods) with macular implant location. Speed had two levels: 4°/s (slow) and 8°/s (fast). There were four combinations of conditions: NV with slow and fast and SPV with slow and fast. Each combination was presented in a block of 40 trials. The subject performed the experiment first in NV, followed by SPV. The order of target speed was counterbalanced across subjects.

All six subjects had no previous experience in pursuit eye movement studies. However, four subjects were experienced in SPV. Before the formal experiment, subjects were allowed practice to learn the task until their performance became stable. Subjects varied in the duration of practice. All subjects quickly learned pursuit eye movements in natural vision. Three subjects (one of them was naive to SPV) took 1 hour of practice for each condition of SPV.

Horizontal variability of pursuit eye movements was significantly higher in SPV than in NV mode ($F_{1,5} = 9.39; P < 0.05$), as shown in Figure 4. No significant effect of interaction between mode and speed or of speed alone was found. Figure 5 shows a sample reconstruction of eye movement traces superimposed on target movement traces and depicts differences in horizontal variability between SPV and NV. On the other hand, no significant difference in vertical variability was found between SPV and NV mode. As shown in Figure 6, the latency of pursuit eye movements was longer in SPV than in NV ($F_{1,5} = 75.84; P < 0.01$) but shorter in pursuing fast than slow targets ($F_{1,5} = 22.23; P < 0.01$). No significant effect of interaction between mode and speed on latency was found.

Results based on the data of five subjects showed significantly ($F_{1,4} = 64.04; P < 0.01$) longer RT in SPV (631 ± 69 ms) than in NV (367 ± 64 ms). No significant differences in HR and
Experiment 2

The purpose of experiment 2 was to assess how prosthesis implant location affects pursuit eye movements at two different target speeds. There were two experimental factors in experiment 2: locus and speed. Locus referred to implant location and had three levels, macula (Macula), 8° superior to fovea (Superior), and 8° nasal to fovea (Nasal). Speed was as defined in experiment 1. There were six combinations of conditions (3 × 2): macula locus with slow and fast target; superior locus with slow and fast target; and nasal locus with slow and fast target. Data for the macula conditions were those collected in SPV mode in experiment 1. The remaining data were collected with the conditions counterbalanced across subjects.

Before the formal experiment, three subjects took little practice, whereas the other subjects took approximately 1 hour of practice for each combination of conditions.

The main effect of locus on horizontal variability (Fig. 7) was significant ($F_{1,4} = 13.69, P < 0.05$). Pairwise comparisons showed that HV was significantly higher at superior ($F_{1,11} = 13.43; P < 0.01$) and at nasal ($F_{1,11} = 31.05; P < 0.01$) than at macula. In addition, HV in nasal condition was significantly higher than in superior ($F_{1,11} = 19.29; P < 0.01$) by approximately 17%. No significant effect of interactions between locus and speed or of speed alone on HV was found. The main effect of speed on vertical variability (Fig. 8) was significant ($F_{1,1} = 32.50; P < 0.01$), with greater VV in slow condition than in fast condition. No significant effect of interactions between locus and speed or of locus alone on VV was found. The main effect of speed on latency (Fig. 9) was significant ($F_{1,1} = 35.62; P < 0.01$) with longer latency in slow condition ($597 \pm 200$ ms) than in fast condition ($411 \pm 88$ ms). The coefficient of variation (CV) for latency was 33.5% in slow condition and 21.4% in fast condition. No significant effect of interactions between locus and speed or of locus alone on latency was found.

Among the four subjects whose data were analyzed, no significant differences in RT, HR, and FA were found among different conditions. Mean RT was $649 \pm 128$ ms, mean HR was $0.51 \pm 0.20$, and mean FA was $0.22 \pm 0.16$. Data of the other two subjects were not included in the analysis because in some conditions the subjects made no manual responses—W54 for eccentric implant locations with fast target and W56 in the conditions of SPV with fast target and at the nasal locus with slow target. At other times, their responses were consistent with those of the other subjects in RT, but they had lower HR and higher FA.

**Discussion**

**Eye Movement Stability**

Our study of horizontal pursuit eye movements finds that horizontal fixation position with respect to target position is less stable in simulated prosthetic vision than in natural vision. In addition, fixation position is less stable with a simulated retinal prosthesis implanted at an eccentric locus than at the macula. In tracking target motion using a simulated retinal prosthesis, most subjects in our study made stepwise saccades, instead of smooth pursuit eye movements. We observed that eye movements were smoother in tracking a horizontally moving target using simulated prosthetic vision representing a retinal prosthesis implanted superior to the fovea than one implanted nasal to the fovea.

By subtracting the horizontal variation in natural vision from that in simulated prosthetic vision with the macular implant location, one obtains the variability caused by reduced spatial resolution. Similarly, variability attributed to implant location can be obtained by subtracting the horizontal variation in simulated prosthetic vision with the macular implant location from that with a peripheral implant location. Our results show that horizontal variability is doubled in simulated prosthetic vision compared with that in natural vision (Fig. 4), that superior implant location contributes an additional 60% over the variability of macular implant location, and that nasal implant location adds another 67% (Fig. 7). Those findings suggest horizontal variability is attributable to two sources, spatial resolution of the simulated retinal prosthesis and implant location.

Similar phenomena have been reported in studies of pursuit eye movements in eccentric viewing. Winterson and Steinman reported that normally sighted subjects could visually pursue a horizontally moving target using the peripheral vision of 6° below the foveal vision in the visual field. Steinbach demonstrated that the eccentricity of a target being pursued could be as far as 15° above foveal vision in the visual field. Peli argued that eye movements are better controlled if the line between PRL and fovea is perpendicular to the direction of target movement. Such a facilitatory effect of superior PRL on horizontal eye movements has also been observed in reading. For example, patients with central scotoma who use a PRL superior to the fovea tend to be less impaired in reading speed. Steinbach suggested that the superior PRL is better for global search. Pidcoe and Wetzel studied smooth eye movements in subjects with a simulated scotoma and found that eye movements became less smooth with increases in scotoma size. Those findings suggest that direction and distance of a PRL are important factors affecting the quality of pursuit eye movements.

Hallum et al. investigated eye-hand coordination as a function of image quality of simulated prosthetic vision. Scheme Q2 of the phosphene profile in their study is similar to that in the present study. In their eye-hand coordination experiment, Hallum et al. calculated the power spectral density of the performance deviation between a simulated phosphene array and a smoothly moving target. They found greater power spectral density in simulated prosthetic vision (scheme Q2) than in...
natural vision, suggesting that manual tracing is less stable in simulated prosthetic vision than in natural vision. Although eye movements and hand movements are different, the results of Hallum et al.\textsuperscript{28} and our results show that motor control is affected by spatial resolution of vision.

In our study, vertical variability in simulated prosthetic vision at superior implant location is found to be less stable in slower eye movements. It is unclear why vertical variability is greater when target speed is lower. One hypothesis is that it is difficult to maintain stable fixation at low spatial resolution and that, therefore, the eye is less stable when target speed is low. This hypothesis is yet to be tested.

**Eye Movement Initiation**

Our results show that in natural vision and simulated prosthetic vision, mean latency is longer under the condition of slower target than fast (Figs. 6, 9). We also found that mean eye movement latency in simulated prosthetic vision is approximately 200 ms, or 65%, longer than that in natural vision (Fig. 6). In simulated prosthetic vision, eye movement latencies have greater variability (approximately 30%) at slow target speed than they do at fast target speed. During examination of hand movement initiation (spacebar press), we found that in detecting a target jump, subjects take longer to press a spacebar in simulated prosthetic vision than in natural vision and have a higher incidence of missing target jumps in simulated prosthetic vision with an eccentric implant location. On the other hand, the visuomanual response time is not affected by target speed. Eye movement in response to target movement and visuomanual response to a target jump share two components—detection of a visual event and enactment of a motor action. Our data lead us to hypothesize that visual event detection is impaired by reduced spatial resolution and is worsened by eccentric viewing and that the enactment of eye movement, but not hand movement, is modulated by target speed.
Task Performance

The functional purpose of eye movements in daily life is to accomplish tasks requiring better sight. Task performance measures allow us to objectively assess functional usefulness of eye movements. In this study, we designed a simple signal detection task by asking the subject to press a key whenever the subject saw the target jumping. We measured the visuo-manual response time, hit rate, and false-alarm rate to characterize task performance. RT is approximately 65% longer in simulated prosthetic vision than in natural vision, suggesting that the low resolution of simulated prosthetic vision delays the viewer’s response to a visual event. Hallum et al. reported visuomanual response time in their Q2 scheme of simulated prosthetic vision to be 20% longer than in natural vision (0.29 second). Our result that RT in simulated prosthetic vision is 70% longer than in natural vision (0.37 second) shows the same pattern found by Hallum et al. The discrepancy in the magnitude of RT may be the result of different viewing conditions. In Hallum et al., subjects viewed the target binocularly through the phosphene array, and the phosphene array was not locked to a certain location on retina. Such experimental conditions may be less demanding in detecting a visual event.

We did not find statistically significant differences in HR and FA between the conditions of natural and simulated prosthetic vision. However, two subjects made too few manual responses, particularly with eccentric implant locations, to be included in statistical analysis. Their performance manifests that there are marked individual differences in tracking target motion using low-resolution vision and that this task can be very difficult for some persons and that it can be even more difficult to detect a visual event in eccentric viewing. The fact that the false-alarm rate is low in natural vision and simulated prosthetic vision may reflect subject bias in decision-making. The observations that eye movement latency and stability, visuomanual response time, and sometimes hit rate are impaired in simulated prosthetic vision provide convergent evidence to support the hypothesis that stable and smooth pursuit eye movements are desired for functional vision.

All six subjects in our study were naive to the eye movement experiments, but four of them had experience using simulated prosthetic vision. Subjects were asked to practice until their performance appeared satisfactory and asymptotic. The amount of time taken for practice was approximately 1 to 2 hours for one experimental condition. Other studies on simulated prosthetic vision have reported that substantial practice is needed before task performance approaches an asymptote. Reviewing those studies, one finds an association between cognitive load of the task and amount of practice. For example, the reading task in Sommerhalder et al. and the virtual maze navigation task in Dagnelie et al. are more cognitively demanding than our signal detection task and the eye-hand coordination task in Hallum et al. Task performance in Hallum et al. generally approaches an asymptote after the first three visits, which amounts to approximately 1 hour of practice, similar to what was observed in the present study. For a simpler task of visual/manual tracking with lower cognitive demand, one can command the task with relative ease.
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References


