Saccadic Adaptation in Visually Normal Individuals Using Saccadic Endpoint Variability From Amblyopia

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Purpose. Saccadic adaptation is affected by the spatial variability of the adapting error signal. Recently, we have shown that saccadic adaptation is reduced in anisometropic amblyopia, possibly impacted by spatially imprecise saccades. Here, we tested this idea by quantifying the saccadic endpoint variability difference between people with anisometropic amblyopia and visually normal individuals. We then applied this difference to the second target step distribution during saccadic adaptation in visually normal people to test whether their performance diminished to a similar extent as participants with amblyopia.

Methods. Ten visually normal adults performed a double-step adaptation task (±19°, followed by 4° back-steps) with the nondominant eye under two conditions: "consistent error," using a constant back-step; and "variable error," using a variable (σ_{diff}) back-step determined by subtracting the saccadic endpoint variability in controls from that in anisometropic amblyopia during amblyopic/nondominant eye viewing. Percentage change in saccadic gains, percentage retention, and adaptation time constants were analyzed.

Results. Percentage change in saccadic gains decreased significantly during the variable error condition (50% ± 10%) compared to the consistent error condition (69% ± 9%; $P = 0.0008$). Percentage retention and time constants did not differ between conditions. The adaptation magnitude during the variable error condition was comparable to the previous percentage adaptation in people with anisometropic amblyopia during the consistent error condition with amblyopic eye viewing.

Conclusions. Our findings indicate that adding exogenous spatial noise to the adapting step consistent with the saccadic endpoint variability difference between amblyopic and visually normal groups is sufficient to reduce saccadic adaptation in healthy individuals.

Keywords: saccadic adaptation, visual error signal, amblyopia, spatial variability

Variability is an inherent feature of all biological systems, including the oculomotor system. Saccadic eye movements, which move the eyes to place the image of a target accurately on the fovea, display characteristic variability in their endpoints.[1] In visually healthy individuals, saccadic performance is monitored by sensorimotor adaptive mechanisms that minimize systematic postsaccadic errors, thereby maintaining saccadic accuracy.[2] In a laboratory setting, artificial postsaccadic errors can be introduced by the use of a double-step target paradigm, where the intended target's position is shifted during the saccadic movement.[3] Over many presentations of these double-step targets, participants modify their saccadic gain to maintain movement accuracy. It is generally believed that saccadic gain adaptation is driven by ongoing comparison of the actual visual errors with estimated errors, and keeping them in unison.[4–6]

There is some evidence that the precision of the spatial error signal is an important factor in determining the strength of the ensuing saccadic adaptation response.[7] In their study, Havermann and Lappe[7] varied the trial-by-trial second step size in a double-step paradigm to manipulate the variability of the spatial error signal supplied to the adapting healthy saccadic system. Their primary aim was to study the general impact of error signal precision on saccadic adaptation in healthy individuals, so they used experimentally exaggerated second-step variability in their study. They concluded that saccadic adaptation was greatly reduced when the precision of the second step was decreased (i.e., when the distribution around the mean second step was more variable).[7]

Amblyopia is a unilateral (or rarely bilateral) loss of vision caused by abnormal visual experience early in childhood. It is a neurodevelopmental disorder that is associated mostly with anisometropia and strabismus in an otherwise normal eye.[8] The visual loss due to amblyopia cannot be attributed to structural abnormality of the eye and cannot be treated immediately by optical means. In addition to the known deficits in spatiotemporal vision,[9] amblyopia is associated with increased *spatial variability* on motor tasks, such as grasping,[10] hand reaching,[11] and saccadic eye movements.[12,13] It is known that individuals with anisometropic amblyopia exhibit imprecise visual localization irrespective of the target's spatial scale.[14] Consistent with these findings, primary saccadic movement endpoints in people with anisometropic amblyopia are also more spatially variable.[12,13] Recently, we investigated saccadic adaptation in people with anisometropic amblyopia and found that they showed reduced adaptive changes in their saccadic gains when

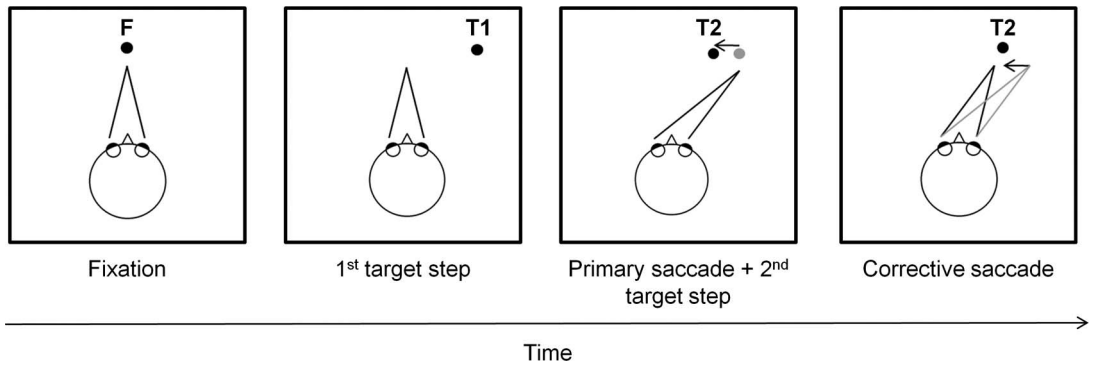

Figure 1. Double-step target paradigm: the participant fixates on a central visual target at the beginning of the trial. After a random interval, the target steps to a new location (T1). As soon as the participant's eyes start moving toward the target, it steps to another location (T2) before returning to central fixation. Participants respond to the double-step targets by reducing the gains of their primary saccades after several repetitions.

the amblyopic eye was involved in viewing (amblyopic eye and binocular viewing).[13] In the context of double stepping targets, less precise primary saccade endpoints mean that the visual spatial error signals that drive saccadic gain adaptation over a number of trials will be more variable and thus less reliable in people with amblyopia. Hence, we postulate that the reduction in saccadic adaptation in participants with amblyopia could be due to more variable spatial error signals generated *endogenously* as a consequence of imprecise primary saccadic movements.

To test our hypothesis, we investigated whether spatial error variability equivalent to the saccadic endpoint variability difference derived from people with anisometropic amblyopia and visually normal people could diminish saccadic adaptation in visually normal participants when applied *exogenously*. To achieve this, we first measured the variance in the endpoint distributions of nonadapting primary saccades in 8 participants with anisometropic amblyopia and 11 visually normal controls during amblyopic/nondominant eye viewing, based on data we have published previously.[13] We then calculated the variance difference of the saccadic endpoint distributions between amblyopic and visually normal participants, and applied this variance difference to the second step during saccadic adaptation in a new sample of visually normal participants with their nondominant eye viewing. We hypothesized that visually normal participants would exhibit a lesser magnitude of saccadic adaptation when the error signal (i.e., second step) is variable as opposed to when the error signal is consistent.

Methods

Participants

Ten visually normal or corrected-to-normal adults (age, 27 ± 5 years; 6 females) were recruited for the study. All participants were naive to the experiment and underwent a standard eye examination performed by a certified orthoptist. The research study was approved by the Research Ethics Board at The Hospital for Sick Children, Toronto, Ontario, Canada, and all experiments conformed with the guidelines of the Declaration of Helsinki.

Setup

The visual target was a red dot (0.2°) that was rear-projected on a tangent screen by using a laser galvanometer (GSI Group, Bedford, MA, USA). The participants were seated 80 cm from the projector screen with their head stabilized on a chin rest. Eye movements were recorded binocularly by using a video-based eye tracker (Chronos Vision, Berlin, Germany) at 200 Hz (see our previous article [Raashid et al.[13]] for more methodological details).

Procedure

Participants made saccades to the visual target on the screen as quickly and as accurately as possible during monocular nondominant eye viewing. Each experiment had 385 trials comprising five blocks: pre-OFF, pre-ON, adaptation, post-OFF, and post-ON, as described below.

Pre-OFF and Pre-ON Blocks. In these two baseline blocks, the target stepped to ±19° horizontally from the central fixation point. In the pre-OFF block (45 trials: 30 in the adapting and 15 in the nonadapting direction, presented randomly), as soon as the participants started moving their eyes to the target, the visual target was extinguished. Therefore, participants did not obtain visual feedback about the target position during the pre-OFF block. The pre-ON block (50 trials: 35 adapting direction, 15 nonadapting direction) was similar to the pre-OFF block except that the visual target always remained on.

Adaptation Block. A double-step target paradigm was used to induce saccadic adaptation.[3] In the adaptation block, the target stepped initially to ±19° horizontally, followed by a 4° step back toward initial fixation (gain-decrease adaptation, Fig. 1) as soon as the primary saccade velocity exceeded the threshold velocity of 50 deg/s. The intrasaccadic target step was provided for saccades in one horizontal direction only (adapting trials) that was chosen randomly across subjects. Saccades in the other horizontal direction did not include the second 4° backward step (nonadapting trials). Additionally, catch trials (±19° vertically) were included in the adaptation block to reduce the effects of prediction and anticipation on adaptation. The entire adaptation block was 200 trials long (120 adapting, 60 nonadapting, and 20 catch trials presented in a predetermined pseudorandom order).

Two separate adaptation blocks were used for the two error conditions. In the "consistent error" condition, the trial-by-trial intrasaccadic step size was a constant 4°, with the overall step size distribution having a standard deviation of 0° (120 trials). In the "variable error" condition the intrasaccadic steps were distributed normally around an amplitude of 4° ± 1.002° (range, 1.6°–6.8°). This second step variability was set to a value ($\sigma = 1.002°$) that corresponded to the difference in the measured saccadic endpoint variability between 8 participants with anisometropic amblyopia and 11 visually normal controls whose data were recorded previously.[13] To achieve this, we measured the probability distribution of saccadic endpoints to

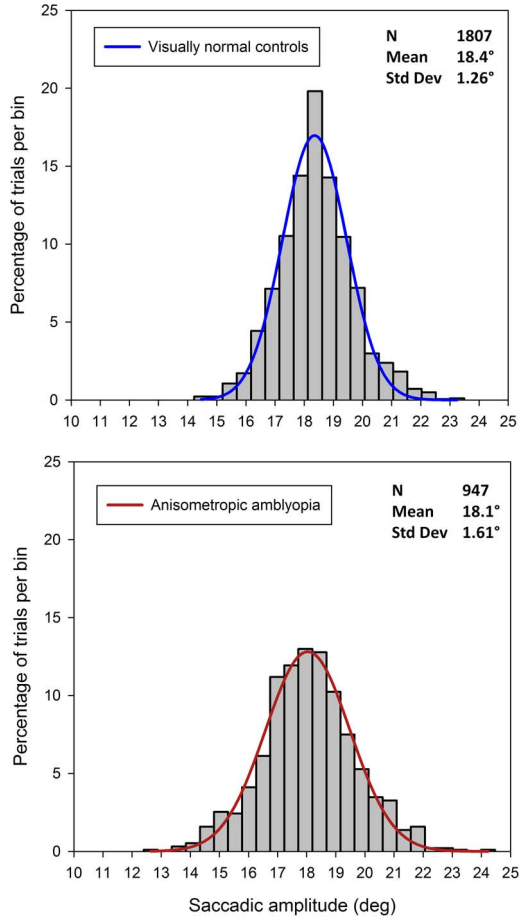

Figure 2. Saccadic endpoint distributions for 11 visually normal controls (*top panel*) and 8 people with anisometropic amblyopia (*bottom panel*) during nondominant eye and amblyopic eye viewing, respectively (from Raashid et al.[13]).

±19° visual targets in both groups during monocular amblyopic/nondominant eye viewing (Fig. 2; subjects from published data[13]). There were no differences in the saccadic endpoints of rightward movements when compared to leftward movements, so saccades in both directions were pooled together for each group. Each participant completed more than 100 baseline saccades within their respective groups ($n_{amblyopia} = 947$ saccades, $n_{control} = 1807$ saccades). Saccadic endpoints were distributed around a mean of 18.1° ± 1.61° within participants with anisometropic amblyopia and around a mean of 18.4° ± 1.26° within visually normal participants (Fig. 2). Saccadic endpoint variance (σ^2) in visually normal participants was subtracted from the saccadic endpoint variance in the participants with anisometropic amblyopia to yield the differential variance in the saccadic movements with their amblyopic/nondominant eye viewing: $\sigma^2_{diff} = \sigma^2_{amblyopia} - \sigma^2_{controls}$. This differential variance ($\sigma^2_{diff} = 1.0045$; $\sigma_{diff} = 1.002°$) was used as the variance of the second target step for the variable error condition.

Post-OFF and Post-ON Blocks. These blocks were similar to the two baseline blocks. The target stepped to ±19° horizontally and was extinguished during saccades in the post-OFF block (45 trials: 30 adapting direction, 15 nonadapting direction), and it stayed on throughout the post-ON block (45 trials: 30 adapting direction, 15 nonadapting direction). Disrupting the visual feedback about target position during the postadaptation period resulted in participants retaining saccadic gain changes they achieved during adaptation. With the onset of visual feedback about target position in the post-ON block, the participants started de-adapting their saccadic gains to baseline levels.

Participants underwent two separate sessions for the "consistent error" and "variable error" conditions at least a week apart to minimize the effects of retention on saccadic adaptation. Only the adaptation block differed between the two sessions; all other experimental blocks were the same.

Data Analysis

All statistical analyses were performed by using the SAS 9.4 software package (SAS Institute, Inc., Cary, NC, USA). Outcome measures were saccadic gain, saccadic latency, normalized saccadic peak velocity, percentage change in saccadic gain, percentage retention, adaptation time constant, asymptotic adaptation gain, and the goodness-of-fit (R^2) values. Saccadic gain was defined as the ratio of saccadic amplitude to the target amplitude. Saccadic latency was defined as the time elapsed between target presentation and the onset of the primary saccades (saccade detection velocity threshold ≥20 deg/s). Mathematically, saccadic peak velocity can be described as a function of amplitude, where increasing movement amplitudes increase the peak velocity in a quasi-linear fashion up to a certain movement eccentricity after which the rise in peak velocities subside.[15] This relation between the saccadic peak velocity and amplitude is commonly known as the main sequence of saccades, and has been quantified by many different methods. To analyze the saccadic main sequence in our study, we used a measure called normalized peak velocity (described by Lebedev and colleagues[16]), where $Normalized\ Peak\ Velocity = Peak\ Velocity / \sqrt{Amplitude}$.

All the trials from each experimental block were used to calculate mean saccadic latencies and normalized peak velocities. To calculate mean saccadic gains, the last 30 trials from each experimental block (or all trials if <30 trials in a block) were used. Percentage change in saccadic gain was calculated by using the following formulae:

$$Observed\ Change\ in\ Saccadic\ Gain = \frac{Mean\ Pre\text{-}ON\ Gain - Mean\ Adaptation\ Gain}{Mean\ Pre\text{-}ON\ Gain} \quad (1)$$

$$Ideal\ Change\ in\ Saccadic\ Gain = \frac{Size\ of\ Intrasaccadic\ Target\ Step\ (4°)}{Size\ of\ the\ Primary\ Target\ Step\ (19°)} \quad (2)$$

$$Percentage\ Change\ in\ Saccadic\ Gain = \frac{Observed\ Change\ in\ Saccadic\ Gain}{Ideal\ Change\ in\ Saccadic\ Gain} \times 100\% \quad (3)$$

Percentage retention during the postadaptation period was calculated by using the following formulae:

$$Retained\ Change\ in\ Saccadic\ Gain = \frac{Mean\ Pre\text{-}OFF\ Gain - Mean\ Post\text{-}OFF\ Gain}{Mean\ Pre\text{-}OFF\ Gain} \quad (4)$$

$$Percentage\ Retention = \frac{Retained\ Change\ in\ Saccadic\ Gain}{Ideal\ Change\ in\ Saccadic\ Gain} \times 100\% \quad (5)$$

To quantify the time course of saccadic adaptation, individual adaptation data were fitted with the exponential equation of the form $G(t) = G_0 + \Delta G e^{-t/\tau}$, where G_0 indicates the asymptotic saccadic gain at the end of adaptation, ΔG

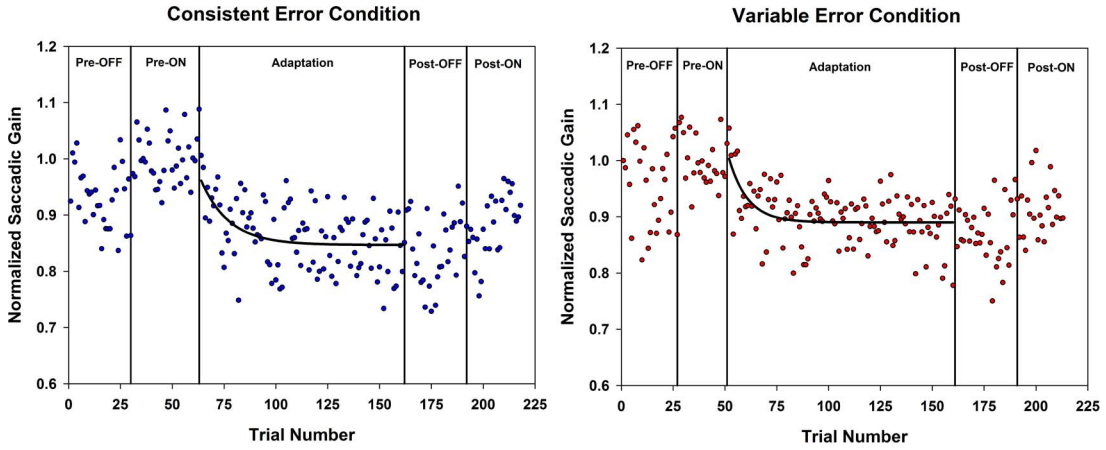

Figure 3. A plot of saccadic gains normalized to the pre-ON gain against trial number for a representative participant. The *left panel* shows the consistent error condition and the *right panel* shows the variable error condition. The *vertical lines* separate the five experimental blocks: pre-OFF, pre-ON, adaptation, post-OFF, post-ON. The participant had a steady saccadic gain during the baseline blocks (pre-OFF and pre-ON) and reduced gain during the adaptation block. This reduction was of a greater magnitude in the consistent error condition than the variable error condition. During the first postadaptation block (post-OFF), the participant retained the gain reduction achieved during adaptation and started increasing the saccadic gain during the second postadaptation block (post-ON).

indicates the gain change from trial $t = 0$, and τ (number of trials) describes the time constant of adaptation. All the parameter estimates obtained from the nonlinear regression fits were first tested by using a *t*-test to determine their statistical significance. Participants were included in the final group analysis only if all three of their computed parameters had a *P* value of ≤ 0.05. The goodness-of-fit (R^2) values were also computed.

Saccadic gain, latency, and normalized peak velocity were submitted to a two-way repeated measures ANOVA with error condition (two levels: consistent error, variable error) and experimental block (five levels: pre-OFF, pre-ON, adapt, post-OFF, post-ON) as the within-subjects factors. Post hoc multiple comparison tests were carried out by using the Tukey-Kramer method. Percentage gain change, percentage retention, asymptotic gains, time constants, and goodness-of-fit values were compared between the two error conditions by using paired *t*-tests with the Holm-Bonferroni correction for multiple comparisons.

Results

Preliminary analysis revealed that there was no effect of target direction (two levels: leftward, rightward) on saccadic gain ($F_{4,32} = 1.4$, $P = 0.25$), saccadic latency ($F_{4,32} = 2.4$, $P = 0.08$), or normalized peak velocity ($F_{4,32} = 2.4$, $P = 0.08$) across all experimental blocks for both consistent error and variable error conditions. There was also no effect of target direction on the percentage change in saccadic gain ($F_{1,8} = 1.6$, $P = 0.24$) or percentage retention ($F_{1,8} = 0.7$, $P = 0.42$) measures across the consistent error and variable error conditions. Therefore, the data were pooled across both horizontal target directions for all subsequent analyses.

Saccadic Gain

Figure 3 depicts the progression of normalized saccadic gains from a representative visually normal participant across the five experimental blocks for both error conditions. Saccadic gains remained steady during the two baseline blocks (pre-OFF and pre-ON) and started decreasing at the onset of the double-step adaptation block. Generally, for all 10 participants, pre-OFF saccadic gains were lower than the pre-ON saccadic gains during both error conditions (pre-OFF: 0.90 ± 0.05, pre-ON: 0.94 ± 0.04; Tukey-adjusted $P = 0.01$). All participants had a significant change in their saccadic gains across different blocks within both consistent error and variable error conditions ($F_{4,36} = 4.9$, $P = 0.003$), albeit of different magnitudes (discussed below). Post hoc analysis revealed that participants significantly reduced their saccadic gains in response to the intrasaccadic target steps during the adaptation block compared to the pre-ON block in both consistent error (pre-ON: 0.96 ± 0.04, adapt: 0.81 ± 0.03; Tukey-adjusted $P < 0.0001$) and variable error conditions (pre-ON: 0.92 ± 0.03, adapt: 0.82 ± 0.03; Tukey-adjusted $P < 0.0001$).

Percentage change in saccadic gain was analyzed to compare the magnitude of reduction in saccadic gains of participants at the end of adaptation during the two error conditions. Figure 4A shows a plot of percentage change in saccadic gain by error conditions for individual participants. All 10 individuals showed a reduction in their percentage gain change values during the variable error condition as compared to the consistent error condition. On average, participants demonstrated a significantly reduced change in their saccadic gains during the variable error condition (50 ± 10%) as compared to during the consistent error condition (69% ± 9%; $t_{(9)} = 5.8$, Holm-Bonferroni corrected $P = 0.0008$; Fig. 4B).

Percentage retention was assessed to determine whether the changes in saccadic gains attained during adaptation were retained in the postadaptation saccadic movements made in the absence of visual feedback about the target position. There was no difference in percentage retention values between the two error condition groups (consistent: 38% ± 21%, variable: 39% ± 23%; $t_{(9)} = -0.1$, Holm-Bonferroni corrected $P = 0.9$), despite participants exhibiting a greater magnitude of adaptation in the consistent error condition.

Saccadic Latency and Normalized Peak Velocity

Mean saccadic latencies did not differ significantly across the five experimental blocks during the consistent error (pre-OFF: 204 ± 38 ms, pre-ON: 179 ± 25 ms, adapt: 192 ± 19 ms, post-OFF: 197 ± 28 ms, post-ON: 202 ± 40 ms) or variable error conditions (pre-OFF: 202 ± 26 ms, pre-ON: 196 ± 21 ms, adapt: 191 ± 16 ms, post-OFF: 202 ± 31 ms, post-ON: 203 ± 23 ms; $F_{4,36} = 1.1$, $P = 0.39$). Normalized saccadic peak velocities did not differ significantly between

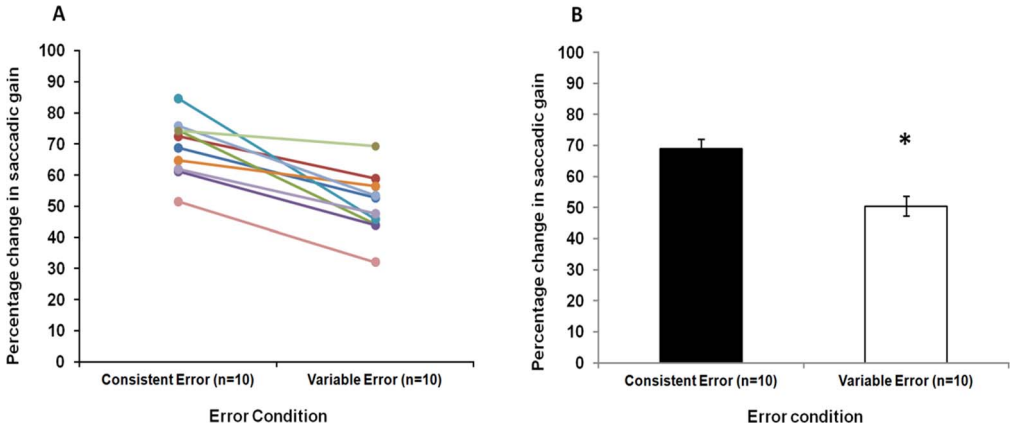

FIGURE 4. Percentage change in saccadic gain plotted by error condition for (**A**) individual participants separately and (**B**) the mean of all participants. *Error bars* indicate ±1 SEM. On average, participants showed a diminished reduction in their saccadic gains during the variable error condition (*asterisk*, $P = 0.0008$).

the two error conditions averaged over all blocks (consistent: 94.8 ± 14.4 $\sqrt{\text{deg}}$/s, variable: 96.0 ± 13.4 $\sqrt{\text{deg}}$/s; $F_{1,18} = 0.7$, $P = 0.42$), but they were significantly lower during the post-ON block (94.2 ± 13.7 $\sqrt{\text{deg}}$/s) compared to the pre-ON block (98.8 ± 12.7 $\sqrt{\text{deg}}$/s; Tukey-adjusted $P = 0.048$) averaged over both error conditions ($F_{4,36} = 2.9$, $P = 0.03$). Interestingly, compared to the pre-ON block (98.8 ± 12.7 $\sqrt{\text{deg}}$/s), normalized peak velocities were also lower during the pre-OFF (95.0 ± 13.8 $\sqrt{\text{deg}}$/s), adaptation (94.7 ± 14.7 $\sqrt{\text{deg}}$/s), and post-OFF (94.3 ± 15.0 $\sqrt{\text{deg}}$/s) blocks, but these reductions were not statistically significant (Tukey-adjusted P values of 0.14, 0.09, and 0.06, respectively).

Exponential Course of Adaptation—Time Constants and Asymptotic Gains

We fitted the adaptation block data for all individuals with an exponential equation of the form $G(t) = G_0 + \Delta G e^{-t/\tau}$, and calculated the time constants τ and the asymptotic gains G_0 from the fits. The exponential fit data for all the participants during both error conditions are shown in Figures 5 and 6 and the Table (along with the goodness-of-fit R^2 values). Adaptation data from participants 5 and 7 during the consistent error condition, and from participants 9 and 10 during the variable error condition (4 of 20 observations; see the Table), yielded a time constant value that was not statistically significant in spite of their data being fitted adequately (regression F statistic $P < 0.05$) with the exponential equation (see Figs. 5, 6). Consequently, these four participants were excluded from the analysis of both time constants and asymptotic gains. The R^2 values did not differ significantly between the two error conditions (consistent: 0.36 ± 0.15, variable: 0.29 ± 0.1; $t_{(9)} = 1.7$, Holm-Bonferroni corrected $P = 0.2$). The averaged time constants of adaptation from these fits were also somewhat similar in the two error conditions (consistent: 23 ± 11 trials, variable: 16 ± 10 trials; $t_{(5)} = 0.5$, Holm-Bonferroni corrected $P = 0.6$; Fig. 7); however, this result should be interpreted with caution, as the power of the statistical test performed was reduced owing to the exclusion of 4 out of 20 observations. To validate the results obtained from the percentage change in saccadic gain measure, we compared the asymptotic gains G_0 obtained from the fits between the two error conditions (with data from participants 5, 7, 9, and 10 excluded). We found that on average participants reached a higher asymptotic gain value during the variable error condition (0.89 ± 0.02) than the consistent error condition (0.85 ± 0.02; $t_{(5)} = -3.5$, Holm-Bonferroni corrected $P = 0.048$). It is noteworthy that unlike the time constant analysis,

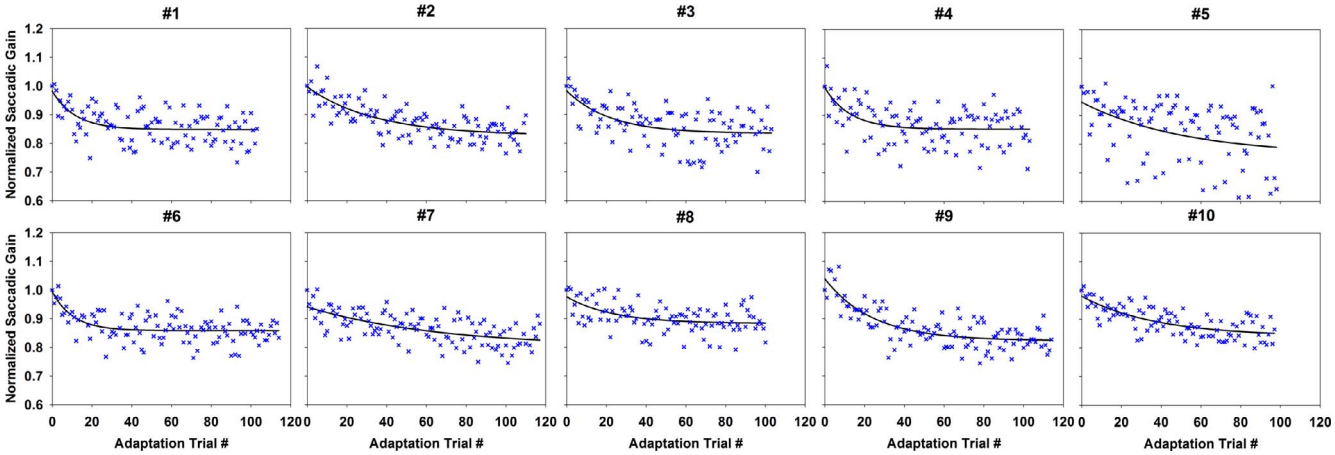

FIGURE 5. A plot of adaptation saccadic gains normalized to the individual pre-ON saccadic gain against trial number during the consistent error condition for all 10 participants. The *blue crosses* indicate individual trials, and the *black line* represents the best fit curve using the exponential equation of the form $G(t) = G_0 + \Delta G e^{-t/\tau}$. It is noteworthy that the exponential fits for participants 5 and 7 yielded time constant parameters that were not statistically significant.

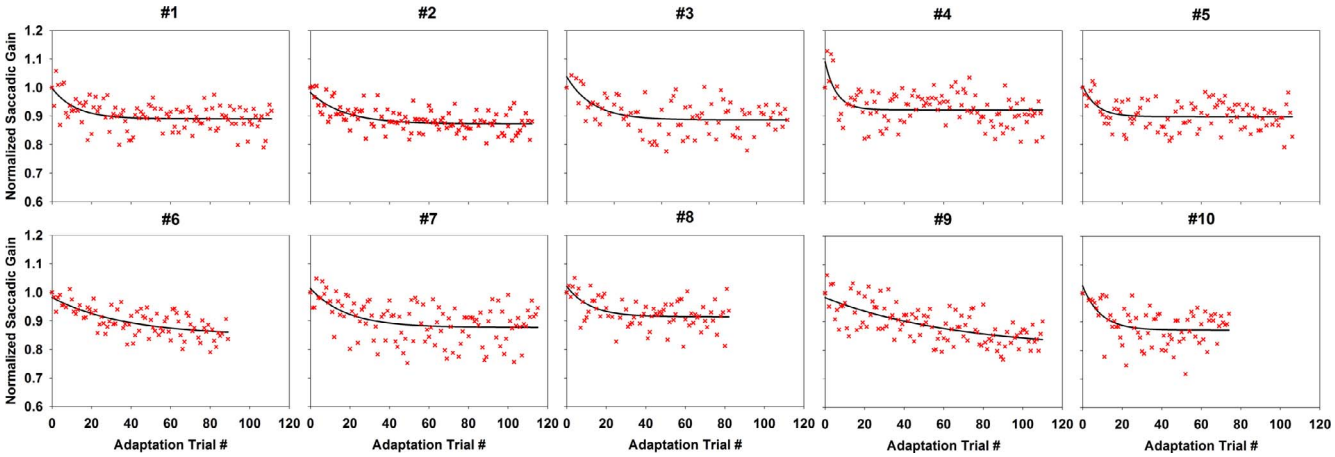

FIGURE 6. A plot of adaptation saccadic gains normalized to the individual pre-ON saccadic gain against trial number during the variable error condition for all 10 participants. The *red crosses* indicate individual trials, and the *black line* represents the best fit curve using the exponential equation of the form $G(t) = G_0 + \Delta G e^{-t/\tau}$. It is noteworthy that the exponential fits for participants 9 and 10 yielded time constant parameters that were not statistically significant.

the asymptotic gain analysis was not impacted by the reduction in statistical power even after the exclusion of 4 out of 20 observations. A higher asymptotic gain during the variable error condition reflects a reduced change in saccadic gain during adaptation, which corroborates our results from the percentage change in saccadic gain measure.

TABLE. Time Constants (τ), Goodness-of-Fit (R^2), and Asymptotic Gain (G_0) Values for All Participants During Both Consistent Error and Variable Error Conditions

Group	ID	τ, No. of Trials	R^2	G_0
Consistent error	1	12	0.2505	0.8485
	2	35	0.5455	0.8272
	3	22	0.3095	0.8348
	4	13	0.238	0.8515
	5	52*	0.15	0.7606†
	6	11	0.3113	0.8582
	7	65*	0.39	0.8032†
	8	24	0.243	0.8832
	9	25	0.6201	0.8236
	10	38	0.5151	0.8402
		23 ± 11	**0.36 ± 0.15**	**0.85 ± 0.02‡**
Variable error	1	12	0.2261	0.8905
	2	18	0.3773	0.8728
	3	11	0.2529	0.8869
	4	6	0.2165	0.9219
	5	7	0.1761	0.898
	6	37	0.4702	0.8485
	7	19	0.2337	0.8771
	8	12	0.26	0.9146
	9	67*	0.43	0.8026†
	10	9*	0.23	0.871†
		16 ± 10	**0.29 ± 0.10**	**0.89 ± 0.02‡**

Bolded values indicate group mean ± standard deviation.

* Indicates time constant values that were not statistically significant ($P > 0.05$). Subsequently, these values were not used in calculating the group means.

† Indicates asymptotic gain values that were statistically significant ($P < 0.05$) but were excluded from group means calculations, as their corresponding time constant values were not statistically significant.

‡ Indicates the pair of group means that were significantly different from each other ($P = 0.048$).

DISCUSSION

In a prior study, we have shown that people with anisometropic amblyopia exhibit diminished adaptation of primary saccadic gains when viewing with the amblyopic eye.[13] Interestingly, we also noticed that they had more variable movement endpoints during the nonadapting primary saccades. We hypothesized that this higher-than-normal endogenous saccadic endpoint variability, which in turn increases spatial error variability for double-step adaptation, could be a key factor in diminishing the adaptation response we observed in our previous study. Here, we introduced spatial error variability experimentally in visually normal people by substituting the computed saccadic endpoint variability difference between visually normal and amblyopic participants during baseline trials (σ_{diff}; see Methods) for the normally occurring spatial variability of the second step during saccadic adaptation. We observed that in response to this experimental increase in second-step variability, visually normal controls exhibited a reduction in their adapting saccadic gains as compared to when the second step was consistent.

The saccadic system requires a spatially accurate and precise visual error signal to achieve a maximal adaptive change in movement gains of a specific vector.[17,18] This is indicated by a previous observation by Havermann and Lappe[7] that when the mean second step (3°) in a double-step gain-

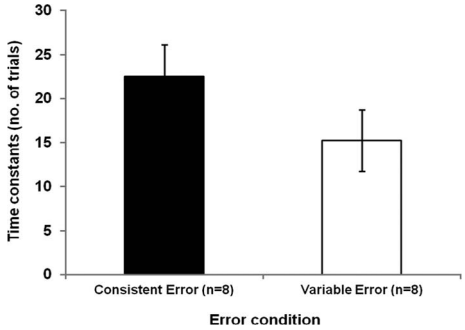

FIGURE 7. Mean time constants for all participants plotted against the two error conditions. *Error bars* indicate ±1 SEM. Participants showed no difference in the time constants of adaptation between the two error conditions ($P = 0.6$).

decrease adaptation paradigm was made more variable spatially by a σ of 2°, the adaptation magnitude was reduced by ≈25% of its initial value.[7] In this previous study, the smallest-tested spatial variability of the second target step when normalized to its mean size (a measure known as relative standard deviation [RSD]) was fairly high (RSD = 67%). In contrast, we tested a much smaller spatial variability: σ_{diff} of 1° on a mean second step of 4°, an RSD of only 25%. Nonetheless, we found that increasing the second-step variability by a σ_{diff} of 1° significantly decreased the magnitude of the adapting saccadic gain change by approximately 27% of its initial value (from 69% to 50%; Fig. 4B), supporting the hypothesis that increased spatial variability of the adapting error signal leads to reduced saccadic adaptation. Another major distinction in our study is that we presented the second step *during* primary saccade execution (before the primary saccade reaches peak velocity), whereas in the study by Havermann and Lappe,[7] the second step was presented *after* the primary saccade had ended. It is known that postsaccadic temporal delays in the adapting error signal presentation of up to 400 ms can have a significant impact on modulating the saccadic adaptation response in humans.[4] Therefore, given that the variability of the error signal reduces saccadic adaptation, it is possible that using a less variable error signal can more efficiently reduce the saccadic adaptation response, compared to a more variable error signal, if it is presented early in the primary saccade execution. This may be a reason why the reduction in adaptation magnitude in our experiment was equivalent to the "$\sigma = 2°$" condition in the study of Havermann and Lappe,[7] despite using a smaller second-step variability ($\sigma_{diff} = 1°$). Importantly, the amount of exogenous spatial error variability we introduced was equivalent to that observed in people with anisometropic amblyopia, which we have reported previously. In addition, the reduction in saccadic adaptation we observed in visually normal participants we tested in the current experiment during the variable error condition (percentage change in saccadic gain = 50% ± 10%) was comparable to that observed in people with anisometropic amblyopia during a consistent second-step condition (percentage change in saccadic gain = 45% ± 11%; [Fig. 3 in Raashid et al.[13]]).

There could be mechanistic differences between (1) the saccadic adaptation decrement associated with anisometropic amblyopia[13] as a consequence of endogenously imprecise saccadic endpoints as opposed to (2) the decrement we observed in this study in response to an experimentally induced more variable second step. The former is likely attributable to increased internal noise in the encoding of sensory signals,[19] which leads to imprecise motor commands due to degraded perception of the visual error signals. On the other hand, the latter is in response to extraneous ambiguity caused by a variable target step that diminishes motor performance because the adapting error signal keeps on changing from trial to trial. Yet, both the aforementioned processes share a common pathway insofar as they both increase the variability of the spatial error signal required for adaptation, either endogenously or exogenously (respectively). Since the estimate of our experimental "noise" (σ_{diff}) was calculated from the *endpoints* of saccadic movements (of both amblyopic and visually normal participants), we cannot pinpoint precisely whether that noise came from a sensory or a motor source. According to van Beers,[20] the inherent variability in saccadic endpoints can either come from errors in detection and localization of the visual target (sensory) or from a combination of signal-dependent and mechanical noise in the torque generated by the extraocular muscles (motor). In his modeling study, van Beers[20] reported that the sensory noise accounted for ≈57%, whereas motor noise accounted for ≈42%, of the overall saccadic endpoint variability in the visually healthy system. It will be interesting to explore the proportion of sensory-to-motor noise in saccades generated by an amblyopic visuomotor system. Until then, based on our current knowledge,[19,21–24] it is the sensory noise that is distinctively elevated in people with amblyopia, and therefore our estimate of experimental "noise" (σ_{diff}) most likely represents variability predominantly from the sensory component of amblyopic saccadic variability.

It is generally believed that gain-decrease adaptation is achieved primarily by adapting the internal model that modifies the dynamics of the ongoing primary saccade, whereas gain-increase adaptation is achieved by updating the sensory representation of the target.[25,26] These two studies reported that the peak velocities of the *adapting* saccades of certain amplitudes were similar to the peak velocities of the *nonadapting* saccades of equivalent amplitudes for the gain-increase adaptation only: gain-decrease adapting saccades showed lower peak velocities than their nonadapting counterparts. In our study, to assess the saccadic dynamics during gain-decrease adaptation for both the consistent and the variable error conditions, we normalized the saccadic peak velocity to the square root of the amplitude.[16] This normalization procedure removed the known dependence of saccadic peak velocity on its amplitude (the main sequence relation[15]) and enabled us to compare the dynamics of the baseline (pre-ON) nonadapting saccades with the adapting saccades of varying amplitudes. We observed a trend toward lower normalized saccadic peak velocity during the adaptation block compared to the pre-ON block across both consistent and variable error conditions. Even though this result was not statistically significant (Tukey-adjusted $P = 0.09$, see Results), it was in line with the trend reported by others[25,26] where saccades during gain-decrease adaptation show a reduction in their peak velocities. We also found that over all experimental blocks, the normalized peak velocities did not differ significantly between the consistent and variable error conditions. This result suggests that gain-decrease saccadic adaptation proceeds with similar modulation of saccade dynamics in both the presence and absence of the trial-by-trial second-step variability.

As described above, we used the calculated saccadic endpoint variability difference from baseline trials as a metric for our experimental spatial error variability. Emerging evidence suggests that baseline motor variability characteristics can accurately predict the propensity for subsequent error-based motor adaptation in both the manual motor[27] and the oculomotor[28] systems. In the former study, Wu et al.[27] showed that a higher level of task-relevant baseline motor variability predicted faster learning on the following manual force field adaptation task. In the latter study, Wong and Shelhamer[28] found that high intertrial correlations (i.e., low variability) in baseline predictive saccades were associated with a subsequent rapid gain-increase saccadic adaptation. At first glance, the two studies seem to offer conflicting viewpoints on the relation between baseline motor variability and adaptation performance; however it is important to note that the two adaptation tasks are vastly different from each other. The target perturbations are consciously perceptible during the adaptation of hand movements,[29] whereas participants are not consciously aware of the perturbations during the adaptation of saccadic eye movements.[30] That may explain why adaptation of hand movements would benefit from a slightly higher baseline motor variability (or "exploration"; see Herzfeld and Shadmehr[31]), while saccadic adaptation appears to be hindered if the baseline movement fluctuations are larger in magnitude, as it will result in a more variable spatial error for adaptation. Nonetheless, both these studies establish a strong link between baseline motor task characteristics and subsequent motor adaptations.

Arguably, the decrement in spatial error precision in our experiment could have been achieved by alternative methods, such as by degrading vision directly with the use of blurring lenses. However, degrading visual acuity in visually normal people to the level of people with anisometropic amblyopia is not identical to increasing spatial imprecision in the visual error signal for two reasons. First, we have previously found no correlation between the severity of visual acuity loss and saccadic variability/saccadic adaptation magnitude in people with anisometropic amblyopia, indicating that the visual acuity loss itself does not explain the reduction in spatial precision/saccadic adaptation in amblyopia.[13] Second, we have shown previously that saccade dynamics, including amplitude and variability in amplitudes, did not change significantly when visually normal participants were asked to make saccades while viewing a visual target with blurring lenses, even after 5 hours of blur adaptation.[32]

To assess the time course of saccadic adaptation we fitted our data with exponential equations and used them to calculate the time constant measure. In contrast, Havermann and Lappe[7] used more conservative linear fits to their data and computed a gain change per trial measure. They found that the linear gain change per trial measure decreased generally with the decreasing second-step consistency, but the decrease was only statistically significant for their lowest consistency "$\sigma = 4°$" condition. They did not report a statistically significant decrease in adaptation rate during their "$\sigma = 2°$" condition.[7] Interestingly, we also could not find any evidence for a difference in the time constants of adaptation between the variable error ($\sigma_{diff} = 1°$) and consistent error groups despite the adapting gains reaching a lower spatial magnitude during the variable error condition. A similar result had been observed in participants with anisometropic amblyopia where they reduced their saccadic gains at a rate similar to that of visually normal people, but showed a decrement in the spatial extent of saccadic adaptation.[13] It is important to note that 4 of 20 observations in our current data set did not yield a statistically significant time constant value (see Table), and therefore our time course analysis is undermined to some extent by the loss of statistical power. Taken together, however, these results suggest that the spatial error variability most likely does not impact the temporal properties of saccadic adaptation.

The retention of saccadic adaptation also seems to be unaffected by the variability of the adapting error signal. We observed that the adapted changes in saccadic gains in both error conditions were retained to the same spatial extent when participants were asked to make saccades without visual feedback after adaptation. However, care should be taken when interpreting this result, as saccades executed without visual feedback tend to be more hypometric than those executed with the benefit of visual feedback.[33] We also observed this phenomenon in the current study—the primary saccades during the pre-OFF block had slightly lower mean amplitude than those during the pre-ON block. Therefore, the observed reduction in the saccadic gains during the post-OFF block can either be due to prior adaptation or purely due to absence of a visual target to foveate during the postadaptation period. Additionally, the ability to retain adapted changes in saccadic gain is a marker of long-term saccadic adaptation,[34] which exhibits different spatiotemporal properties than the short-term saccadic adaptation that we tested in this study.[35]

In conclusion, we found that exogenous spatial error variability equivalent to the primary saccadic endpoint variability difference between people with anisometropic amblyopia and visually normal people is sufficient to reduce the spatial extent of saccadic adaptation in visually normal people. Interestingly, this decrement in saccadic adaptation using a spatially variable error in normal subjects corresponds to the reduction in saccadic adaptation using a spatially consistent error in people with anisometropic amblyopia. Despite the significant reduction in the spatial extent of saccadic adaptation, its temporal and gain retention properties appear to be unaffected by the variability of the adapting error signal.

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