Effects of Strabismic Amblyopia and Strabismus without Amblyopia on Visuomotor Behavior, I: Saccadic Eye Movements

Ewa Niecbwiej-Szwedo,1 Manokaraananthan Chandrakumar,1 Herbert C. Goltz,1,2 and Agnes M. F. Wong1,2

PURPOSE. It has previously been shown that anisometropic amblyopia affects the programming and execution of saccades. The aim of the current study was to investigate the impact of strabismic amblyopia on saccade performance.

METHODS. Fourteen adults with strabismic amblyopia, 13 adults with strabismus without amblyopia, and 14 visually normal adults performed saccades and reach-to-touch movements to targets presented at ±5° and ±10° eccentricity during binocular and monocular viewing. Latency, amplitude, and peak velocity of primary and secondary saccades were measured.

RESULTS. In contrast to visually normal participants who had shorter primary saccade latency during binocular viewing, no binocular advantage was found in patients with strabismus with or without amblyopia. Patients with amblyopia had longer saccade latency during amblyopic eye viewing (P < 0.0001); however, there were no significant differences in saccade amplitude precision among the three groups across viewing conditions. Further analysis showed that only patients with severe amblyopia and no stereopsis (n = 4) exhibited longer latency (which was more pronounced for more central targets; P < 0.0001), and they also had reduced amplitude precision during amblyopic eye viewing. In contrast, patients with mild amblyopia (n = 5) and no stereopsis had normal latency and reduced precision during amblyopic eye viewing (P < 0.0001), whereas those with gross stereopsis (n = 5) had normal latency and precision. There were no differences in peak velocity among the groups.

CONCLUSIONS. Distinct patterns of saccade performance according to different levels of visual acuity and stereoscopic losses in strabismic amblyopia were found. These findings were in contrast to those in anisometropic amblyopia in which the altered saccade performance was independent of the extent of visual acuity or stereoscopic deficits. These results were most likely due to different long-term sensory suppression mechanisms in strabismic versus anisometropic amblyopia. (Invest Ophthalmol Vis Sci. 2012;53:7458–7468) DOI:10.1167/iovs.12-10550

Amblyopia is a neural disorder caused by inadequate visual stimulation during the early critical period of development.1 Amblyopia is commonly associated with two risk factors: strabismus (eye misalignment) and anisometropia (difference in refractive errors between the eyes).2 Patients with amblyopia have reduced visual acuity and contrast sensitivity, as well as other perceptual deficits.3–10 which are most pronounced during amblyopic eye viewing; however, they are also evident during fellow eye viewing, albeit to a lesser extent.11–15

The effects of amblyopia on visuomotor behavior have not been examined as extensively as the sensory/perceptual deficits. This is surprising because a fundamental function of the brain is to use sensory information from all modalities to make purposeful, goal-directed behaviors through the process of sensorimotor integration. Vision provides critical information about the location and properties of objects that we want to interact with or avoid. To see an object in detail, the fovea—the area of highest resolution on the retina—has to be directed toward the object, which is achieved via saccadic eye movements. Visual information is combined across eye movements to form internal spatial representations of the external world.14,15Thus, saccadic eye movements are an essential component of the action–perception loop, and play an important role in guiding flexible behaviors while people interact with objects in dynamic environments.

Our group has been studying the effects of impaired spatiotemporal visual functions in amblyopia on motor behavior. In a series of detailed investigations, we have recently reported the impact of anisometropic amblyopia on saccadic eye movements.16 reaching movements of the upper limb.17,18 and eye–hand coordination19 during visually guided reaching. Specifically, we have shown that patients with anisometropic amblyopia had significantly longer and more variable saccade latency during amblyopic eye viewing,16 lower peak acceleration and a longer acceleration phase during reaching,18 and a different temporal pattern of eye–hand coordination.19 Importantly, the effects of amblyopia on reaching movements were evident not only during amblyopic eye viewing, but also during binocular and fellow eye viewing.

As a next step in our systematic investigations, we examined whether different subtypes of amblyopia affect motor behaviors differentially. Previous studies have demonstrated several differences in perceptual deficits among patients with anisometropic versus strabismic amblyopia. For example, patients with anisometropic amblyopia exhibited...
deficits in contrast detection and spatial localization across the entire visual field, whereas patients with strabismic amblyopia exhibited more pronounced deficits in the central visual field than those in the peripheral visual field. A study of 427 amblyopic patients has also shown distinctive patterns of visual deficits among different amblyopia subtypes. Patients with anisometropic amblyopia and moderate loss of acuity had normal/subnormal contrast sensitivity and were more likely to have gross stereopsis, whereas those with strabismic amblyopia and moderate loss of acuity had better than normal contrast sensitivity at low spatial frequencies and were more likely to have reduced/absent stereopsis.

The effects of strabismic amblyopia on saccadic eye movements have only been investigated in two previous studies. Schor examined saccades in five patients using a predictable, square-wave stimulus to elicit saccades. He reported no difference in latency and a significant increase in amplitude variability when patients viewed with their amblyopic eye. Ciuffreda and colleagues tested six patients using an unpredictable stepping target and found longer saccade latencies in some patients. However, they did not include a visually normal control group and their sample size was small, which precluded a more detailed analysis of the effects of visual acuity or stereocuity on saccade performance. Previous studies of children with strabismus without amblyopia found no difference in saccade latency between children with and without binocular vision and in comparison to children with normal vision. However, adults with strabismus showed an impairment in binocular coordination of saccades that was most pronounced in patients without binocular vision.

The objective of the current study was to investigate saccadic eye movements during a visually guided reaching task in patients with strabismic amblyopia, as well as the effects of visual acuity and stereocuity deficits on saccade performance. We hypothesized that impairments in saccade performance would be largest in patients with amblyopia during amblyopic eye viewing. We also hypothesized that patients' performance would be affected by their level of visual acuity and stereocuity deficits. Specifically, we hypothesized that saccades will be delayed and have reduced precision in patients with poorer acuity and negative stereopsis. Results of the reaching movement are the focus of our next study.

**METHODS**

**Participants**

All participants were adults and underwent a complete orthoptic assessment by a certified orthoptist, which included visual acuity (Snellen chart), prism cover test (simultaneous and alternate) of eye alignment, and measurement of stereocuity using the Titmus test. Exclusion criteria were any ocular cause for reduced visual acuity, previous intraocular surgery, or any neurologic disease. All participants were right-handed to reduce the variability in motor performance.

Fourteen patients with strabismic amblyopia (6 females; age: 31.7 ± 9.9 years; see Table 1 for clinical characteristics) were recruited. Strabismic amblyopia was defined as an interocular acuity difference ≥2 lines on a Snellen chart, and subjects with a history of childhood strabismus and manifest eye deviation. Visual acuity was tested with current refractive correction. The difference in refractive error between the two eyes was ≤1 diopter (D) of spherical or cylindrical power, to rule out a potentially amblyogenic astigmatic component (i.e., to rule out mixed-mechanism amblyopia). When stereocuity was absent, the presence or absence of sensory fusion was determined using Worth’s 4-dot test and Bagolini-striated glasses. Ten patients had mild amblyopia, with acuity in the amblyopic eye ranging from 20/50 to 20/60. Five of the patients with mild amblyopia had gross stereocuity (range: 120–800 seconds of arc), whereas the other five patients had negative stereocuity. Four patients had severe amblyopia (20/200 in the ambylopic eye) and negative stereocuity. Visual acuity in the fellow eye was 20/20 or better in all patients. All patients with strabismus without amblyopia (acuity 20/25 or better in both eyes) were also recruited (6 females; age: 30.1 ± 4.0 years; see Table 1 for clinical characteristics). All patients had manifest eye deviation. Nine patients were tested negative for stereocuity, two had stereocuity of 3000 seconds of arc, and the remaining two had stereocuity of 50 and 80 seconds of arc.

Fourteen visually normal participants (6 females; age: 31.7 ± 9.9 years) with corrected-to-normal visual acuity (20/20 or better) in both eyes and stereocuity ≤40 seconds of arc were recruited. Eye dominance in visually normal participants was determined using the Dolman “hole-in-card” test.

The study was approved by the Research Ethics Board at The Hospital for Sick Children, and all protocols adhered to the guidelines of the Declaration of Helsinki. Informed consent was obtained from each participant.

**Apparatus and Experimental Protocol**

Details of the apparatus and experimental procedure have been described in a previous article. Briefly, the visual target was a white square (visual angle: 0.5°) presented on a black background on a cathode ray tube computer monitor (Diamond Pro 2070SB, resolution 1600 × 1200 at 85 Hz; NEC/Mitsubishi Electric Visual Systems, Tokyo, Japan). Testing was conducted in a dimly lit room. Eye movements were recorded binocularly at 200 Hz using a video-based pupil/iris tracking system (Chronos Vision, Berlin, Germany). Reaching movements of the upper limb were also recorded simultaneously at 200 Hz using an infrared illumination-based motion-capture system (Optotrak Certus; Northern Digital, Waterloo, Canada).

Participants were seated at a table with their heads stabilized on a chin rest. They fixated a cross at the beginning of each trial. The viewing distance was 42 cm. After a variable delay of 1.5 to 3 seconds, the fixation cross was extinguished and one visual target appeared randomly at one of four eccentricities ±5 or ±10 along the horizontal axis. There was no temporal delay between the offset of the fixation point and the presentation of the target (simultaneous fixation offset and target onset). Participants were instructed to look at the target and to make a reaching movement to touch the target with their index finger as quickly and as accurately as possible. Details of the reaching task have been described previously. In 50% of the trials, the target was switched off at the onset of hand movement. For the other 50% of the trials, the target remained on the screen. Trials with and without visual feedback of the target were randomized on a trial-by-trial basis.

Participants performed the experiment in three viewing conditions: (1) binocular viewing; (2) monocular viewing with the dominant eye (i.e., the fellow eye for patients with amblyopia, and the nondeviating eye for patients with strabismus without amblyopia); and (3) monocular viewing with the nondondeviating eye (i.e., the amblyopic eye for patients with amblyopia, and the deviating eye for patients with strabismus without amblyopia). Data were collected in blocks for each viewing condition, and the order of viewing conditions was randomized across participants. All participants completed 10 trials in each combination of the experimental conditions for a total of 240 trials/session. Practice trials were completed before the experiment was begun to familiarize the participants with the experimental procedure. All data were collected in one session (1–1.5 hours), which included calibration of the apparatus, practice, and experimental trials.

**Analysis: Saccadic Eye Movements**

Eye position data were low-pass filtered using a second-order dual-pass Butterworth filter with a cutoff frequency of 50 Hz. Eye velocity was obtained using a two-point differentiation method. A custom-written
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PD, prism diopter; Hx, history; W4D, Worth 4 Dot test; Bagolini, Bagolini striated glasses; ET, esotropia; XT, exotropia; X, exophoria; E, esophoria; HT, hypertropia; Hypo, hypotropia; H, hyperphoria; Int. fusion, intermittent fusion; IET, infantile esotropia; ARC, anomalous retinal correspondence; AET, alternating esotropia; DVD, dissociated vertical deviation; surgery, surgical treatment of strabismus.
Effects of Stereopsis in Patients with Strabismus without Amblyopia.

The procedure developed by Conover and Iman. The ANOVA had severe amblyopia (i.e., acuity 20/200) and negative stereopsis (Table 1: and negative stereopsis (mild and strabismus without amblyopia, a separate repeated-measures ANOVA on the ranked data was performed on each outcome measure. For this analysis, patients with strabismus without amblyopia were divided into two subgroups: stereo positive (n = 4), and stereo negative (n = 9). The ANOVA had Subgroup as a between-subjects factor (i.e., stereo+, stereo-) and two within-subjects factors: Viewing Condition (binocular, monocular dominant eye, and monocular nondominant eye) and Target Location (5°, 10°).

Effects of Strabismic Eye Deviation. Spearman correlation analysis was performed to investigate the relation between the amount of eye deviation and primary saccade outcome measures (latency, amplitude accuracy [mean] and precision [SD], peak velocity). The correlation coefficient was calculated separately for patients with strabismic amblyopia and patients with strabismus without amblyopia for the different viewing conditions.

RESULTS

Primary Saccades

Figure 1 shows representative eye velocity tracings from a visually normal participant and individual patients with strabismic amblyopia (mild–stereo+, mild–stereo-, severe), and strabismus without amblyopia (stereo+, stereo-). The visually normal participant showed highly stereotypical saccades in all viewing conditions. The largest deviation from the stereotypical saccade behavior was seen in the patient with severe amblyopia (negative stereopsis) during amblyopic eye viewing and in the patient with strabismus without amblyopia (negative stereopsis) in all viewing conditions. Both patients showed delayed and highly variable saccades.

Latency. The main effect of Viewing Condition (F_{2,76} = 16.81, P < 0.0001) and the interaction between Group and Viewing Condition were significant (F_{4,152} = 6.92, P < 0.0001; Fig. 2A). Post hoc tests revealed that mean saccade latency increased significantly when patients with strabismic amblyopia viewed with their amblyopic eye (218 ± 49 ms), compared with viewing with their fellow eye (172 ± 36 ms) or binocularly (177 ± 39 ms). Patients with strabismus without amblyopia had comparable saccade latency in all viewing conditions (binocular: 191 ± 29 ms; dominant eye: 190 ± 23 ms; nondominant eye: 198 ± 32 ms). In contrast, visually normal participants had significantly shorter saccade latency when viewing binocularly (173 ± 27 ms), compared with monocular viewing with the dominant eye (190 ± 25 ms) or nondominant eye (191 ± 26 ms).

The three-way interaction between Group (strabismic amblyopia, strabismus without amblyopia, visually normal), Viewing Condition, and Target Location was also significant (F_{6,76} = 5.12, P = 0.0002; Fig. 3A). Post hoc testing indicated that patients with strabismic amblyopia had significantly longer latency during amblyopic eye viewing for saccades to the 5° target (227 ± 52 ms) compared with the 10° target (209 ± 44 ms). Target Location did not affect saccade latency in patients with strabismus without amblyopia and visually normal participants in any viewing condition.

The comparison among patients within the amblyopia subgroup (mild–stereo+, mild–stereo-, severe) showed a significant interaction between Subgroup and Viewing Condition (F_{4,22} = 9.34; P < 0.0001, Fig. 2B). Post hoc tests indicated that patients with severe amblyopia had significantly longer saccade latency when viewing with the amblyopic eye (273 ± 36 ms), compared with binocular (165 ± 41 ms) or fellow eye viewing (160 ± 33 ms), and to the other subgroups (i.e., mild amblyopia with and without stereopsis). Patients with mild amblyopia and negative stereopsis also had significantly longer saccade latency during amblyopic eye viewing (187 ± 34 ms), compared with binocular (165 ± 25 ms) or fellow eye viewing (165 ± 35 ms). In contrast, patients with mild amblyopia and

Saccadic Eye Movements in Strabismic Amblyopia

this analysis, patients with strabismus without amblyopia were divided into two subgroups: stereo positive (n = 4), and stereo negative (n = 9). The ANOVA had Subgroup as a between-subjects factor (i.e., stereo+, stereo-) and two within-subjects factors: Viewing Condition (binocular, monocular dominant eye, and monocular nondominant eye) and Target Location (5°, 10°).

Statistical Analysis

All continuous dependent variables were submitted to repeated-measures ANOVA with one between-subjects factor: Group (strabismic amblyopia, strabismus without amblyopia, visually normal) and three within-subjects factors: Viewing Condition (binocular, monocular dominant eye [fellow eye for patients with amblyopia], and monocular nondominant eye [amblyopic eye for patients with amblyopia]), Target Location (5°, 10°), and Visual Feedback of Target (on, off).

The frequency of corrective saccades was compared using Pearson’s χ² statistic. The frequency of saccades was first compared between patients and visually normal participants, then the effect of Viewing Condition was examined within each group, both using Pearson’s χ² statistic.

All statistical analyses were performed using a commercial statistical analysis software program (SAS Software, version 9.2; SAS Institute Inc., Cary, NC). Descriptive statistics were reported as the mean and corresponding SD. All main effects and interactions were analyzed further using Tukey-Kramer post hoc tests to adjust for multiple comparisons. The significance level was set at P < 0.05. Preliminary analysis of all the data showed that Visual Feedback of Target had no significant effect on any outcome measures; therefore, data with or without visual feedback were collapsed for subsequent analysis and reporting. Saccades to the left and right targets at each eccentricity were pooled together for statistical analysis.

Effects of Severity of Amblyopia and Stereopsis. To investigate further the effects of severity of amblyopia and stereopsis, a separate repeated-measures analysis was performed on each outcome measure. For this analysis, patients with amblyopia were stratified into three subgroups: (1) mild amblyopia (i.e., acuity <20/60) and gross stereopsis (mild–stereo+; Table 1: patients 1-5); (2) mild amblyopia and negative stereopsis (mild–stereo-; Table 1: patients 6-10); and (3) severe amblyopia (i.e., acuity 20/200) and negative stereopsis (Table 1: patients 11-14). Since the number of subjects in each subgroup was small, a nonparametric approach was used. All data were transformed to ranks and then submitted to a repeated-measures ANOVA following the procedure developed by Conover and Iman. The ANOVA had Subgroup as a between-subjects factor (i.e., mild–stereo-, mild–stereo-, severe) and two within-subjects factors: Viewing Condition (binocular, monocular fellow eye, and monocular amblyopic eye) and Target Location (5°, 10°).

Effects of Stereopsis in Patients with Strabismus without Amblyopia. To investigate the effects of stereopsis in patients with strabismus without amblyopia, a separate repeated-measures ANOVA on the ranked data was performed on each outcome measure. For

Viewing Condition was examined within each group, both using Pearson’s χ² statistic.
FIGURE 1. Representative eye velocity tracings from individual trials during monocular viewing with the nondominant/amblyopic eye (left column), monocular viewing with the dominant/fellow eye (middle column), and binocular viewing (right column) when the target was shown 10° to the right. Top row: a visually normal participant; second row: a patient with mild amblyopia and gross stereopsis (200 seconds of arc) (Table 1, ID 4); third row: a patient with mild amblyopia and negative stereopsis (Table 1, ID 6); fourth row: a patient with severe amblyopia and negative stereopsis (Table 1, ID 14); fifth row: a patient with strabismus and stereopsis (80 seconds of arc) (Table 1, ID 16); last row: a patient with strabismus without amblyopia and negative stereopsis (Table 1, ID 21).
gross stereopsis had similar saccade latencies across all viewing conditions (binocular viewing: 200 ± 43 ms; fellow eye viewing: 190 ± 35 ms; amblyopic eye viewing: 205 ± 29 ms).

The three-way interaction between Amblyopia Subgroup (mild–stereo⁺, mild–stereo⁻, severe), Viewing Condition, and Target Location was also significant ($F_{6,22} = 2.88; P = 0.0315$; Fig. 3B). Post hoc testing indicated that only patients with severe amblyopia had significantly longer latency during amblyopic eye viewing for saccades to the 5° targets (294 ± 7 ms) compared with the 10° targets (252 ± 21 ms). Target location did not affect saccade latency in patients with amblyopia who had mild acuity deficits with and without stereopsis.

There was no significant difference among patients with strabismus without amblyopia with and without stereopsis for saccade latency in any viewing condition. There was no relation between the extent of eye deviation and latency in both patient groups.

**Amplitude.** There was a significant main effect of target location for saccade amplitude ($F_{1,38} = 1255.91; P < 0.0001$). Saccades to the 10° target had higher amplitude than those to the 5° target in all experimental conditions for visually normal participants and all patients (Table 2). No other significant main effects or interactions were present for mean saccade amplitude. There were also no differences among patients with amblyopia. The distribution of primary saccade amplitude for each target location across viewing conditions for a few representative participants in each subject group is shown in Supplementary Figure S1 (see Supplementary Material and Supplementary Fig. S1, http://www.iovs.org/lookup/suppl/doi:10.1167/iovs.12-10550/-/DCSupplemental).

Saccade amplitude precision (i.e., variability) was not significantly different when patients with amblyopia were compared with visually normal participants and patients with strabismus without amblyopia ($F_{4,76} = 3.12; P = 0.064$). There was a main effect of target location ($F_{1,38} = 114.08; P < 0.0001$); however, interaction between Group and Target Location was not significant. Further subgroup analysis revealed that only patients with severe visual acuity deficits due to amblyopia and negative stereopsis (shown in blue) had a significant longer saccade latency ($P = 0.0515$) during amblyopic eye viewing to targets located closer to fixation compared with more peripheral targets.
TABLE 2. Mean Primary Saccade Amplitude and Peak Velocity

<table>
<thead>
<tr>
<th>Target</th>
<th>Dominant (Fellow Eye)</th>
<th>Nondominant (Amblyopic) Eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak Velocity, deg/s Ampl</td>
<td>4.87 ± 0.29</td>
<td>5.18 ± 0.36</td>
</tr>
<tr>
<td>5 Target</td>
<td>4.67 ± 0.22</td>
<td>4.72 ± 0.14</td>
</tr>
<tr>
<td>10 Target</td>
<td>4.79 ± 0.14</td>
<td>4.76 ± 0.14</td>
</tr>
</tbody>
</table>
| Location did not reach significance ($F_{1,38}$ = 2.33; $P = 0.056$). All subjects exhibited larger variability for the 10° target (visually normal: 1.07 ± 0.52°; patients with strabismic amblyopia: 1.32 ± 0.65°; patients with strabismus without amblyopia: 1.50 ± 0.68°) compared with the 5° target (visually normal: 0.68 ± 0.34°; patients with strabismic amblyopia: 0.88 ± 0.48°; patients with strabismus without amblyopia: 0.85 ± 0.42°).

There was a significant interaction between Amblyopia Subgroup and Viewing Condition ($F_{4,22} = 6.89; P = 0.0009; \text{Fig. 4A}$) for saccade amplitude precision. Post hoc testing showed that patients with severe amblyopia had significantly reduced precision of saccade amplitude during ambyopic eye viewing (2.08 ± 0.86°) compared with binocular (1.12 ± 0.52°) or fellow eye viewing (0.71 ± 0.32°). Similarly, patients with mild amblyopia and negative stereopsis had reduced saccade amplitude precision during ambyopic eye viewing (1.62 ± 0.55°) compared with binocular (1.18 ± 0.32°) or fellow eye viewing (1.07 ± 0.46°). In contrast, patients with mild amblyopia and gross stereopsis had similar saccade amplitude precision across viewing conditions (binocular viewing: 0.81 ± 0.40°; fellow eye viewing: 1.18 ± 0.64°; ambyopic eye viewing: 0.77 ± 0.25°), which was comparable to visually normal participants (binocular viewing: 0.94 ± 0.64°; dominant eye viewing: 0.85 ± 0.37°; nondominant eye viewing: 0.94 ± 0.52°) and to patients with strabismus without amblyopia (binocular viewing: 1.27 ± 0.76°; dominant eye viewing: 1.21 ± 0.73°; nondominant eye viewing: 1.16 ± 0.57°).

There was no significant difference among patients with strabismus without amblyopia with and without stereopsis for saccade amplitude in any viewing condition. There was no relation between the extent of eye deviation and amplitude or precision in both patient groups.

**Peak Velocity.** There was a significant main effect of target location for saccade peak velocity ($F_{1,38} = 712.87; P < 0.0001$). Saccades to the 10° target had higher peak velocity than those to the 5° target in all experimental conditions for visually normal participants and all patients. There was also a main effect of viewing condition ($F_{4,26} = 4.67; P = 0.012$) for peak velocity. Saccades had higher peak velocity during binocular viewing compared with monocular viewing, which was most evident for saccades to the 10° target in all groups, except for patients with strabismus without amblyopia and negative stereopsis (Table 2).

There was no significant difference among patients with strabismus without amblyopia with and without stereopsis for peak velocity in any viewing condition. There was no relation between the extent of eye deviation and peak velocity in both patient groups.

**Secondary Corrective Saccades**

**Frequency.** The overall frequency of corrective saccades was greater in patients with strabismic amblyopia (16.3%) and patients with strabismus without amblyopia (15.1%) compared with visually normal participants (15.5%; $\chi^2_{1,2g+1} = 8.61, P = 0.013$). However, there was no difference in the frequency of secondary saccades among viewing conditions for patients with strabismic amblyopia (binocular viewing: 6.3%, fellow eye viewing: 5.6%, amblyopic eye viewing: 4.4%), patients with strabismus without amblyopia (binocular viewing: 5.8%; dominant eye viewing: 4.9%; nondominant eye viewing: 4.9%), and visually normal participants (binocular viewing: 4.1%; dominant eye viewing: 4.8%; nondominant eye viewing: 4.6%).

Subgroup analysis of patients with amblyopia showed a significant frequency difference in corrective saccade frequency ($\chi^2_{1,2g+1} = 49.00, P < 0.001$). Specifically, patients with mild...
amblyopia and gross stereopsis made fewer secondary saccades (3.1%) compared with patients with mild amblyopia and negative stereopsis (6.4%) and patients with severe amblyopia (6.8%). Differences among viewing conditions are shown in Table 5.

**Latency.** The latency of corrective saccades was comparable across all viewing conditions for patients with strabismic amblyopia, patients with strabismus without amblyopia, and visually normal participants. The subanalysis of patients with amblyopia also yielded no significant differences.

**Amplitude and Peak Velocity.** There was a significant interaction between Group and Viewing Condition for corrective saccade amplitude ($F_{4,62} = 4.49; P = 0.003$). Post hoc testing indicated that patients with strabismic amblyopia had significantly greater secondary saccade amplitudes during amblyopic eye viewing (2.44 ± 1.14°) compared with binocular (1.58 ± 0.78°) and fellow eye viewing (1.43 ± 0.90°), which were comparable to visually normal participants (binocular viewing: 1.39 ± 0.92°; dominant eye viewing: 1.34 ± 0.61°; nondominant eye viewing: 1.42 ± 0.80°) and to patients with strabismus without amblyopia (binocular viewing: 1.72 ± 0.92°; dominant eye viewing: 1.37 ± 0.66°; nondominant eye viewing: 1.47 ± 0.45°). The interaction between Group and Viewing Condition for corrective saccade peak velocity did not reach significance ($F_{4,62} = 1.97; P = 0.111$).

Further analysis of patients with amblyopia revealed a main effect of Viewing Condition for secondary saccade amplitude ($F_{2,11} = 10.05; P = 0.001$) and peak velocity ($F_{2,11} = 4.70; P = 0.024$). Data presented in Table 5 indicate that patients with negative stereopsis had significantly larger amplitude and peak velocity of secondary saccades during ambyopic eye viewing compared with binocular and fellow eye viewing.

**Amplitude Variability after Secondary Saccade.** The comparison between patients with amblyopia, patients with strabismus without amblyopia, and visually normal participants was not statistically significant. The mean precision of the final amplitude after the secondary saccade was less than 1° for all groups (range: 0.65–0.98°). In contrast, analysis of patients with amblyopia revealed a main effect of Subgroup ($F_{2,11} = 13.70; P = 0.001$). Post hoc analysis indicated that amplitude variability after secondary saccade was larger in patients with mild amblyopia and negative stereopsis compared with the other groups in all viewing conditions, with the exception of patients with severe amblyopia during ambyopic eye viewing. There was also an interaction between Subgroup and Viewing Condition ($F_{4,22} = 8.91; P = 0.0002$; Fig. 4B). Post hoc analysis indicated that patients with severe amblyopia had significantly lower precision (i.e., increased variability) of the final amplitude after secondary saccade during ambyopic eye viewing (1.33 ± 0.22°) compared with binocular (0.77 ± 0.28°) and fellow eye viewing (0.50 ± 0.16°), as well as with

![Figure 4](https://iovs.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/932978/)

**Table 3.** Frequency and Kinematics of Secondary Saccades for Patients with Strabismic Amblyopia

<table>
<thead>
<tr>
<th>Mild–Stereo+ ($n = 79$)</th>
<th>Mild–Stereo− ($n = 163$)</th>
<th>Severe–Stereo− ($n = 173$)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Binocular</td>
<td>Fellow Eye</td>
</tr>
<tr>
<td>Frequency, %</td>
<td>5.0</td>
<td>2.0</td>
</tr>
<tr>
<td>Latency, ms</td>
<td>209 ± 24</td>
<td>225 ± 17</td>
</tr>
<tr>
<td>Amplitude, °</td>
<td>1.65 ± 0.71</td>
<td>1.27 ± 0.24</td>
</tr>
<tr>
<td>Peak velocity, deg/s</td>
<td>122 ± 45</td>
<td>102 ± 24</td>
</tr>
</tbody>
</table>

* Total number of trials that contained secondary saccades in each group of patients.
† Saccade amplitude and peak velocity were greater during ambyopic eye viewing for patients with amblyopia with negative stereopsis.
patients with mild amblyopia with and without stereopsis, as illustrated in Figure 4B.

**Discussion**

This study examined saccades in patients with strabismic amblyopia and compared their performance to that of patients with strabismus without amblyopia and visually normal participants. The major findings are: (1) patients with strabismic amblyopia and patients with strabismus without amblyopia showed no binocular advantage for saccade initiation; (2) latency and amplitude of primary saccades were affected by the severity of amblyopia and the presence of stereopsis; (3) amblyopic patients without stereopsis initiated secondary saccades more frequently compared with visually normal participants. These secondary saccades improved the final precision of saccade amplitude; however, the precision remained significantly worse in patients with severe amblyopia during amblyopic eye viewing; and (4) these findings were unique to patients with strabismic amblyopia, because they were not observed in patients with strabismus without amblyopia.

**Patients Lack Binocular Advantage for Saccade Initiation**

Binocular advantage refers to improvements in performance (e.g., visual acuity, contrast sensitivity, and detection of dim stimuli) during binocular viewing compared with monocular viewing in normal people. It has been proposed that when sensory signals from the eyes are summed, uncorrelated signals (i.e., noise) cancel out and correlated signals are amplified (binocular summation). This binocular summation, however, is impaired in patients with amblyopia. Levi and colleagues found no improvement in contrast sensitivity during binocular viewing compared with fellow eye viewing in three patients with strabismic amblyopia and one patient with anisometropic amblyopia. Our findings provide additional evidence that patients with strabismic amblyopia lack binocular advantage in their oculomotor system; their saccade latency was comparable during binocular and fellow eye viewing.

We also found slightly higher peak velocity during binocular viewing compared with that during monocular viewing, which was evident in all groups, except for patients with strabismus without amblyopia and negative stereopsis. The difference was statistically significant, but it was quite small (~5% for 10° saccades). Although we cannot explain this effect at present, we will continue to investigate it in the future by examining the saccade main sequence in patients to determine whether viewing binocularly or monocularly affects the saturation velocity of saccades.

**Effects of Severity of Amblyopia and Stereopsis**

Although the number of patients with strabismic amblyopia in each subgroup was small in the current study, we found significant differences in saccade latency and precision among patients with different levels of visual acuity and stereoaucity deficits. With respect to acuity deficit, our analysis yielded two important findings. First, saccade latency was prolonged only in patients with a severe acuity deficit (20/200) but not in patients with a mild deficit (20/60) during amblyopic eye viewing. These results are in contrast to those in patients with anisometropic amblyopia who had significaantly longer saccade latencies during amblyopic eye viewing, irrespective of whether they had a mild or severe acuity deficit, using the same criteria and experimental paradigm. Second, patients with strabismic amblyopia and severe acuity deficits experienced more difficulty orienting to targets closer to central fixation (i.e., the 5° vs. 10° target). This is in contrast to patients with anisometropic amblyopia whose saccade latencies were not affected by Target Location. Our current and previous results can be interpreted as the motor consequences of different long-term sensory suppression mechanisms in strabismic versus anisometropic amblyopia. Suppression of the central field helps to eliminate central diplopia arising from eye misalignment and allows some degree of peripheral fusion. In contrast, the prolonged saccade latency that is independent of Target Location in patients with anisometropic amblyopia is consistent with sensory suppression of a blurred image across the entire visual field. Interestingly, we found no correlation between the amount of strabismus and saccade latency for different target locations. A larger sample size is required for a more robust correlation analysis.

The prolonged saccade latency for a more centrally located target is consistent with stronger sensory suppression of the central visual field in strabismic amblyopia as found in both humans and cats. This pattern of behavior is not likely to be due to interocular suppression because longer latency was found only when patients were viewing with the amblyopic eye and not during binocular viewing. However, it is possible that the chronic suppression of the deviated eye during binocular viewing extends to the monocular viewing conditions. A previous brain imaging study showed a lower level of cortical activation during foveal stimulation of the amblyopic eye, and may explain the longer saccade latency to more centrally located targets.

A second important finding is that patients with negative stereopsis had significantly reduced precision of primary saccades during amblyopic eye viewing, regardless of the visual acuity deficit. In particular, we found that saccade amplitude precision was significantly worse in patients with strabismic amblyopia and negative stereopsis compared with patients who had gross stereopsis and a similar acuity deficit. It is possible that despite having good acuity in the ambylic eye, the signal from the amblyopic eye in patients with negative stereopsis may remain under suppression during natural binocular viewing, which also habitually extends to monocular amblyopic eye viewing during the brief experimental period. Our findings are consistent with a recent neuroimaging study on patients with strabismic amblyopia, which showed that the decrease in neural activation in V1/V2 during amblyopic eye stimulation was dependent on the suppressive effects of the fellow eye: activity was more reduced when the fellow eye was open than when it was closed. Taken together, our findings and those of others suggest that the amblyopic eye is under chronic suppression during both monocular and binocular viewing, albeit to a different extent.

Previous studies have used perceptual and psychophysical tasks to demonstrate spatial localization deficits in amblyopia. Patients showed a systematic localization bias in the direction of the deviated eye, and exhibited increased spatial uncertainty that was more pronounced in central vision compared with the periphery. Using a saccade task, we provide additional evidence that patients with amblyopia have deficits in spatial localization as shown by increased variability (i.e., reduced precision) in primary saccade amplitude especially during amblyopic eye viewing. We also observed a gradation of effects of strabismic amblyopia: in patients with a severe acuity deficit (and negative stereopsis), both detection (i.e., longer saccade latency) and localization (i.e., increased saccade amplitude variability) deficits were evident. In patients with mild amblyopia, however, evidence that patients with strabismic amblyopia lack binocular advantage for saccade initiation; (2) latency and amplitude of primary saccades were affected by the severity of amblyopia and the presence of stereopsis; (3) amblyopic patients without stereopsis initiated secondary saccades more frequently compared with visually normal participants. These secondary saccades improved the final precision of saccade amplitude; however, the precision remained significantly worse in patients with severe amblyopia during amblyopic eye viewing; and (4) these findings were unique to patients with strabismic amblyopia, because they were not observed in patients with strabismus without amblyopia.
with mild amblyopia and negative stereopsis, a localization deficit was evident but not a detection deficit (i.e., normal saccade latency), whereas in those with mild amblyopia and gross stereopsis, no localization or detection deficit was present. The distinct pattern found in patients with mild amblyopia and negative stereopsis could be explained by a speed-accuracy tradeoff: saccades were initiated with normal latency but with a greater than normal scatter of landing positions. This behavior might have led to a large inaccuracy; however, the errors in primary saccade amplitude were corrected by secondary saccades as discussed in the following text.

**Secondary Saccades**

Primary saccades have a tendency to undershoot the target by approximately 10%. Secondary saccades are initiated to correct the amplitude error remaining after the primary saccade. Two sources of error feedback have been proposed for the generation of secondary saccades. One is based on extraretinal information derived from the efference copy of the oculomotor command. Another is based on retinal feedback derived from the position of the target image on the retina at the end of the primary saccade.

Our data show two important findings. First, only patients with amblyopia (mild and severe) and negative stereopsis initiated secondary saccades more frequently. Second, saccades initiated by these patients with negative stereopsis during amblyopic eye viewing had higher amplitudes and peak velocities. Since we also found that these patients had lower primary saccade amplitude precision, these secondary saccades were initiated to correct the amplitude error remaining after the primary saccade. Patients with mild amblyopia were able to correct the error significantly more compared with patients with severe amblyopia, as indicated by improved final amplitude precision after the secondary saccade. These results can be interpreted by considering that the retinal feedback is more impaired in patients with severe amblyopia. Consequently, patients with less reliable retinal position error signals may need a larger visual error signal before initiating a secondary saccade, which in turn leads to higher amplitude and, thus, peak velocity of the corrective eye movement. In addition, our data indicate that the error detection process is impaired in patients with severe amblyopia because they made significantly fewer secondary saccades during amblyopic eye viewing. Our findings highlight the importance of a reliable retinal feedback signal for the initiation of secondary corrective saccades.

In conclusion, our study adds to the growing body of literature that recognizes amblyopia as a heterogeneous disorder of both visual and visuomotor functions. We found a distinct pattern of deficits in patients with strabismic amblyopia that, unlike that in anisometropic amblyopia, was dependent on the level of visual acuity and stereocuity losses. Gross stereopsis was associated with better saccade performance in terms of detection and localization, regardless of viewing condition. In addition, these deficits were unique to patients with strabismic amblyopia, because they were not found in patients with strabismus without amblyopia. Our results suggest that the evaluation of the effectiveness of treatment regimens for amblyopia should also consider motor improvement, rather than solely on visual acuity.

**References**


