Comparison of Two Methods of Producing Adaptation of Saccade Size and Implications for the Site of Plasticity

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Scudder, Charles A., Ekatherina Y. Batourina, and George S. Tunder. Comparison of two methods of producing adaptation of saccade size and implications for the site of plasticity. J. Neurophysiol. 79: 704–715, 1998. Saccade accuracy is known to be maintained by adaptive mechanisms that progressively reduce any visual error that consistently exists at the end of saccades. Experimentally, the visual error is induced using one of two paradigms. In the first, the horizontal and medial recti of trained monkeys are tenectomized and allowed to reattach so that both muscles are paralytic. After patching the unoperated eye and forcing the monkey to use the “paretic eye,” saccades initially undershoot the intended target, but gradually increase in size until they almost acquire the target in one step. In the second, the target of a saccade is displaced in midsaccade so that the saccade cannot land on target. Again saccade size adapts until the target can be acquired in one step. Because adaptation with the latter paradigm is very rapid but adaptation using the former is slow, it has frequently been questioned whether or not the two forms of adaptation depend on the same neural mechanisms. We show that the rate of adaptation in both paradigms depends on the number of possible visual targets, so that when this variable is equated, adaptation occurs at similar rates in both paradigms. To demonstrate further similarities between the result of the two paradigms, an experiment using intrasaccadic displacements was conducted to show that rapid adaptation possesses the capacity to produce gain changes that vary with orbital position. The relative size of intrasaccadic displacements were graded with orbital position so as to mimic the position-dependent dysmetria initially produced by a single parietal extraocular muscle. Induced changes in saccade size paralleled the size of the displacements, being largest for saccades into one hemifield and being negligible for saccades into the other hemifield in the opposite direction. Collectively, the data remove the rational for asserting that adaptation produced by the two paradigms depends on separate neural mechanisms. We argue that adaptation produced by both paradigms depends on the cerebellum.

INTRODUCTION

Because saccades have too short a duration for vision to directly control their final position, saccade accuracy must be maintained over the long term by mechanisms that assess saccade error at the end of each saccade and modify subsequent movements. That such adaptive mechanisms do exist was dramatically demonstrated in patients with paresis of the extraocular muscles in one eye (Abel et al. 1978; Kommerell et al. 1976; Optican et al. 1985). Whereas the normal eye was able to saccade to visible targets accurately, the paresis in the other eye necessarily rendered its eye movements much smaller. Hence, when the patient was forced to use the “paretic eye” by patching the normal eye, saccades initially undershot the target (hypometria). Over days of forced use of the paretic eye however, saccades increased in size until they were nearly accurate. When the patch was switched and the normal eye was used again, saccades in this eye overshot the target initially (hypermetria), but adaptive mechanisms restored normal accuracy over succeeding days.

Experimentally, two paradigms have been used to investigate saccade adaptation. The first is a more controlled version of the clinical situation described above. Monkeys had their medial and lateral rectus muscles of one eye surgically weakened and were forced to use this eye by patching the other. The initial saccadic hypometria was gradually eliminated over time (Optican and Robinson 1980). Switching the patch and forcing the monkey to use the normal eye produced saccadic hypermetria that also was gradually eliminated. The changes in saccade size had an approximately exponential time course with time constants of <1 day and 0.5 days respectively.

In the second method for producing saccadic adaptation, the eye muscles are unaltered, but the visual target is perturbed so that saccade does not initially land on the target. Although optical devices have been used for this purpose (Hensen 1978), the most common method has been to displace the target during each saccade so that there will always be an error. Typically, the target is displaced intrasaccadically either backward or forward (here to be called the intrasaccadic step, or ISS) collinearly with the initial target step (Deubel et al. 1986; McLaughlin 1967; Miller et al. 1981). Saccade size gradually decreases or increases, respectively, so that saccades eventually land on target. The rate of change varies widely. In monkeys undergoing steps of multiple sizes, the modification of saccade size was fit with an exponential having a rate constant of 200–600 trials (Deubel 1987; Fuchs et al. 1996; Straube et al. 1997), but in humans generating saccades between just two target locations, adaptation of saccade size may be completed in as few as 6 trials (McLaughlin 1967; Miller et al. 1981; Weisfeld 1972). Adaptation produced by the ISS-paradigm has sometimes been called “rapid” saccadic adaptation to distinguish it from that produced by the paretic-muscle paradigm, which seems to be an order of magnitude slower.

The flexibility of the ISS-paradigm has allowed an investigation of the parameters that influence the rate or extent of adaptation and allowed some insight into its mechanisms. For instance, it has been shown repeatedly that adaptation is not simply a parametric gain adjustment that is applied to all saccades. The presentation of intrasaccadic steps during saccades in one direction but not in the opposite produces a modification of saccade size in the trained direction only (Deubel et al. 1986; Wolf et al. 1984). Similarly, adaptation of saccades in one direction generalizes little or not at all to
perpendicular saccades (Deubel 1987; Frens and van Opstal 1994). Adaptation to target steps of one amplitude only partially generalizes to target steps of a different amplitude (Albano 1996; Frend and van Opstal 1994; Straube et al. 1997), whereas adaptation produced at one eye position generalizes well, albeit incompletely, to saccades at different eye positions (Albano 1996).

Differences in the outcomes of adaptation produced by the ISS-paradigm and the paretic-muscle paradigm, particularly the differing rates of gain changes, have led investigators to question whether they share the same underlying mechanism (Fitzgibbon et al. 1986; Optican 1985). However, differences may be more apparent than real because the two types of adaptation have not been investigated under similar conditions. In the paretic-muscle paradigm, monkeys and humans make spontaneous saccades to self selected targets at widely varying displacements, directions, and positions in space, so that generalization of adaptation is minimal. In the human experiments where typically only one muscle is paretic (Abel et al. 1978; Kommerell et al. 1976), the innervation required to make saccades of the same size varies enormously with eye position in the orbit (Optican et al. 1985). It could be the case that saccades of a certain size, direction, and position adapt almost independently and do not benefit from adaptation of saccades of other sizes, directions, and positions. In contrast, saccades produced in the ISS-paradigm are of restricted size, direction, and position in space. Under these latter conditions, generalization insures that adaptation of saccades with mildly different parameters will be mutually reinforcing and the overall rate of adaptation will increase. A second difference is that subjects in the ISS-paradigm are required to acquire the target, whereas subjects with a paretic eye may tolerate considerable error. If, for instance, corrective saccades convey an error signal for adaptation as some have postulated (Albano and King 1989; Schweighofer et al. 1996), mandatory acquisition of the target would be expected to increase the rate of adaptation.

This study shows that the properties of adaptation produced by the ISS- and paretic-muscle paradigms under comparable conditions are, in fact, much more similar than previously supposed. Three approaches are used. First, experiments show that the rate of adaptation in the ISS-paradigm depends on the complexity of the pattern of targets (defined as the number of targets and dimensionality of the pattern). Second, experiments show that a suitably chosen gradient of intrasaccadic steps can mimic the outcome of adaptation to a single paretic muscle. And third, results show that adaptation produced in the paretic-muscle paradigm by using a target pattern of low complexity occurs at a rate comparable to ISS-adaptation. Results are discussed in the context of the underlying neurophysiology.

**METHODS**

Five juvenile rhesus monkeys were used in these experiments. All procedures were approved by the Institute Animal Care and Use Committee and conform to guidelines issued by the National Institutes of Health. Two to four monkeys were used in each of the eye-movement recording paradigms described below.

**Surgery**

Monkeys were prepared for eye movement recording during an aseptic surgery in which they were deeply anesthetized with halothane (1.5% in oxygen/nitrous oxide) after induction with ketamine. A 16-mm, 3-turn magnetic search coil (Cooner A-632) was sutured to the sclera of the right eye under the conjunctivum by using a method modified from Judge et al. (1980). Lead wires were passed under the skin to a connector on the top of the skull. Three lugs for the stabilization of the head were built from dental acrylic layered about stainless screws attached to the skull. One lug was positioned at the top front center of the skull and two at the back sides behind both ears. These lugs mated with bars rigidly attached to the primate chair in which monkeys sit during the recording sessions.

Three monkeys underwent a subsequent surgical procedure to weaken the eye muscles and to implant a search coil in the left eye. The medial and lateral recti were detached from the globe, were cut to about 2/3 their normal length, and allowed to reattach to the back of the globe without assistance. The search-coil was implanted as above. Monkeys also had a recording chamber implanted at this time that was used for extracellular single neuron recording from the cerebellum. In one monkey, a few sessions of eye-movement adaptation were conducted after the neuronal recordings had begun.

**Behavioral apparatus and tasks**

Experiments were conducted in a dimly illuminated soundproof booth with the monkeys seated in a primate chair and their heads restrained. Surrounding their heads were two perpendicular Helmholtz coils, which were used in conjunction with the implanted search coil for the measurement of eye movements (CNC Engineering). Eye movement signals were calibrated by having the monkey alternately fixate stationary targets at ±15° horizontal and vertical eccentricity.

Monkeys viewed a red, 0.3° target spot projected onto a textureless white screen formed into a vertically oriented quarter cylinder and situated 75 cm in front of the monkey. The target spot was generated by a laser diode and deflected by an X-Y mirror galvanometer system (General Scanning) under computer control (PPD 11/73). The computer determined the target location, monitored eye movements, and dispensed applesauce reward when on-target conditions were met. For training, food-deprived monkeys were required to fixate the target spot within an error "window" of 6° in all directions to receive a dollop (about 0.1 ml) of applesauce. As performance improved, the error window was reduced to 2° and monkeys were required to fixate at least 1.5 s after an on-target saccade.

Three target patterns were used: a 5×3 (horizontal × vertical) rectangular array of potential target locations with 10° spacing; a 5×1 linear horizontal array with 10° spacing; and a 2×1 array with 20° spacing. Target locations were chosen pseudo-randomly by the computer with all targets having equal probability. The final target of one saccade was used as the starting point for the next. Consequently for the 5×3 pattern, most target steps were oblique and the distribution of horizontal and vertical component sizes was not flat. Ten-degree components were most numerous (53% of horizontal and 64% of vertical components), followed by 20° components (37% H and 36% V) and 30° and 40° components, which comprised the remainder. The introduction of ISSs smeared the distribution of step sizes, but the modal value was still 10°. A new target was presented every 1.5–2.5 s while the monkey was on target.

Target patterns were slightly modified for monkeys viewing through the muscle-weakened left eye. The reattached eye muscles did not provide as wide a range of horizontal eye movements as normal and one side was always more limited than the other (usu-
ally medial). Therefore, to improve the linearity between target position and innervation, the whole pattern was displaced 4–8° away from the more limited side and the $5 \times 3$ pattern was scaled by 75% horizontally.

**Adaptation paradigms**

Two methods were used for inducing adaptive modification of saccade size. In the intrasaccadic step (ISS) paradigm, the target was stepped to a location in one of the above patterns (the primary target) and then displaced collinearly forward by 20% or backward by 30% of the original target displacement. These fractions were chosen because they yield about the same size error given that the primary saccades normally fall about 5% short of the primary target. ISSs were initiated $\sim 8–30$ ms after primary saccade onset. Within each adaptation session, only one type of ISS was presented and ISSs were triggered for every trial. Two or more days typically intervened between sessions or if not, ISSs of opposite directions were used on successive days. There was no evidence of carry-over from day to day, with preadaptation saccade size as a measure.

One special ISS pattern was instituted to mimic the very nonuniform adaptation produced by having one paretic eye muscle (Optican et al. 1985). For saccades in one horizontal direction (which will always be denoted as right), there were no ISSs. In the opposite (left) direction, there were no ISSs if the target was located in the right visual field, but targets located in the left visual field were followed by ISSs whose relative size varied linearly with the distance of the primary target from the vertical meridian at rate of 25% per 10° eccentricity (a target landing at 10° left would be followed by a 25% ISS). The stimulus was designed to produce adaptation in only one direction and one half of the visual field. This paradigm will be called the “position-dependent ISS” paradigm.

In the second, “paretic-muscle,” paradigm, adaptation of saccade size was produced by forcing the monkey to view the world through the eye having surgically weakened eye muscles. Vision in the normal unoperated eye was blocked by using an opaque rigid patch that mated with a receptacle attached to the front acrylic lug on the monkeys head. Recovery was produced by patching the weak eye. In either case, monkeys wore the patch typically 7 days, but a minimum of 3 days, before adaptation experiments were conducted in which the patch was switched to the opposite eye. At the end of the experiment, the patch was typically left on that eye and another 3–7 days elapsed before another experiment.

**Data collection and analysis**

Eye movement and target data were collected before adaptation, at the start of adaptation (the initiation of ISSs or patch-switching), at the end of adaptation, and after adaptation (after the termination of ISSs or returning the patch to the original eye). These will be referred to as the pre-, start-, end-, and postadaptation records. Data were also collected at 0.5-, 1-, 2-, 3-h, and sometimes at the intervening 0.5-h intervals. Typically data from 100 trials were collected. One minute usually intervened between start of the adaptation paradigm and the collection of the “start-adaptation” data and 100–130 trials intervened between the start of adaptation and the midpoint of the start-adaptation data. Horizontal and vertical eye and target position were digitized on-line and encoded on VCR tape (Vetter 4000A) for backup. Data were sampled every 5 ms. A record of the number of primary target steps and the monkeys performance was also kept. Performance was measured as time-on-target, which was the fraction of the total running time that the monkey was within the reward window. Monkeys were counted as being on target after a target step if they acquired the target within 0.5 s during a normal trial (no ISS) or 0.8 s during any adaptation trial (ISS or paretic-muscle). Because the monkeys performance had a measurable effect on the results of ISS adaptation, no data were used after the cumulative performance fell below 90% or after performance fell below 80% in a particular 30-min interval. In the paretic-muscle paradigm, unlike the ISS-paradigm, recovery does not ensue when the monkey makes spontaneous saccades instead of following the target. Hence the 90% cumulative performance criterion was dropped, but the 80% interval criterion was maintained.

Saccade metrics were computed from the digitized data by using an interactive program similar to that used previously (Scudder et al. 1988). The user manually scrolled the data and placed a cursor near desired saccades. The computer (PD4 1173 or 80486-based) found peak velocity and independently searched backward and forward in time for the first point where eye position reached steady-state initial or final eye positions. The computer marked these points and the user accepted them or manually marked those that were in error. Relevant derived values include reaction times and the amplitudes of the horizontal and vertical saccadic components. Saccade gain, defined as saccade amplitude divided by target displacement was computed for polar values as well as component values (e.g., horizontal component size/horizontal target displacement). Most of the data reported below refer to the gain of the horizontal component. In the paretic-muscle paradigm, gain was always computed for the viewing (unpatched) eye.

Saccades were excluded from the statistical analysis if the reaction times were too short (<70 ms) or too long (>600 ms), if the monkey was not initially on target (≥1.5°), if the saccade was clearly not directed at the target, or if the gain was 3.5 standard deviations away from the mean for the particular data set (about 0.3% of the data). Usually, like conditions (with versus without ISSs) were compared for computing changes in gain, that is, pre- and postadaptation data, start- and end-adaptation data, or start- and mid-adaptation data. With the $5 \times 3$ target pattern, gains associated with $5–15°$ and $15–25°$ steps were always similar and not significantly different, despite the higher proportion of $10°$ target steps. Consequently, saccades of all sizes were pooled. Similarly, leftward and rightward saccade data were pooled except for the position-dependent ISS paradigm. In the paretic-muscle paradigm, leftward and rightward saccade gains were frequently dissimilar, but were averaged because their difference was not currently of interest. The pooled variance was computed from the separate left- and right-saccade variances, and so did not include the difference between the means. Because data were collected at fixed times and not fixed trial numbers, small gain corrections were sometimes made so gains could be compared at the fixed trial numbers of 950 and 1,900 (the mean number of trials at 30 and 60 min.). The exponential best fit of gain versus trials (see below) was displaced so as to pass through the actual gain, and the gain at 950 or 1,900 trials was computed from the displaced exponential. In the ISS paradigm, these adjustments amounted to a few percent of the original value, but the performance rate in the paretic-muscle paradigm differed systematically, so adjustments were up to 10%. Gains were statistically compared using Student’s t-test with one-tailed probabilities because there was always a clear prediction about the direction of the changes.

In the position-dependent ISS paradigm, the dependence of saccade gain on the target position at the end of the primary target step was measured with linear regression. Separate regressions were computed for pre-, start-, end-, and postadaptation data. Also, separate regressions were initially computed for $5–15°$ and $15–25°$ primary target steps. In most cases, the slopes were similar ($±40°$) so the data were pooled and a final regression was computed for the pooled data. In one monkey ($G$), the slopes were consistently different and only the smaller saccades were used.

To facilitate comparisons between data from the ISS-paradigm and paretic-muscle paradigm, gain changes were also normalized. Gains changes were expressed as a percentage of the maximum
Figure 2 shows that the rate of adaptation depends on the direction of the ISSs and the complexity of the target pattern. The four traces illustrate the results of four sessions taken from the data of monkey M that approximately represent the average changes occurring during forward ISSs (Fig. 2A) and backward ISSs (Fig. 2B), with the $2 \times 1$ and the $5 \times 3$ patterns. Plotted are the changes in the gain of the horizontal component relative to the gain measured immediately after the “start” of ISSs. Differences between this value and gains at earlier and later times are plotted against the number of intervening trials. It can be seen that the gain at the start of adaptation differed considerably from that recorded in the preadaptation test trials (leftmost symbols), as will be discussed more fully below. As shown in Fig. 2 and tabulated in Table 1, gain changed very slowly after the start of forward ISSs using the $5 \times 3$ pattern. On average, gain increased by only 0.034 (about 3.6%) over the first 950 trials. Gain changed somewhat faster with the $2 \times 1$ pattern, i.e., by 0.056 (about 5.9%). The difference in rates between the two patterns was statistically significant. Similarly, gain changes after about 1,900 trials (0.059 and 0.11) for the two patterns were significantly different. Adaptation was more rapid with backward ISSs. Gain decreased by 0.078 (8.2%) change theoretically possible, which was computed as the difference between the initial (start-adaptation) gain and the theoretical limit. For the 20%-forward and 30%-backward ISSs, the limits were taken as 1.15 and 0.65 respectively and represent the ratio of the secondary to primary target displacements minus 0.05 to account for the tendency of normal and adapted saccades to undershoot. It was clearly necessary to account for saccade undershoot because in the backward-iss sessions, average saccade gain frequently fell below 0.7 (see also, Deubel 1989; Henson 1978). For the paretic-muscle paradigm, the theoretical limit was taken as 0.95 when viewing with the normal eye, and 0.95, 0.85, or 0.65 for monkeys G, M, or W when viewing with the paretic eye. These numbers represent the average gain measured after long-term (days) viewing with the paretic eye. The normalized gain data were plotted against number of trials and were fit with exponentials having variable asymptotes and rate constants using the method of least squares.

RESULTS

Basic results from the ISS paradigm

Adaptation using intrasaccadic steps produced reliable changes in saccade gain in all cases, albeit at disparate rates that depended on the target pattern. Figure 1 illustrates typical trials obtained from the pre-, start-, end-, and post-adaptation records ($A$–$D$, respectively) during a session with backward ISSs with the $2 \times 1$ target pattern. With the onset of ISSs ($B$), saccades consistently overshot the primary target position. After about 2,000 trials ($C$) however, saccades were reduced sufficiently in size that many of them accurately acquired the final target position. Cessation of the ISSs ($D$) caused the saccades to severely undershoot the target.
TABLE 1.  Gains and gain changes produced by ISS-adaptation

<table>
<thead>
<tr>
<th>Target pattern</th>
<th>5 × 3</th>
<th>5 × 3</th>
<th>2 × 1</th>
<th>2 × 1</th>
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<tbody>
<tr>
<td>ISS displacement</td>
<td>+20%</td>
<td>−30%</td>
<td>+20%</td>
<td>−30%</td>
</tr>
<tr>
<td>Sessions</td>
<td>n = 9</td>
<td>n = 7</td>
<td>n = 7</td>
<td>n = 6</td>
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</table>

**Horizontal component gains**

| Preadaptation, −130 trials | 0.939 (0.023) | 0.954 (0.028) | 0.920 (0.040) | 0.945 (0.066) |
| Start-adaptation, 0 trials | 0.953 (0.027) | 0.909 (0.038) | 0.956 (0.027) | 0.867 (0.022) |

**Vertical component gain changes (×100)**

| Change at 30', 950 trials | −4.47 (1.7) | 3.56 (2.6) | −7.77 (2.0) |
| Change at 60', 1,900 trials | −8.04 (2.4) | 5.91 (1.3) | −14.3 (1.1) |

Averaged saccade component gains and gain changes (×100) observed preadaptation, at start of adaptation, and at 30 and 60 min (adjusted to correspond to 950 and 1,900 trials respectively). Prestart is 100% difference between pre- and start-adaptation gains. Likewise, postend is 100% difference between post- and end-adaptation gains. Columns tabulate results from each ISS paradigm. Standard deviations are enclosed in parentheses. ISS, intrasaccadic step.

Rapid and very rapid adaptation

As illustrated in Fig. 2, there were sizable differences between the gain measurements obtained during the preadaptation test trials and the trials at the start of adaptation. Compared to the preadaptation gains, the start-adaptation gains were consistently higher during forward-ISS trials and lower during backward-ISS trials. The average size of these differences depended on both the direction of ISS steps and the target pattern in a manner very similar to the rates of change reported above (Table 1). Changes were smallest for the forward-ISS trials using the 5 × 3 pattern (0.0141; 1.5%) and largest for the backward-ISS trials with the 2 × 1 pattern (−0.078; −8.2%). All differences were significantly different from zero (P < 0.025).

Average normalized gain changes of horizontal component produced by adaptation in ISS-paradigm (top) and paretic-muscle paradigm (bottom). A normalized gain of 100 means gain adapted to its theoretical limit. Rate constants are expressed as number of trials. Heading at top of each column identifies target configuration and source of dysmetria. +20% and −30% refer to size of ISSs; N → P means that monkeys had been using their normal eye (N) and patch was switched to paretic eye (P) to observe course of adaptation. Standard deviations are enclosed in parentheses. Sample sizes are the same as in Tables 1 and 3. ISS, intrasaccadic step.
For completeness, the possibility that ISSs had a direct effect on the course of an ongoing saccade was tested in one monkey by interleaving +20%-ISS, -30%-ISS, and 0%-ISS (normal) trials in a pseudorandom order using the 5×3 pattern. This paradigm produced no consistent differences between the gains associated with the +20% and -30%-ISS trials.

**Position-dependent ISS paradigm**

Figure 3 illustrates the results of adapting a monkey using the position-dependent adaptation paradigm. In this paradigm, only leftward saccades directed at targets in the left visual field were associated with backward ISSs, while all other saccades were associated with no ISSs. Figure 3 shows that saccade gain adapted faithfully according to the pattern of ISSs. The gains of end- and postadaptation leftward saccades (● and △) were significantly smaller than the gains of the pre- and start-adaptation control saccades (○ and □). Overall, after adaptation, there was a significant trend for saccades landing further to the left to have lower gains than those landing to the right. At the leftmost (20°) targets, saccade gain was about 20% lower than before adaptation. In contrast, the gains of rightward preadaptation and rightward postadaptation saccades were substantially the same (● and □), as were the gains of rightward start- and end-adaptation saccades (not illustrated).

Data for adapted saccades from all sessions in all monkeys are summarized in Fig. 4 by comparing the slopes of the linear regression lines of saccade gain against target position at the end of the primary step. Slopes have the units of percent-change in saccade size per degree of eccentricity. Figure 4 only illustrates the results of saccades in the adapted (leftward) direction. The gray and the black bars represent the slopes fit to the pre- and start-adaptation data, respectively, and the white and hatched areas represent the incre-
TABLE 3. Gains and gain changes (×100) produced by paretic eye adaptation

<table>
<thead>
<tr>
<th></th>
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<td>N → P</td>
<td>P → N</td>
<td>N → P</td>
<td>P → N</td>
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<tr>
<td>Start-adaptation gain, 0 trials</td>
<td>0.613</td>
<td>1.451</td>
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<td>(0.16)</td>
<td>(0.09)</td>
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<td>Change at 30', 950 trials</td>
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<td></td>
<td>(4.6)</td>
<td>(12)</td>
<td>(3.4)</td>
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<tr>
<td>Change at 60', 1,900 trials</td>
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Averaged gains and gain changes (×100) of horizontal component produced by adaptation in paretic-muscle paradigm. Heading at top of each column identifies target configuration and eye to be adapted. N → P means that monkeys had been using their normal eye (N) and patch was switched to paretic eye (P) to observe course of adaptation. Standard deviations are enclosed in parentheses. For 5 × 3 N → P, n = 3; otherwise, n = 5.

TABLE 3. Gains and gain changes (×100) produced by paretic eye adaptation

The positive slopes fit to the preadaptation data reflect the normal tendency for centripetal saccades (leftward saccades landing at 10° R and 0°) to be slightly larger than centrifugal saccades (those landing at −20° and −10°; cf. Becker 1989). The larger slopes seen at the start of adaptation (cf. monkey S) presumably are the product of the very rapid adaptation that was reported earlier for ordinary ISS adaptation. The existence of a positive slope indicates that the gain change was graded with the size of the ISS at each eccentricity rather than being uniformly depressed.

The main point of Fig. 4 is that the position-dependent adaptation paradigm produced a significant, or significantly greater, tendency for the gain of leftward saccades to decrease in association with more leftward target positions. On average, postadaptation slopes were larger than preadaptation slopes by 0.46%/deg (±0.19 SD) and end-adaptation slopes were larger than start-adaptation slopes by 0.47%/deg (±0.17). Hence on average, saccades to the 20°-left targets were 9.5% smaller than those to 0°-targets after adaptation. Within-session comparisons were all significant at the P < 0.05 level and most (14/17) were significant at the P < 0.01 level or better.

In the unadapted (right) direction, pre- versus post-, and start- versus end-adaptation slopes were usually negligibly different from each other or from zero. The mean postpreadaptation difference was 0.003 ± 0.120 and the mean end-start adaptation difference was 0.013 ± 0.127. Only once did the slope differences approach magnitudes found in the adapted direction (0.215 ± 0.228), but this and the other smaller differences were never statistically significant (P > 0.05).

Paretic-muscle paradigm

In the paretic-muscle paradigm, monkeys viewed their environment for several days while wearing a patch over either the normal or the paretic eye. Switching the patch to the other eye and requiring the monkey to follow targets landing on the 2 × 1 or 5 × 3 grid produced significant within-session changes in saccade gain in all cases (Table 3). As seen in Fig. 5, when monkeys were forced to use their normal eye after previous adjustment to using their paretic eye, the gains of horizontal saccades were initially very high (top, Paretic → Normal; Table 3). Over the course of a few thousand trials, saccade gain declined and became almost equal to that obtained after long-term viewing with the normal eye. Exponentials fit to the normalized data from individual sessions with the 2 × 1 target pattern all reached an asymptote of about 100% (nonnormalized gain = 0.95). With the 5 × 3 target pattern, saccade gain declined more slowly and usually did not reach the 100% theoretical limit. In fact, exponential fits only twice had asymptotes near 100% and the fit asymptotes for all sessions averaged 80% (Table 2; nonnormalized gain = 1.16). At the end of the experimental session, the patch was switched back to the paretic eye to compare pre- and postadaptation gain changes in that eye.

When monkeys were forced to use their weak eye after previous adjustment to using their normal eye, saccade gain increased, albeit very slowly (Fig. 5, bottom, Normal → Paretic). Saccade gain never reached an asymptotic value within the experimental session. Exponential fits to the normalized data revealed long time constants of over 3,000 trials and asymptotes slightly over 70%. When the patch was switched back to the normal eye at the end of the experimental session, the raw gain changes were always smaller in the paretic eye than in the (just adapted) normal eye, as would be expected because eye movements are smaller in general in the paretic eye. In normalized values, the gain of saccades measured in paretic eye changed 60%, which compares favorably with the average 80% change measured in the normal eye.

When monkeys were forced to use their weak eye after previous adjustment to using their normal eye, saccade gain increased, albeit very slowly (Fig. 5, bottom, Normal → Paretic). Saccade gain never reached an asymptotic value within the experimental session. Exponential fits to the normalized data revealed long time constants of over 3,000 trials and asymptotes slightly over 70%. When the patch was switched back to the normal eye at the end of the experimental session, the raw gain changes were always larger than in the (just adapted) paretic eye. Again, this would be expected from the relative mobility of the two eyes. In normalized values, the gain measured in the normal eye changed 47%, which is just slightly larger than the average 44% change measured in the paretic eye. The small differences found between the normalized gains in the normal and paretic eye are probably the product of nonlinearities in the paretic eye and not monocular adaptation (Snow et al. 1985).

The rates of adaptation obtained under different conditions were compared as they were for the standard ISS-paradigm. Normalized gains were used for these comparisons to compensate for the wide variations in initial gain. Gain increases produced by viewing with the paretic eye were equally slow whether using the 2 × 1 or the 5 × 3 target pattern. As listed in Table 2 (bottom), gain changes were very similar at the 950- and 1900-trial benchmarks and the time constants were also similar. Gain decreases produced by viewing with normal eye were significantly faster than the gain increases for both the 2 × 1 and 5 × 3 target patterns (P < 0.05). Comparing the rates of gain decrease for the two target patterns, the rate was significantly slower with the 5 × 3 pattern according to the 950-trial 1900 trial, and time-constant measures (P < 0.05 to P < 0.01).

A major goal of this study was to compare the rates of adaptation produced by the paretic-muscle paradigm with those produced by the ISS paradigm under similar conditions. Comparing the data in Table 2, it is obvious that the rates were comparable and certainly not different by an order of magnitude. In fact, the rates for the gain decreasing experiments are nearly identical (columns 2 and 4). For both the 2 × 1 and 5 × 3 pattern, normalized gains at the 950 and
1,900-trial benchmarks differed by only a couple percent and the time constants were similar: 794 and 820 trials for ISS and paretic-muscle paradigms, respectively. These measures differed more for the gain-increasing experiments, but usually not substantially. The data show that with the $5 \times 3$ pattern, the paretic-muscle paradigm produced slightly faster adaptation than did the ISS-paradigm, while the opposite was true for the $2 \times 1$ pattern (columns 1 and 3).

**DISCUSSION**

The results of this study support the hypothesis that adaptation of saccade gain by the ISS-paradigm and the paretic-eye paradigm share the same adaptive mechanisms. The major objection to this hypothesis was that the rates of adaptation produced by each paradigm seemed to be extremely different (Optican 1985; Optican and Robinson 1980). The current experiments provide an explanation for this apparent difference, and show that when examined under similar circumstances, adaptation produced by the two paradigms have similar features. The first experiment showed that the rate of adaptation became slower as the complexity of the target array increased and, in fact, was extremely slow when produced by gain-increasing forward ISSs using the most complex ($5 \times 3$) target pattern. This situation is most comparable to previous studies with the paretic-muscle paradigm in which gain increases occurred as monkeys or humans scanned the multiplicity of targets provided by the real world (Able et al. 1978; Kommerell et al. 1976; Optican et al. 1985; Optican and Robinson 1980). The third experiment showed that the rate of adaptation produced with the paretic-muscle paradigm had a similar dependence on target complexity. Moreover, a direct comparison of the rates of adaptation produced by each paradigm, using targets of the same complexity, showed that they are similar and, in fact, adaptation using the paretic-muscle paradigm could sometimes be slightly faster. Hence the point is no longer tenable that differing rates produced by the two adaptation paradigms must reflect the existence of separate adaptation mechanisms. Finally, the results of the position-dependent ISS paradigm show that adaptation produced by the ISS paradigm possesses a capacity required for adaptation to naturally occurring extraocular muscle paresis, namely the capacity to adjust saccade size according the location of the target in head-referenced space (Optican et al. 1985).

**Dependence of adaptation rate on the complexity of the target array**

The first experiment showed that backward ISSs produced gain decreases more rapidly than forward ISSs produced gain increases, as was shown by others in monkeys and humans (Deubel 1987; Straube et al. 1997; Straube and Deubel 1995). More importantly, the experiment showed that both forward and backward ISSs produced gain changes more slowly with the $5 \times 3$ target pattern than with the $2 \times 1$ pattern. Quantitatively, gain increases were about 47% slower and gain decreases were 36% slower. A similar trend was reported for human subjects (Miller et al. 1981). The rate dependence on the number of targets is a direct consequence of the finding reported by others that adaptation is relatively specific to the size, direction, and position of the adapting target steps (Albano 1996; Deubel 1987; Frens and van Opstal 1994, 1997; Miller 1981; Straube et al. 1997). Adaptation produced by exposure to target steps of a single size and direction transfers (generalizes) only to saccades directed at targets having similar sizes and directions. Frens and van Opstal (1994) described this restricted region as
the “adaptation field.” In contrast, if adaptation were mediated by parametric gain control, all trials would produce the same incremental gain change for all saccades regardless of the size, direction, or position of the target step. Because this is not the case, the total number of trials is divided among the different adaptation fields. This causes each adaptation field to receive less exposure to the adapting stimuli and saccades directed at that field will change gain proportionally less.

Considering the current results, it is not clear what dimension (size, direction, or position) was most responsible for the reduced adaptation rate with the $5 \times 3$ target pattern, but collectively, evidence indicates all were important. There has never been any debate that adaptation of saccades to target steps of one direction generalizes poorly to saccades of other directions (Deubel 1987; Frens and van Opstal 1994; Straube et al. 1997). A possible reduction in the transfer of gain changes to saccades that differ in size from the adapted size has been more controversial (Deubel et al. 1986; Wolf et al. 1984), but the majority of the more recent studies using monkeys and humans have clearly shown such transfer is limited (Albano 1996; Frens and van Opstal 1994, 1997; Straube et al. 1997). A reduction in the transfer of adaptation to saccades outside the trained position in space has been the hardest to demonstrate (Albano 1996; Semmlow et al. 1989). Probably, the nervous system is predisposed to transfer adaptation to a wide region of space, but will restrict adaptation to a specific region when such transfer is contraindicated. For instance, in the position-dependent ISS paradigm, the large ISSs that accompany target steps to $20^\circ$ left produced adaptation at that location, which might have transferred to other target positions in the absence differential training. The smaller ISSs associated with target steps to these other positions, however, indicate to the nervous system that the transfer of such a large gain change is inappropriate. In this circumstance, the nervous system clearly manages to restrict the transfer and to grade the amount of adaptation on the basis of the landing position of the primary target step.

**Rate of adaptation: from very rapid to very slow**

A consistent finding in these experiments was that the gain measured during preadaptation trials (no ISSs) differed from that measured during start-adaptation trials (with ISSs). The direction and magnitude of these changes correlated with the direction and magnitude of the longer-term within-session changes and so were quite sizable with the $2 \times 1$ target pattern. Experiments showed that this was a very rapid form of adaptation, which took place within the space of 20 or so trials.

Indications of such rapid adaptation have been seen in other monkey studies (Fuchs et al. 1996; Straube et al. 1997) but have not been systematically examined. A valid question is why such changes, which could be quite large, have not been reported more often. A methodological answer may lie in the common practice of analyzing the data by generating a scatter plot of saccade gain against trial number and fitting the entire data set with an exponential. The initial rapid drop would be fit as part of the exponential and the discontinuity in rate obscured by the large scatter of saccade gains. A more intriguing answer is that it has been seen and corresponds to the very rapid changes seen in some human experiments (Erkelsens and Hulleman 1993; McLaughlin 1967; Miller et al. 1981; Semmlow et al. 1989; Wiesfeld 1972). As in the current study, the very rapid changes were most prominent when there were only two target locations and the subjects simply made saccades back and forth. The normalized gain changes were smaller in monkeys ($-7.77/ -30\%$ ISS = 26\%, Table 1) than in humans ($-40\%$ to $-70\%$) (Abrams et al. 1992; Albano 1996; Albano and King 1989; Erkelsens and Hulleman 1993; Miller et al. 1981; Semmlow et al. 1989), but not so much as to preclude the possibility that rapid gain changes in both species were produced by similar mechanisms. The proposal that monkeys and humans share this form of very rapid adaptation is consistent with the idea that other differences between monkey and human saccade adaptation (cf. Deubel 1987) are simply quantitative and not qualitative.

In the body of the session, the rate of change measured by the rate constants of the exponential fits ranged from an average of $800 - 5,000$ trials. In comparing these rates with the results of other studies, it is important to remember that the trial counts include target steps of many sizes and directions. So for backward ISSs with the $2 \times 1$ target pattern, the gain of rightward saccades declined with a rate constant of $400 (800/2)$ trials, as did the gain of leftward saccades. Despite the greater predictability of target locations in our study, these rates are comparable to those observed in other monkey studies using target steps of a fixed size (Deubel 1987; Fuchs et al. 1996; Straube et al. 1997). Similarly, the 830-trial rate-constant observed for gain increases of leftward and rightward saccades ($1,660/2$) is also comparable to rate constants seen in these same studies. Rate constants for the $5 \times 3$ target pattern cannot be compared with other studies because similar experiments have not been done.

There may be adaptation at rates still slower than those observed during the body of the training session. In the gain-decreasing experiment, the asymptotic gains approached the theoretical limit, but this was not observed in all published experiments, and was definitely not observed by us or others in gain-increasing experiments. Adaptation was projected to stop after gains reached $\sim 75\%$ of their ideal value. Note that this is not the result of the normal tendency for saccades to undershoot, as this was taken into account by the normalization procedure. Nor is it possible that adaptation had reached the limits of its capacity, because much larger gain changes were observed in the paretic-muscle experiments. The proposition that adaptation ceases at a nonideal value leads to the dissatisfying conclusion that the nervous system is willing to tolerate large saccadic errors. An alternative explanation for the seeming asymptotes is that adaptation was still occurring, but at a slower rate. In fact, one must reach this conclusion for the paretic-muscle experiments because saccade gains did ultimately reach their theoretical limits; these limits were defined as the final gains achieved after long-term viewing.

**Short- and long-term mechanisms**

Previously, questions about the mechanisms of saccadic adaptation were framed in terms of the paradigms used to
produce adaptation. “Short-term” adaptation was the product of the ISS paradigm and “long-term” adaptation was the product of the paretic-muscle paradigm. This study shows that the paradigm is irrelevant when considering the existence of long- and short-term mechanisms of adaptation. Indeed, it is difficult to see why the nervous system would care whether dysmetria were produced by displacing a target or by muscle tenectomy. Both interventions result in a visual error and require a corrective saccade to reach the target [but see Miller et al. (1981) for a discussion of the theoretical importance of proprioception]. But, having dissociated the paradigm from the issue of short- and long-term adaptation, the question still remains whether or not there are separate short- and long-term mechanisms. The current experiments may not address this issue, because it is likely that adaptation in the paretic-muscle paradigm, as currently conducted, invoked the same short-term mechanisms as did the ISS-paradigm. On the other hand, as argued above, there is reason to believe that both paradigms invoke a spectrum of mechanisms from very rapid to very slow.

An issue closely related to the separate existence of short- and long-term mechanisms is the idea that they might be mediated at different anatomic sites. Long-term adaptation, as induced using the paretic-muscle paradigm, is dependent on the integrity of the cerebellum (Optican and Robinson 1980). The locus of short-term adaptation, as induced by the ISS-paradigm, is uncertain. Fitzgibbon et al. (1986) thought it might be upstream of the superior colliculus, because the size of saccades evoked by microstimulation of the superior colliculus were not modified after the size of visually evoked saccades was adaptively changed. Moreover, they argued that inflections in the velocity profiles of partially adapted saccades were the product of programming of two nearly simultaneous saccades. Similar velocity inflections were seen in our experiments during gain-decreasing adaptation with the paretic-muscle paradigm, but were mainly evident when the monkeys were not fully aroused. The evidence implicating the superior colliculus is not compelling however, because the same group also found that short-term adaptation was abolished after large lesions of the fastigial nucleus (Goldberg et al. 1993). This would seem to indicate that the cerebellum also mediates short-term adaptation. Moreover Frens and van Opstal (1997) found that neuronal discharges in the superior colliculus did not change during short-term adaptation using the ISS paradigm. Although it could be the case that both long- and short-term adaptation each reside at more than one site, we wish to consider the possibility that both do take place in the cerebellum.

A comparable model where this might be true is adaptation of the vestibuloocular reflex (VOR). The behavioral situations that produce VOR adaptation are analogous to those that produce saccade adaptation, but the sites that might mediate VOR adaptation have been more thoroughly examined. VOR adaptation is an enduring phenomenon that is frequently produced as subjects make normal head and eye movements while they wear the appropriate optical devices (Melvill Jones 1985; Miles and Eighmy 1980). This is analogous to having monkeys or patients naturally view the world while their nonparetic eye is patched. On the other hand, enduring VOR adaptation can also be rapidly produced by using the same optical devices and continuous forced vestibular stimulation, or by simulating the visual-vestibular conflict produced by these devices using optokinetic and smooth pursuit stimuli (Lisberger et al. 1984; Scudder and Fuchs 1992). This is, of course, similar to the rapid adaptation produced in this and similar experiments. A final similarity is that gain increases proceed more slowly than gain decreases (Miles and Eighmy 1980). Regarding the site of plasticity, VOR adaptation, whether short or long-term, was shown to require the cerebellum (Lisberger et al. 1984; Robinson 1976; Zee et al. 1981) and neurophysiological changes that might be the source of VOR gain changes were recorded in the vestibulocerebellum and its target structure, the vestibular nucleus (Lisberger et al. 1994a,b). Thus the changes that accompany adaptation would seem to be limited to the cerebellum and its deep nuclei, and the different rates in adaptation may reflect different cellular mechanisms acting at perhaps different synapses within the same system (Crepel and Jailard 1991; Ito 1989; Linden et al. 1991; Llano et al. 1991; Racine et al. 1986).

The idea that short-term, as well as long-term adaptation of saccade size is mediated by the cerebellum fits with known physiology. The existence of “adaptation fields” (Frens and van Opstal 1994) indicates that short-term adaptation takes place in a structure receiving retinotopically place-coded information. Neurons in the brainstem saccadic burst generator are not place coded (cf. Fuchs et al. 1985) so it is very unlikely that adaptation occurs there. Neurons in the superior colliculus are place coded, but for adaptation to take place there, it might require a rapid and massive reorganization of the numerous inputs that converge from many cortical areas to produce a modified sensory-motor transformation (Sparks and Hartwich-Young 1989; Wurtz and Albano 1980). Moreover, this modified transformation would need to vary with eye position in the orbit to produce the results of the position-dependent ISS paradigm. The recent findings of Frens and van Opstal (1997) confirm the absence of any neural correlates of adaptation in the superior colliculus. The “oculomotor vermis,” on the other hand, receives place-coded input from other structures (Crandall and Keller 1985; Ohtsuka and Noda 1992) as well as information about eye position in the orbit via mossy-fiber inputs (Kase et al. 1980). Although eye-position information is only weakly encoded at the output of the cerebellum in normal animals (Fuchs et al. 1993), it could be used when needed e.g., to compensate for severe orbital nonlinearities produced by paresis of one extraocular muscle. The inflections in saccade velocity that were sometimes observed here and elsewhere (Fitzgibbon et al. 1986), as well as the consistently observed alterations in saccade dynamics (Albano and King 1989; Straube and Duebel 1995; Straube et al. 1997) are probably the product of incompletely coordinated cerebellar input signals arriving from different sources (Melis and van Gisbergen 1996) and cerebellar output signals directed at different neuronal pools in the pontine saccadic burst generator (Noda et al. 1990). Finally, the cerebellum is an intricate structure possessing many levels, types of cells, and types of synapses, and is accordingly richly endowed with a variety plastic mechanisms (Crepel and Jailard 1991; Ito 1989; Linden et al. 1991; Llano et al. 1991; Racine et al. 1986). In summary, there is ample reason to
consider that all adaptation in the saccadic system takes place in the cerebellum and that the spectrum of adaptation rates reflects a spectrum of plastic mechanisms.

This work was supported by National Eye Institute Grants EY-09210 and P30 EY-08098 and the Eye and Ear Institute Foundation of Pittsburgh. Address for reprint requests: C. A. Scudder, Dept. of Otolaryngology, University of Pittsburgh, 200 Lothrop St., Pittsburgh, PA 15213.

Received 15 May 1997; accepted in final form 14 October 1997.

REFERENCES


ADAPTATION OF SACCADE SIZE


