Effects of Induced Monocular Blur versus Anisometropic Amblyopia on Saccades, Reaching, and Eye-Hand Coordination

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Purpose. We previously showed that anisometropic amblyopia affects the programming and execution of saccades and reaching movements. In our current study, we investigated whether these amblyopia-related changes simply are due to a reduction in visual acuity alone by inducing artificial blur in one eye in visually-normal participants.

Methods. Twelve visually-normal participants performed saccades and reach-to-touch movements to targets presented on a computer screen during binocular and monocular viewing. A contact lens was used to blur the vision of one eye to a mean acuity level of 20/50. Saccades and reaching kinematics were compared before blur, immediately after blur, and 5 hours after blur was induced. The 5 hours after blur kinematic data from visually-normal participants also were compared to those from 12 patients with anisometropic amblyopia who had comparable acuity in the amblyopic eye.

Results. Primary saccades (latency, amplitude, peak velocity), reaching movements (reaction time, movement time, peak acceleration, duration of the acceleration phase), and eye-hand coordination (saccade-to-reach planning interval, saccade-to-reach peak velocity interval) were not affected by induced monocular blur in visually-normal participants, either immediately or 5 hours after blur. Compared to visually-normal participants after 5 hours of blur, patients with anisometropic amblyopia had significantly longer and more variable saccade latency during amblyopic eye viewing, lower peak acceleration, and a longer acceleration phase during reaching, and a different temporal pattern of eye-hand coordination.

Conclusions. Artificially-induced monocular blur in visually-normal participants did not affect saccades, reaching movements, and eye-hand coordination during a simple reach-to-touch task even after a period of blur exposure. In contrast, patients with anisometropic amblyopia demonstrated significantly different kinematics while performing the same task. These results indicate that loss of visual acuity alone cannot explain the kinematic changes seen in patients with mild anisometropic amblyopia. (*Invest Ophthalmol Vis Sci.* 2012; 53:4354–4362) DOI:10.1167/iovs.12-9855

Amblyopia is a developmental disorder characterized by reduced vision in one or both eyes that cannot be corrected immediately by optical means.[1] It affects 3–5% of the world population[2] and presents a significant health care issue. People with amblyopia (including those treated successfully and those whose treatment failed) have reduced quality-of-life and career choices due to difficulties with distance and depth estimation, visual disorientation, and fear of losing vision in the better seeing eye.[3]

Amblyopia is associated most commonly with early childhood strabismus (eye misalignment), anisometropia (difference in refractive errors between the eyes), or both (i.e., mixed mechanism).[4] In addition to reduced visual acuity and contrast sensitivity, patients with amblyopia also exhibit perceptual deficits, including abnormal global form detection,[5] spatial distortions and temporal instability,[6,7] spatial and temporal crowding,[8] poor stereopsis,[9] abnormal global motion detection,[10,11] and deficits in extracting motion-defined form.[12] These deficits are most pronounced during amblyopic eye viewing; however, they also are evident during fellow eye viewing, albeit to a lesser extent.[13–15]

A primary function of the senses (e.g., vision) is to collect information to guide motor behaviors, including eye movements and reaching/grasping movements of the limbs. Although the visual impairment in amblyopia has been studied extensively, to our knowledge the effects of amblyopia on visuomotor behavior have not been investigated until recently.[16,17] In a series of detailed investigations, our group has reported the effects of anisometropic amblyopia on saccadic eye movements,[18] reaching movements,[19,20] and eye-hand coordination[21] 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,[18] lower peak acceleration and a longer acceleration phase during reaching,[20] and a different temporal pattern of eye-hand coordination.[21] Importantly, the effects of amblyopia on reaching movements were evident not only during amblyopic eye viewing, but also during binocular and fellow eye viewing.

A question that was raised repeatedly by previous reviewers was whether the altered saccade and reaching behaviors seen in patients with anisometropic amblyopia were due to a loss of visual acuity alone, or whether it was specific to amblyopia as a result of abnormal visual development during early childhood. In our current study, we addressed this question by investigat-

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ing the effects of induced monocular blur on saccadic eye movements, reaching movements, and the temporal pattern of eye-hand coordination in visually-normal participants before and after exposure to monocular blur. We also compared their performance after blur exposure to that of a selected group of patients with anisometropic amblyopia who had comparable acuity levels in their amblyopic eyes. Data from this selected group of patients have been reported previously.[18,20,21]

Methods

Participants

We recruited 12 visually-normal participants (7 females, age 31.8 ± 8.0 years) with corrected-to-normal visual acuity (20/20 or better) in both eyes and stereoacuity ≤40 seconds of arc. They all wore contact lenses habitually for myopia (refractive error ranged from −1.00 to −7.50 diopters [D]). All participants underwent a complete orthoptic assessment by a certified orthoptist, which included visual acuity (Snellen chart at 6 feet), prism cover test of eye alignment, measurement of refractive errors, and stereoacuity 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.

We also tested 12 patients with anisometropic amblyopia (10 females, age 24 ± 7.5 years; see Table 1 for clinical characteristics). The patient data have been reported previously as part of a larger study that included patients with mild and severe acuity deficits.[18,20,21] Anisometropic amblyopia was defined as an interocular acuity difference ≥2 lines in the presence of a difference in refractive error between the two eyes of ≥1 D of spherical or cylindrical power. All patients studied had mild amblyopia, with a mean visual acuity of 20/50 (range 20/30–20/60) in the amblyopic eye, and 20/20 or better in the fellow eye. Six patients were orthophoric and 6 had monofixation syndrome, which is defined as a microtropia ≤8 prism diopters (PD, as a result of a foveal scotoma arising from anisometropia; it was not the cause of the amblyopia), inability to bifixate, and presence of fusional vergence. All patients had residual stereopsis (50–3000 seconds of arc). 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

The visual target was a white square (visual angle 0.5°) presented on a black background on a CRT computer monitor (Diamond Pro 2070SB, resolution 1600 x 1200 at 85 Hz; NEC/Mitsubishi, Itasca, IL). Eye movements and reaching movements of the upper limb were recorded simultaneously at 200 Hz. Details of the apparatus were described previously.[18,20]

Experimental Conditions and Procedure

Using the same experimental protocol described previously,[18,20] participants were seated at a table fixating on a cross presented on a computer screen with their index finger at sagittal midline. After a variable delay of 1.5–3 seconds, the fixation cross was extinguished, and the target appeared randomly at four eccentricities at ±5° or ±10° along the horizontal axis. Participants were instructed to look at and point to the target as quickly and as accurately as possible using their right index finger. 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 target were randomized on a trial-by-trial basis.

Visually-normal participants performed the experiment in 3 separate sessions (normal viewing, immediately after blur was induced, and 5 hours after blur was induced). In the first session (i.e., no blur), participants wore their own contact lenses such that their visual acuity was 20/20 in both eyes. During this session, the orthoptist also determined the power of a contact lens that blurred the vision of the nondominant eye to 20/50 (blurring contact lens power ranged from 0.75–2.00 D). In the second session (i.e., immediate blur), participants wore the required contact lens to induce blur. After the second session, participants engaged in regular activities (e.g., reading, writing, walking) while wearing the blur contact lens for 5 hours, and then returned for the third session (i.e., 5-hour blur). In contrast to visually-normal participants, patients with amblyopia performed the experiment in a single session. Visual acuity and stereopsis were tested by a certified orthoptist before each session was conducted. Although we used a contact lens that blurred the vision of the nondominant eye to 20/50 as determined during the first visit, visual acuity of the nondominant eye varied from 20/30–20/80 during the second and third sessions in 6 participants. Nevertheless, the group mean acuity after blur was 20/50, which was comparable to the mean acuity of the amblyopic eye of patients.

For all participants (visually-normal and patients), each experimental session was performed during 3 viewing conditions: binocular viewing, monocular dominant (nonblurred) eye viewing (monocular fellow eye for patients), and monocular nondominant (blurred) eye viewing (monocular amblyopic eye for patients). 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. In total, 731–932 saccade trials and 816–924 reaching trials were analyzed for different experimental and viewing conditions.

Analysis

Saccadic Eye Movements. Eye position data were low-pass filtered using a second-order dual-pass Butterworth filter with a cut-off frequency of 50 Hz. Eye velocity was obtained using a two-point differentiation method. A custom-written script (MatLab; MathWorks, Natick, MA) was used to identify primary saccades using a velocity threshold of 20°/s. All trials were inspected visually to ensure that saccades were identified correctly by the computer script. Outcome measures were primary saccade latency, amplitude, and peak velocity. The means of each outcome measure were analyzed using separate repeated-measures ANOVAs with 4 within-subjects factors: blur condition (no blur, immediate blur, 5-hour blur), viewing condition (binocular, monocular dominant/nonblurred eye, and monocular nondominant/blurred eye), target location (±5°, ±10°), and visual feedback of target (on or off).

All trials were inspected for the presence of secondary saccades, which were marked manually for each trial. Secondary saccades that occurred within 250 ms of the primary saccades were defined as corrective saccades. The frequency of corrective saccades in each viewing condition was compared separately for visually-normal participants before, immediately after blur, and 5 hours after induced monocular blur using Pearson's χ^2 statistic. The latency, amplitude, and peak velocity of corrective saccades were analyzed using a repeated measures mixed ANOVA with blur condition and viewing condition as a within-subjects factors.

Preliminary analysis showed that visual feedback of the target had no significant effect on eye movement outcome measures. Therefore, the results for eye movements reported herein are pooled across the two visual feedback conditions (on and off).

Reaching Movements. Hand position data were filtered using a second-order dual-pass (bidirectional) Butterworth filter with a cut-off frequency of 7.5 Hz. Hand velocity was obtained using a 2-point differentiation method. Position data were differentiated twice to obtain acceleration. A custom-written MatLab script was used to identify the initiation of the hand movement, defined as the point at

Table 1. Characteristics of Patients with Anisometropic Amblyopia

			Snellen Visual Acuity (LogMAR)		Refractive Error		
ID	Age	Sex	Right	Left	Right	Left	Stereoacuity (arc sec)
1	36	F	20/15 (−0.10)	20/40 (0.30)	−1.50	1.50 + 1.00 ×15	200
2	28	F	20/50 (0.40)	20/15 (−0.10)	2.50 + 0.75 × 50	0.25	3000
3	35	F	20/15 (−0.10)	20/60 (0.48)	−4.25	−0.75	3000
4	25	F	20/40 (0.30)	20/15 (−0.10)	1.00 + 0.025 × 22	Plano	400
5	20	F	20/15 (−0.10)	20/50 (0.40)	Plano	1.50	120
6	19	F	20/20 (0.00)	20/40 (0.30)	−3.50 + 1.50 × 90	−3.50 + 2.50 × 102	200
7	33	M	20/15 (−0.10)	20/30 (0.18)	−0.75	2.00	140
8	14	F	20/50 (0.40)	20/15 (−0.10)	3.25 + 1.25 × 90	2.00	50
9	25	F	20/20 (0.00)	20/50 (0.40)	−1.50 + 1.50 × 80	−3.00 + 2.50 × 80	120
10	17	M	20/20 (0.00)	20/40 (0.30)	Plano + 0.25 × 94	−1.00 + 1.00 × 92	80
11	18	F	20/15 (−0.10)	20/40 (0.30)	Plano	+2.00 + 0.025 × 130	60
12	18	F	20/20 (0.00)	20/60 (0.48)	−1.50 + 0.50 × 80	1.00 + 1.25 × 95	200

which the velocity of the finger along the y-axis (i.e., elevation) exceeded 30 mm/s. The end of the reaching movement was identified when the finger reached the computer screen, and the velocity of the finger in the z-axis (depth) fell to and stayed below 30 mm/s. All trials were inspected visually to ensure that the reaching movement was identified correctly by the MatLab script.

The following outcome measures (including constant and variable error along azimuth and elevation) were calculated to examine reaching performance: reaction time (latency), movement time, peak acceleration, and duration of the acceleration phase (the interval from movement onset to peak velocity; i.e., the zero-crossing on the acceleration trajectory). All kinematic outcome measures were submitted to repeated-measures ANOVAs with 4 factors: blur condition, viewing condition, target location, and visual feedback of target.

Temporal Pattern of Eye-Hand Coordination. Temporal coordination between eye and hand movements was examined in two stages of the reaching movement: the planning stage (i.e., from target onset to reach initiation) and the execution stage (i.e., from reach onset to the end of the reach movement). The saccade-to-reach planning interval was calculated on a trial-by-trial basis by subtracting saccade reaction time (latency) and saccade duration from the reach reaction time (from this point this interval will be referred to as the saccade-to-reach planning interval).[21] Eye-hand coordination during the execution stage of the reaching response was assessed by calculating the time interval between the end of the saccade and the hand reaching peak velocity (PV; from this point referred to as the saccade-to-reach PV interval).[21] Eye-hand coordination during the execution stage of the reaching response also was assessed by examining the frequency of secondary saccades. As in our previous study,[21] secondary saccades that occurred during the reach and >250 ms after the primary saccades were defined as reach-related saccades. We reasoned that these saccades were reach-related and were not secondary "corrective" saccades after the primary saccades under- or overshot because secondary "corrective" saccades typically occur with a latency of 100–250 ms.[22–24] The latency (with respect to the initiation of the reaching response), amplitude, and peak velocity of the reach-related saccades were calculated.

All continuous dependent variables (saccade-to-reach planning interval, saccade-to-reach PV interval, latency, amplitude, and peak velocity of reach-related saccades) were submitted to repeated-measures ANOVAs with 4 factors: blur condition, viewing condition, target location, and visual feedback of target.

The effect of blur on the frequency of reach-related saccades was compared using Pearson's χ^2 statistic.

Comparison between Visually-Normal Participants with Induced Blur and Patients with Anisometropic Amblyopia. We previously compared saccades and reaching movements between patients with anisometropic amblyopia and visually-normal participants without blur using the same experimental paradigm.[18,20,21] In the current study, we also compared the performance of visually-normal participants after 5 hours of blur exposure to that of patients with mild anisometropic amblyopia. Data were submitted to mixed factor ANOVAs with one between-subject factor: group (patients and visually-normal participants 5 hours after blur) and 3 within-subject factors: viewing condition (binocular, fellow/dominant eye, amblyopic/blurred eye), target location, and visual feedback of target.

All statistical analyses were performed using the SAS 9.2 software package (SAS Institute, Cary, NC). The significance level was set at $P < 0.05$. All significant main effects and interactions were analyzed further using post-hoc pairwise comparison *t*-tests.

Table 2. Mean (± SD) Outcome Measures for Primary Saccades

	Visually-Normal Participants											
	No Blur			Immediate Blur			5-Hour Blur			Patients		
	BE	FE	AE	BE	FE	AE	BE	FE	AE	BE	FE	AE
Latency (ms)	171 ± 28	192 ± 31	188 ± 30	173 ± 29	183 ± 29	189 ± 31	177 ± 32	193 ± 34	192 ± 31	189 ± 52	185 ± 29	221 ± 67*
5° target												
Amplitude (°)	4.9 ± 0.3	4.8 ± 0.3	4.7 ± 0.3	4.8 ± 0.3	4.8 ± 0.2	4.9 ± 1.0	4.7 ± 0.3	4.9 ± 0.8	4.8 ± 0.4	4.9 ± 0.6	4.6 ± 0.4	4.8 ± 0.3
Velocity (°/s)	238 ± 39	237 ± 36	234 ± 30	239 ± 43	245 ± 35	236 ± 39	236 ± 42	239 ± 37	241 ± 33	253 ± 32	236 ± 32	244 ± 33
10° target												
Amplitude (°)	9.6 ± 0.7	9.4 ± 0.8	9.2 ± 0.6	9.3 ± 0.6	9.4 ± 0.6	8.9 ± 0.8	9.3 ± 0.5	9.1 ± 0.8	9.5 ± 0.9	9.6 ± 0.5	9.4 ± 0.5	9.5 ± 0.5
Velocity (°/s)	352 ± 59	349 ± 51	341 ± 52	349 ± 56	358 ± 60	330 ± 52	344 ± 63	342 ± 60	353 ± 53	363 ± 38	350 ± 51	362 ± 44

BE, binocular viewing; FE, dominant/fellow eye viewing; AE, nondominant/amblyopic eye viewing.
* $P < 0.0001$.

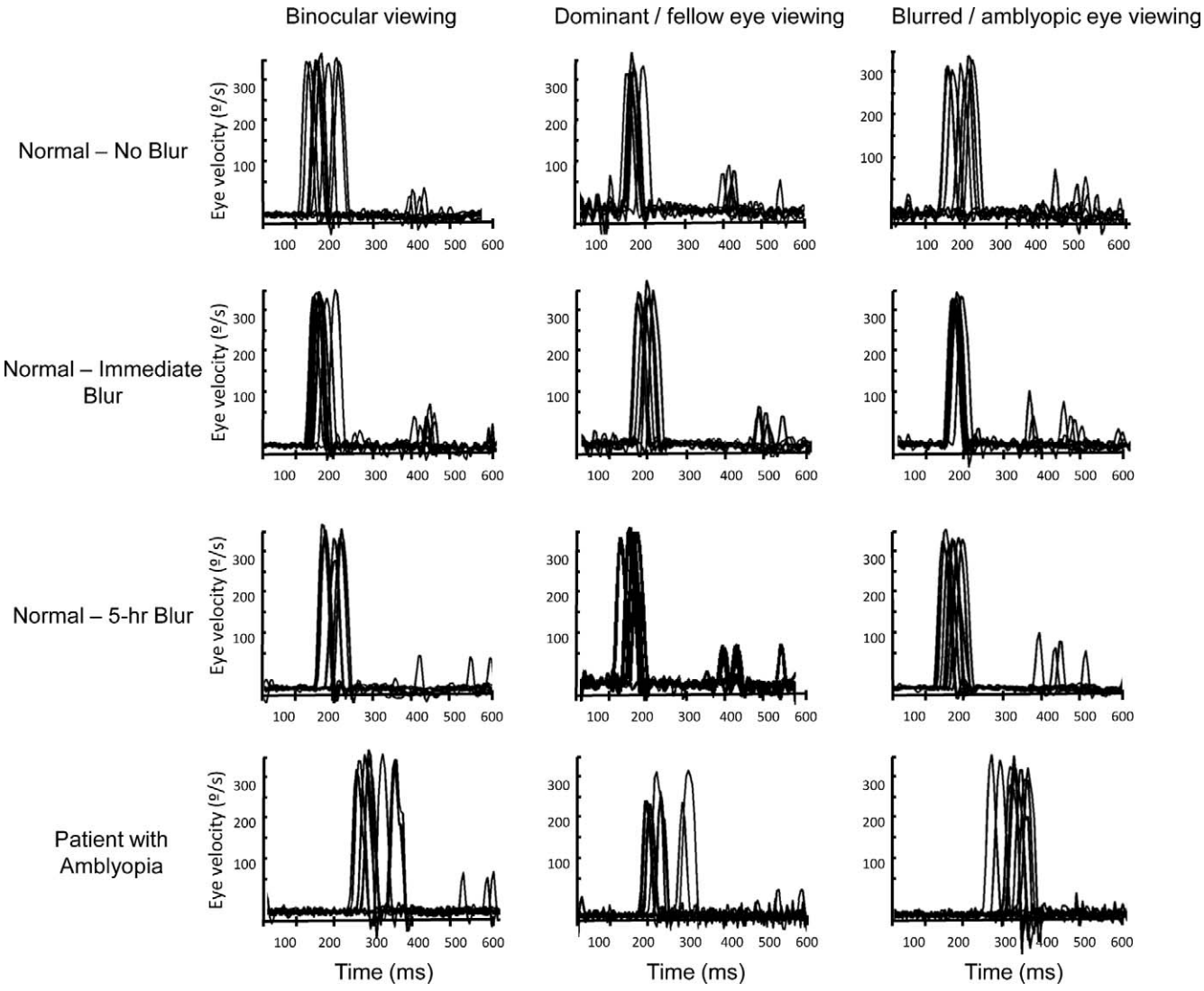

Figure 1. Representative eye velocity tracings from individual trials during binocular viewing (*left column*), monocular viewing with the dominant (nonblurred)/fellow eye (*middle column*), and monocular viewing with the nondominant (blurred)/amblyopic eye (*right column*) when the target was shown 10° to the right. *Top row*: Visually-normal participant — no blur. *Second row*: Visually-normal participant during the first blur session — immediate blur. *Third row*: Visually-normal participant during the second blur session — 5-hour blur. *Last row*: Patient with anisometropic amblyopia. Saccades executed by the visually-normal participant were not affected by induced blur. In contrast, the patient had longer and more variable saccade latencies.

Results

Primary Saccades (Table 2)

Figure 1 shows representative eye velocity tracings from a visually-normal participant and a patient with anisometropic amblyopia. Saccades executed by the visually-normal participant were not affected by induced blur. In contrast, saccades initiated by the patient had longer latency and were more variable.

Latency

For visually-normal participants, the effect of viewing condition was significant ($F_{[2,22]} = 24.22$, $P < 0.0001$); however, the effect of blur ($F_{[2,22]} = 0.86$, $P = 0.4371$) and the interaction did not reach significance ($F_{[4,44]} = 2.42$, $P = 0.0621$). Regardless of induced blur, mean saccade latency was shorter during binocular viewing (i.e., binocular advantage). No other significant main effects or interactions were observed for mean saccade latency.

The comparison between patients and visually-normal participants in the 5-hour blur condition showed a significant interaction between group and viewing condition ($F_{[2,44]} = 5.36$, $P = 0.008$). Post-hoc tests indicated that patients had longer saccade latency when viewing with the amblyopic eye (221 ± 67 ms) in comparison to binocular viewing (189 ± 52 ms), fellow eye viewing (185 ± 29 ms), and visually-normal participants in all viewing conditions (binocular 177 ± 32 ms, dominant eye 193 ± 34 ms, blurred eye 192 ± 31 ms).

Amplitude and Peak Velocity

There was a significant main effect of target location for saccade amplitude ($F_{[3,33]} = 1457.65$, $P < 0.0001$) and peak velocity ($F_{[3,33]} = 363.86$, $P < 0.0001$). Saccades to the 10^0 target had higher amplitude and peak velocity than those to the 5^0 target in all experimental conditions for visually-normal

participants and patients. No other significant main effects or interactions were present for primary mean saccade amplitude or peak velocity.

Secondary Corrective Saccades

The frequency of secondary saccades was comparable among viewing conditions ($\chi^2_{[df=2]} = 0.36$, $P = 0.834$) when visually-normal participants viewed with normal acuity (binocular 4.8%, dominant eye 4.6%, nondominant eye 4.6%). Immediately after blur, visually-normal participants initiated fewer secondary saccades when viewing with the blurred eye (3.4%), compared to viewing binocularly (5.3%) or with the dominant eye (4.0%; $\chi^2_{[df=2]} = 12.55$, $P = 0.002$). The frequency of secondary saccades remained reduced 5 hours after blur when visually-normal participants viewed with the blurred eye (2.5%), compared to binocular (3.8%) and dominant eye (3.4%) viewing ($\chi^2_{[df=2]} = 6.02$, $P = 0.049$).

A similar pattern also was observed in patients. Patients initiated fewer secondary saccades when viewing with the amblyopic eye (5.3%), compared to binocular (6.2%) and fellow eye viewing (8.3%; $\chi^2_{[df=2]} = 16.64$, $P = 0.0002$).

There were no significant effects for latency, amplitude, or peak velocity of secondary saccades for visually-normal participants or patients.

Reaching Movement Kinematics (Table 3)

Accuracy and Precision. For visually-normal participants, there were no significant differences in accuracy or precision along the azimuth or elevation before or after blur. The interaction between blur and viewing condition also was not significant. The comparison between patients and visually-normal participants in the 5-hour blur condition also showed no significant difference in accuracy and precision.

Reaction Time and Movement Time. There were no statistically significant differences for reach reaction time or movement time due to blur. Patients exhibited a trend toward longer movement time (703 ± 128 ms) compared to visually-normal participants in the 5-hour blur condition (621 ± 121 ms); however, the difference did not reach significance ($F_{[1,22]} = 3.30$, $P = 0.083$).

Acceleration Phase. Figure 2 shows representative reach acceleration tracings from a visually-normal participant and a patient with amblyopia. Reaching kinematics were not affected by induced blur in the visually-normal participant. In contrast, the patient had reduced peak acceleration and a longer acceleration phase.

As a group, there were no statistically significant differences for peak acceleration or duration of acceleration phase due to blur for visually-normal participants. Patients had lower peak acceleration (6.62 ± 2.1 m/s^2) compared to visually-normal participants in the 5-hour blur condition (8.37 ± 2.9 m/s^2); however, the effect did not reach statistical significance ($F_{[1,22]} = 3.30$, $P = 0.083$). There was a significant difference for the duration of acceleration phase between patients and visually-normal participants in the 5-hour blur condition ($F_{[1,22]} = 4.74$, $P = 0.041$). Patients had a longer acceleration phase regardless of viewing condition (binocular 234 ± 43 ms, fellow eye 262 ± 62 ms, amblyopic eye 260 ± 61 ms) compared to visually-normal participants with induced blur (binocular 202 ± 68 ms, dominant eye 201 ± 72 ms, blurred eye 204 ± 61 ms).

Eye-Hand Coordination

Saccade-to-Reach Planning Interval. For visually-normal participants, there were no significant differences for saccade-to-reach planning interval due to blur.

Table 3. Mean (± SD) Outcome Measure for the Reaching Movement

	Visually-Normal Participants									Patients		
	No Blur			Immediate Blur			5-Hour Blur					
	BE	FE	AE	BE	FE	AE	BE	FE	AE	BE	FE	AE
Accuracy												
Azimuth (mm)	0.91 ± 3.1	0.63 ± 2.7	0.66 ± 2.3	0.72 ± 2.4	0.80 ± 2.5	1.39 ± 2.6	0.53 ± 2.4	0.18 ± 2.0	0.75 ± 2.5	0.36 ± 1.8	0.09 ± 2.08	0.07 ± 2.3
Elevation (mm)	2.08 ± 3.0	0.94 ± 2.8	−0.35 ± 2.7	2.45 ± 4.0	1.80 ± 3.4	1.19 ± 3.7	3.09 ± 4.3	2.30 ± 3.9	2.02 ± 4.7	−0.74 ± 4.4	−1.61 ± 4.7	−1.86 ± 5.1
Precision												
Azimuth (mm)	1.20 ± 0.5	1.31 ± 0.4	1.31 ± 0.6	1.14 ± 0.3	1.43 ± 0.4	1.34 ± 0.4	1.30 ± 0.4	1.33 ± 0.4	1.45 ± 0.5	1.12 ± 0.4	1.19 ± 0.4	1.36 ± 0.4
Elevation (mm)	1.38 ± 0.3	1.39 ± 0.4	1.40 ± 0.4	1.41 ± 0.3	1.48 ± 0.4	1.51 ± 0.4	1.42 ± 0.5	1.39 ± 0.4	1.55 ± 0.6	1.16 ± 0.4	1.20 ± 0.4	1.36 ± 0.5
Kinematics												
Reaction time (ms)	343 ± 87	351 ± 75	362 ± 85	340 ± 60	355 ± 69	357 ± 76	340 ± 68	355 ± 68	365 ± 73	357 ± 76	375 ± 90	359 ± 65
Movement time (ms)	578 ± 70	610 ± 91	622 ± 78	609 ± 102	632 ± 115	627 ± 121	609 ± 113	628 ± 119	623 ± 124	673 ± 88	724 ± 149	710 ± 113
Peak accel (mm/s^2)	9.55 ± 2.5	8.64 ± 2.4	8.47 ± 2.1	8.82 ± 3.9	8.04 ± 3.2	8.72 ± 3.8	8.55 ± 3.1	8.28 ± 2.9	8.30 ± 2.3	6.93 ± 2.1	6.36 ± 2.1	6.59 ± 2.0
Duration of acceleration phase (ms)	172 ± 48	198 ± 58	201 ± 58	200 ± 71	217 ± 79	197 ± 68	202 ± 68	201 ± 65	204 ± 61	234 ± 43*	262 ± 62*	260 ± 61
Saccade-reach plan interval (ms)	134 ± 86	117 ± 74	137 ± 77	128 ± 61	132 ± 68	126 ± 77	122 ± 76	123 ± 72	134 ± 82	128 ± 80	151 ± 84	104 ± 86
Saccade-to-reach PV interval (ms)	305 ± 92	315 ± 93	337 ± 97	328 ± 78	349 ± 91	322 ± 79	322 ± 91	325 ± 84	336 ± 92	361 ± 101	412 ± 127*	366 ± 128

* $P < 0.05$.

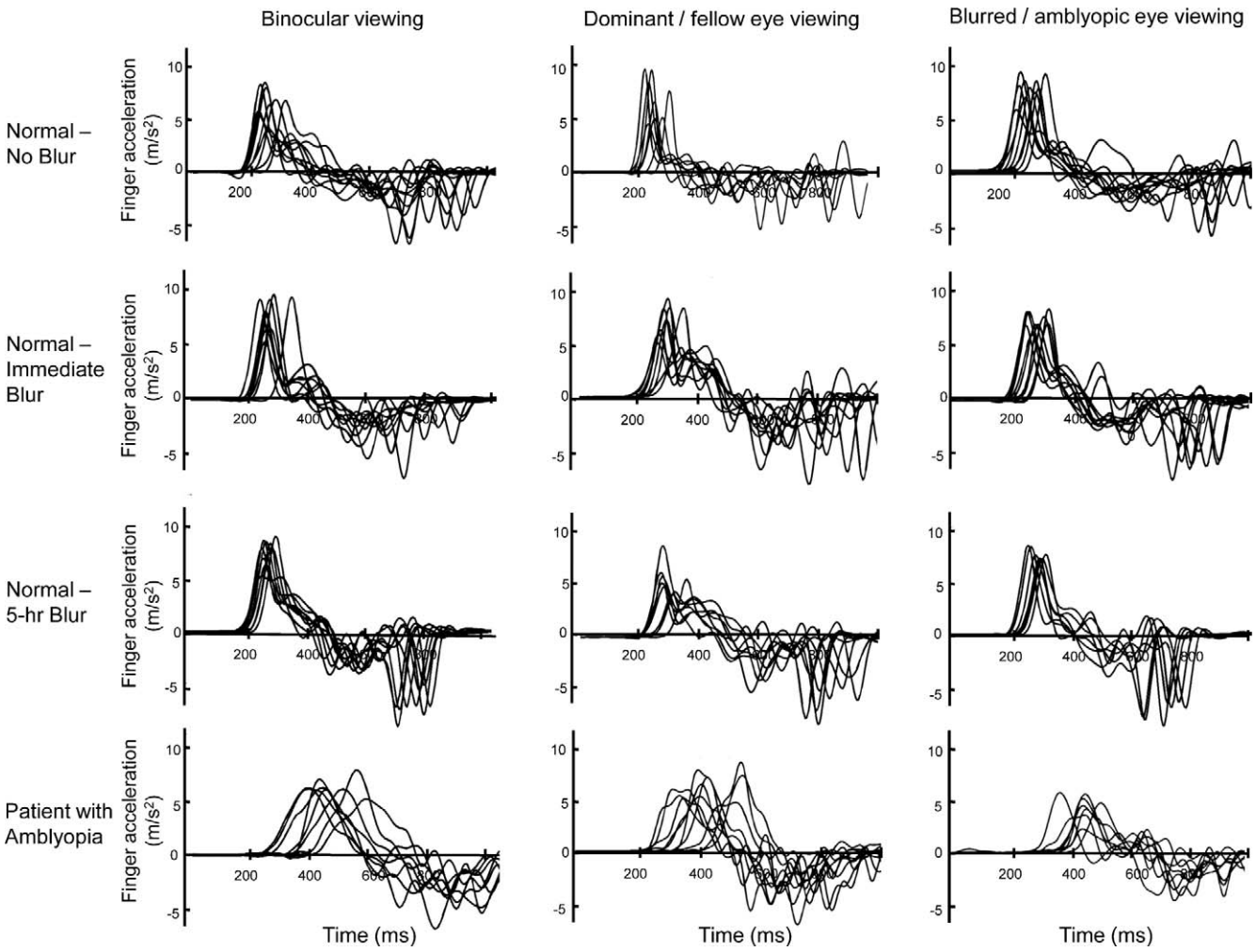

Figure 2. Reach acceleration trajectory during binocular viewing (*left column*), monocular viewing with the dominant (nonblurred)/fellow eye (*middle column*), and monocular viewing with the nondominant blurred/amblyopic eye (*right column*) when the target was shown 10° to the right. *Top row*: Visually-normal participant — no blur. *Second row*: Immediate blur. *Third row*: 5-hour blur. *Last row*: Patient with anisometropic amblyopia. Reaching kinematics were not affected by induced blur. In contrast, patient had reduced peak acceleration and a longer duration of acceleration phase when reaching.

The comparison between patients and visually-normal participants with induced 5-hour blur showed a significant interaction between group and viewing condition ($F_{[2,44]} = 5.96$, $P = 0.005$). Post-hoc tests indicated that saccade-to-reach planning interval was comparable among viewing conditions for visually-normal participants with induced blur (binocular 122 ± 76 ms, dominant eye 123 ± 72 ms, blurred eye 134 ± 82 ms). For patients, saccade-to-reach planning interval was shorter during amblyopic eye viewing (104 ± 86 ms), compared to fellow eye (151 ± 84 ms) and binocular viewing (128 ± 80 ms).

Saccade-to-Reach PV Interval. For visually-normal participants, there was no significant difference for the saccade-to-reach PV interval due to blur.

The comparison between patients and visually-normal participants with induced 5-hour blur showed a significant interaction between group and viewing condition ($F_{[2,44]} = 3.51$, $P = 0.038$). Post-hoc tests indicated that patients took longer to reach peak velocity after the primary saccade was completed when viewing with the fellow eye (412 ± 127 ms), compared to binocular (361 ± 101 ms) and amblyopic eye (366 ± 128 ms) viewing, and to visually-normal participants in all viewing conditions (binocular 322 ± 91 ms, dominant eye 325 ± 84 ms, blurred eye 336 ± 92 ms).

Frequency of Reach-Related Saccades

The frequency of reach-related saccades increased significantly in the induced blur conditions ($\chi^2_{[df=2]} = 11.43$, $P = 0.003$). When viewing with normal acuity, the overall frequency of reach-related secondary saccades was 21.2% (binocular 19.1%, dominant eye 20.2%, nondominant eye 24.4%). It increased to 24.7% immediately after blur (binocular 24.8%, dominant eye 24.3%, blurred eye 24.4%) and remained at 24.5% 5 hours after blur (binocular 25.1%, dominant eye 26.2%, blurred eye 22.6%).

The frequency of reach-related saccades was not significantly different between visually-normal participants with induced blur and patients ($\chi^2_{[df=1]} = 2.74$, $P = 0.098$). For patients, the frequency of reach-related saccades was 28.2% during binocular viewing, 27.7% during fellow eye viewing, and 24.2% during amblyopic eye viewing.

There were no significant effects for latency, amplitude, or peak velocity of reach-related secondary saccades.

Discussion

Our study examined the effects of induced monocular blur on saccades, reaching movements, and eye-hand coordination in visually-normal participants, and compared their performance to that of patients with anisometropic amblyopia. We found that saccades and reaching performance were not affected by induced monocular blur in visually-normal participants, which was in striking contrast to the performance of patients with anisometropic amblyopia who had a comparable level of acuity loss in the amblyopic eye.

Effect of Induced Blur on Eye Movements

We demonstrated previously that patients with anisometropic amblyopia exhibited a significant increase in saccade latency during amblyopic eye viewing and a lack of binocular advantage (i.e., saccade latency during binocular viewing was not reduced as compared to monocular viewing). An unanswered question was whether the impaired performance in these patients simply was due to a loss of visual acuity. In the current study, we demonstrated that saccades in visually-normal participants were unaffected by induced blur, and binocular advantage was reduced only slightly but still evident, even after 5 hours of blur exposure. Therefore, decreased monocular visual acuity alone cannot explain the deficits in saccadic performance in patients with mild anisometropic amblyopia.

We proposed previously that the longer saccade latency during amblyopic eye viewing represents a slower visual processing in the afferent (sensory) pathway, rather than a deficit in the efferent (motor) pathway of the saccadic system.[18] One factor contributing to the delay in response initiation might be a chronic suppression of the input presented to the amblyopic eye.[25] It is possible that because of suppression, it takes longer for the sensory signals to reach threshold, resulting in longer saccade latency during amblyopic eye viewing. Since visually-normal individuals do not experience interocular suppression, their saccade latency is not affected while wearing a blurring lens.

Inducing monocular blur in visually-normal participants did not affect the execution of primary saccades; however, the frequency of secondary saccades was affected by induced blur. We examined 2 types of secondary saccades based on their latencies: corrective saccades that followed the primary saccade within 250 ms,[24] and reach-related saccades that were initiated after the reaching movement had started. We found that the frequency of corrective saccades was slightly but significantly reduced in both blur sessions when participants viewed with the blurred eye. These findings are similar to the behavior of patients with amblyopia who also initiated fewer corrective saccades during amblyopic eye viewing.[18]

Two sources of error feedback have been proposed for the generation of secondary saccades that follow the primary saccade.[24,26,27] One is based on extraretinal information derived from the efference copy of the oculomotor command, suggesting that the secondary saccade might be programmed before the end of the primary saccade.[28] Another is based on retinal feedback derived from the position of the target image on the retina at the end of the primary saccade.[29] The relative contribution of extraretinal and retinal mechanisms to the generation of secondary saccades depends on the availability of visual feedback[27,29] and target eccentricity.[24,28] Specifically, the frequency of secondary saccades increases when visual feedback is available at the end of the primary saccade, whereas extraretinal contribution becomes important when the target is located farther in the periphery (>15°). Our findings show that visually-normal participants exposed to a relatively low level of blur initiated significantly fewer secondary corrective saccades. Since we used targets located within 10° from the fovea, our finding that fewer secondary saccades were initiated when participants viewed with the blurred eye provided further support that retinal feedback has a bigger role than extraretinal feedback in the generation of secondary saccades.

In addition to corrective saccades, we found that the frequency of reach-related secondary saccades also was affected by induced blur. Visually-normal participants initiated reach-related secondary saccades slightly more frequently in both blur sessions, similar to patients with amblyopia who also showed increased number of reach-related secondary saccades.[21] One possible explanation is that when visually-normal participants experienced monocular blur, the reaching movements were planned and initiated based on a less reliable visual input. Subsequently, reach-related secondary saccades were executed with greater frequency during the reaching movement, presumably in an attempt to extract more information to improve the accuracy and precision of the reach.

Effect of Induced Blur on Reaching

Several previous studies have investigated the effect of induced blur in visually normal participants using variety of perceptual and motor tasks.[30–45] These studies showed that the effect of blur was highly dependent on the complexity of the task, with decreasing performance as complexity of the task increased. To our knowledge, only two previous studies have examined the effect of induced blurred vision in visually-normal participants on reaching and grasping movements specifically. In the first study, a convex lens of +2.00 to +3.75 D was used to reduce the stereoacuity of individual subjects to 400–800 arc sec (with visual acuity ranging from 0.72–0.96 logMAR).[35] After blur, reaching errors were significantly greater when compared to the normal acuity condition, with participants undershooting the target in depth by approximately 3 mm and overshooting the target along the azimuth by approximately 2.5 mm during blur. In a second study, the effect of low (+2.00 to +3.00 D) and high (+3.50 to +5.00 D) power convex lenses on prehension skills was examined.[36] It was found that when vision was blurred, participants exhibited longer grip application times and made more errors during the grasping phase. These results were similar to the grasping deficits exhibited by patients with amblyopia tested using the same paradigm.[17]

Our study differed significantly from previous studies[35,36] in the degree of induced blur and the level of stereoacuity. Previous studies used higher power convex lenses to induce blur, which effectively reduced stereoacuity.[35,36] In contrast, we used a lower level of blur (range 0.75–2.00 D) such that stereoacuity remained normal (at 40 arc sec) in 8 participants and was reduced only slightly in the remaining 4 participants (50–80 arc sec). We found that induced blur did not affect the accuracy, precision, or reaching kinematics in visually-normal participants whether they viewed binocularly or monocularly with either their blurred or nonblurred eye. These results are in contrast to the performance of patients with anisometropic amblyopia who had lower peak acceleration and an extended duration of acceleration phase when performing the same task during binocular or monocular amblyopic and fellow eye viewing.[20] We suggested previously that the lower peak acceleration and prolonged acceleration phase may represent a strategy or adaptation of feedforward and feedback control in amblyopia to optimize reaching performance in face of the degraded visual input.

The findings that reaching performance was not affected during dominant eye viewing in visually-normal participants after blur, whereas it was impaired during fellow eye viewing

in patients with amblyopia, also provide further support that fellow eye involvement is unique to amblyopia.[14,15,46,47] Specifically, the acuity of the fellow eye was 20/20 or better in all our patients, so the expectation might be that the reaching movements would be comparable to those made by visually-normal participants. However, this was not the case—patients showed the same reach control strategy while viewing with the fellow eye as when viewing with the amblyopic eye. One possible explanation is that due to the developmental nature of amblyopia, patients' internal model for motor control[48,49] did not develop optimally due to early anomalous visual experience. Another possibility is that temporal integration of visual and proprioceptive signals about limb position/velocity or the relative weighting given to these two signals may differ because of deficits in visual acuity and stereopsis.

Although visual acuity during the induced blur session was comparable between visually-normal participants and our patients, all patients had abnormal stereoacuity whereas it was normal in our visually-normal participants, suggesting that stereoacuity has a crucial role in reaching movements. Previous studies that examined motor skills using clinical tests also demonstrated a relation between poor stereoacuity and poor motor performance.[50,51] Taken together, these results indicate that intact stereopsis is an important visual cue for programming and execution of reaching and grasping movements.

Effect of Blur Adaptation

Several studies have examined the effect of blur adaptation on visual acuity, contrast sensitivity, and blur sensitivity.[52–56] For example, Mon-Williams et al. tested emmetropes on a letter recognition task following 30 minutes of adaptation to binocular blur induced with +1.00 D lenses.[53] All participants exhibited slightly better acuity after 30 minutes of adaptation (mean improvement 0.089 logMAR). In another session, the same participants were tested on a contrast sensitivity task after adapting to optical defocus induced with +2.00 D lenses. Following adaptation, participants exhibited reduced sensitivity to middle spatial frequencies (range 5–25 cpd) while visual acuity improved slightly. Since changes in acuity and contrast sensitivity were not associated with any changes in the refractive status, Mon-Williams et al. suggested that blur adaptation resulted from neural rather than optical compensation.[53] In another study, Rosenfield et al. investigated whether people with myopia exhibit similar adaptation to blur.[54] They tested 22 participants with refractive errors ranging from −1.00 to −3.50 D on a letter acuity task immediately after removing their corrective lenses and 3 hours after exposure to blur. The mean improvement in visual acuity after blur exposure was 0.23 logMAR, which was not accompanied by any significant changes in refractive error.

Similar to the study by Rosenfield et al.,[54] our participants also were myopic, and blur was induced by using a contact lens that "undercorrected" the myopic deficit and produced a retinal defocus ranging from −0.75 to −2.00 D. However, unlike Rosenfield et al.,[54] we did not find any significant blur adaptation—most of our participants showed no difference in visual acuity immediately and 5 hours after blur. Only 4 participants had reduced (rather than improved) acuity after 5 hours of blur exposure; however, the difference never exceeded 2 Snellen lines (i.e., 0.2 logMAR), which is within the limits of test-retest variability.[57] The discrepancy of findings might be related to the experimental design—while we induced monocular blur in the current study, other studies examined the effect of binocular blur or of monocular blur when one eye was patched.

In conclusion, induced monocular blur had no effect on the programming or execution of primary saccades or reaching movements in visually-normal participants, either immediately after blur was induced or after 5 hours of exposure to blur. Our results suggest that the motor performance deficits seen in patients with mild anisometropic amblyopia are not simply due to a loss of visual acuity alone. Amblyopia is a developmental brain disorder resulting from the imbalance of binocular inputs to visual areas and suppression of the amblyopic eye, which leads to impairments in visual acuity, contrast sensitivity, and binocularity. Since visual information provides important sensory input for the planning and execution of eye and hand movements, early anomalous visual experience most likely disturbs the normal development of visuomotor behavior. Therefore, the visuomotor deficits and subsequent adaptations of motor behavior seen in patients with amblyopia arise from the developmental nature of the disorder and are not seen in visually-normal adults exposed to brief periods of blurred vision.

References

1. American Academy of Ophthalmology. Preferred practice pattern guidelines. Amblyopia PPP – September 2007. Available online at: http://one.aao.org/CE/PracticeGuidelines/PPP_Content.aspx?cid=930d01f2-740b-433e-a973-cf68565bd27b. Accessed September 2007.
2. Membreno JH, Brown MM, Brown GC, Sharma S, Beauchamp GR. A cost-utility analysis of therapy for amblyopia. *Ophthalmology*. 2002;109:2265–2271.
3. van de Graaf ES, van der Sterre GW, Polling JR, van Kempen H, Simonsz B, Simonsz HJ. Amblyopia & strabismus questionnaire: design and initial validation. *Strabismus*. 2004;12:181–193.
4. Hensch TK. Critical period plasticity in local cortical circuits. *Nat Rev Neurosci*. 2005;6:877–888.
5. Hess RF, Wang YZ, Demanins R, Wilkinson F, Wilson HR. A deficit in strabismic amblyopia for global shape detection. *Vision Res*. 1999;39:901–914.
6. Sireteanu R, Bäumer CC, Sarbu C, Iftime A. Spatial and temporal misperceptions in amblyopic vision. *Strabismus*. 2007;15:45–54.
7. Barrett BT, Pacey IE, Bradley A, Thibos LN, Morrill P. Nonveridical visual perception in human amblyopia. *Invest Ophthalmol Vis Sci*. 2003;44:1555–1567.
8. Bonneh YS, Sagi D, Polat U. Spatial and temporal crowding in amblyopia. *Vision Res*. 2007;47:1950–1962.
9. Holopigian K, Blake R, Greenwald MJ. Selective losses in binocular vision in anisometropic amblyopes. *Vision Res*. 1986;26:621–630.
10. Simmers AJ, Ledgeway T, Hess RF, McGraw PV. Deficits to global motion processing in human amblyopia. *Vision Res*. 2003;43:729–738.
11. Simmers AJ, Ledgeway T, Mansouri B, Hutchinson CV, Hess RF. The extent of the dorsal extra-striate deficit in amblyopia. *Vision Res*. 2006;46:2571–2580.
12. Ho CS, Giaschi DE, Boden C, Dougherty R, Cline R, Lyons C. Deficient motion perception in the fellow eye of amblyopic children. *Vision Res*. 2005;45:1615–1627.
13. McKee SP, Levi DM, Movshon JA. The pattern of visual deficits in amblyopia. *J Vis*. 2003;3:380–405.
14. Woo GC, Irving EL. The non-amblyopic eye of a unilateral amblyope: a unique entity. *Clin Exp Optometry*. 1991;74:1–5.
15. Mirabella G, Hay S, Wong AM. Deficits in perception of real-world scenes in patients with a history of amblyopia. *Arch Ophthalmol*. 2011;129:176–183.

16. Grant S, Moseley MJ. Amblyopia and real-world visuomotor tasks. *Strabismus*. 2011;19:119–128.
17. Grant S, Melmoth DR, Morgan MJ, Finlay AL. Prehension deficits in amblyopia. *Invest Ophthalmol Vis Sci*. 2007;48: 1139–1148.
18. Niechwiej-Szwedo E, Goltz HC, Chandrakumar M, Hirji ZA, Wong AM. Effects of anisometropic amblyopia on visuomotor behavior, I: saccadic eye movements. *Invest Ophthalmol Vis Sci*. 2010;51:6348–6354.
19. Niechwiej-Szwedo E, Goltz HC, Chandrakumar M, Wong AM. The effect of sensory uncertainty due to amblyopia (lazy eye) on the planning and execution of visually-guided 3d reaching movements. *PLoS ONE*. 2012;7:e31075.
20. Niechwiej-Szwedo E, Goltz H, Chandrakumar M, Hirji ZA, Crawford JD, Wong AM. effects of anisometropic amblyopia on visuomotor behavior, part 2: visually-guided reaching. *Invest Ophthalmol Vis Sci*. 2011;52:795–803.
21. Niechwiej-Szwedo E, Goltz HC, Chandrakumar M, Hirji Z, Wong AM. Effects of anisometropic amblyopia on visuomotor behavior, III: temporal eye-hand coordination during reaching. *Invest Ophthalmol Vis Sci*. 2011;52:5853–5861.
22. Troost BT, Weber RB, Daroff RB. Hypometric saccades. *Am J Ophthalmol*. 1974;78:1002–1005.
23. Robinson DA. The mechanics of human saccadic eye movement. *J Physiol*. 1964;174:245–264.
24. Prablanc C, Massé D, Echallier JF. Error-correcting mechanisms in large saccades. *Vision Res*. 1978;18:557–560.
25. Li J, Thompson B, Lam CS, et al. The role of suppression in amblyopia. *Invest Ophthalmol Vis Sci*. 2011;52:4169–4176.
26. Weber RB, Daroff RB. Corrective movements following refixation saccades: type and control system analysis. *Vision Res*. 1972;12:467–475.
27. Prablanc C, Jeannerod M. Corrective saccades: dependence on retinal reafferent signals. *Vision Res*. 1975;15:465–469.
28. Becker W, Fuchs AF. Further properties of the human saccadic system: eye movements and correction saccades with and without visual fixation points. *Vision Res*. 1969;9: 1247–1258.
29. Deubel H, Wolf W, Hauske G. Corrective saccades: effect of shifting the saccade goal. *Vision Res*. 1982;22:353–364.
30. Wurm LH, Legge GE, Isenberg LM, Luebker A. Color improves object recognition in normal and low vision. *J Exp Psychol Hum Percept Perform*. 1993;19:899–911.
31. Vale A, Scally A, Buckley JG, Elliott DB. The effects of monocular refractive blur on gait parameters when negotiating a raised surface. *Ophthalmic Physiol Opt*. 2008;28:135–142.
32. Vale A, Buckley JG, Elliott DB. Gait alterations negotiating a raised surface induced by monocular blur. *Optom Vis Sci*. 2008;85:1128–1134.
33. Post RB, Leibowitz HW. The effect of refractive error on central and peripheral motion sensitivity at various exposure durations. *Percept Psychophys*. 1981;29:91–94.
34. Norman JF, Beers AM, Holmin JS, Boswell AM. Effective 3-D shape discrimination survives retinal blur. *Atten Percept Psychophys*. 2010;72:1569–1575.
35. Melmoth DR, Storoni M, Todd G, Finlay AL, Grant S. Dissociation between vergence and binocular disparity cues in the control of prehension. *Exp Brain Res*. 2007;183:283–298.
36. Melmoth DR, Finlay AL, Morgan MJ, Grant S. Grasping deficits and adaptations in adults with stereo vision losses. *Invest Ophthalmol Vis Sci*. 2009;50:3711–3720.
37. Mann DL, Ho NY, De Souza NJ, Watson DR, Taylor SJ. Is optimal vision required for the successful execution of an interceptive task? *Hum Mov Sci*. 2007;26:343–356.
38. Higgins KE, Wood J, Tait A. Vision and driving: selective effect of optical blur on different driving tasks. *Human Factors*. 1998;40:224–232.
39. Bulson RC, Ciuffreda KJ, Hung GK. The effect of retinal defocus on golf putting. *Ophthalmic Physiol Opt*. 2008;28: 334–344.
40. Buckley JG, Heasley KJ, Twigg P, Elliott DB. The effects of blurred vision on the mechanics of landing during stepping down by the elderly. *Gait Posture*. 2005;21:65–71.
41. Brooks JO, Tyrrell RA, Frank TA. The effects of severe visual challenges on steering performance in visually healthy young drivers. *Optom Vis Sci*. 2005;82:689–697.
42. Bravo MJ, Farid H. Object recognition in dense clutter. *Percept Psychophys*. 2006;68:911–918.
43. Ball K, Sekuler R. Improving visual perception in older observers. *J Gerontol*. 1986;41:176–182.
44. Applegate RA. Set shot shooting performance and visual acuity in basketball. *Optom Vis Sci*. 1992;69:765–768.
45. Anand V, Buckley J, Scally A, Elliott DB. The effect of refractive blur on postural stability. *Ophthalmic Physiol Opt*. 2002;22: 528–534.
46. Ho CS, Giaschi DE. Stereopsis-dependent deficits in maximum motion displacement in strabismic and anisometropic amblyopia. *Vision Res*. 2007;47:2778–2785.
47. Giaschi DE, Regan D, Kraft SP, Hong XH. Defective processing of motion-defined form in the fellow eye of patients with unilateral amblyopia. *Invest Ophthalmol Vis Sci*. 1992;33: 2483–2489.
48. Wolpert DM, Ghahramani Z. Computational principles of movement neuroscience. *Nat Neurosci (suppl)*. 2000;3:1212–1217.
49. Desmurget M, Grafton S. Forward modeling allows feedback control for fast reaching movements. *Trends Cogn Sci*. 2000;4: 423–431.
50. Webber AL, Wood JM, Gole GA, Brown B. The effect of amblyopia on fine motor skills in children. *Invest Ophthalmol Vis Sci*. 2008;49:594–603.
51. O'Connor AR, Birch EE, Anderson S, Draper H. The functional significance of stereopsis. *Invest Ophthalmol Vis Sci*. 2009;51: 2019–2023.
52. Pesudovs K, Brennan NA. Decreased uncorrected vision after a period of distance fixation with spectacle wear. *Optom Vis Sci*. 1993;70:528–531.
53. Mon-Williams M, Tresilian JR, Strang NC, Kochhar P, Wann JP. Improving vision: neural compensation for optical defocus. *Proc Biol Sci*. 1998;265:71–77.
54. Rosenfield M, Hong SE, George S. Blur adaptation in myopes. *Optom Vis Sci*. 2004;81:657–662.
55. Rosenfield M, Abraham-Cohen JA. Blur sensitivity in myopes. *Optom Vis Sci*. 1999;76:303–307.
56. George S, Rosenfield M. Blur adaptation and myopia. *Optom Vis Sci*. 2004;81:543–547.
57. Bailey IL, Bullimore MA, Raasch TW, Taylor HR. Clinical grading and the effects of scaling. *Invest Ophthalmol Vis Sci*. 1991;32:422–432.