

Facilitation of saccadic adaptation by the memory of previous learning.

(先行学習によるサッケード適応の促通)

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Introduction

Saccades, rapid shifts in the direction of gaze, enable the primate to acquire a visual target with the fovea. Because of the small size of the fovea, efficient collection of visual information depends heavily on the accuracy of saccades. Unlike somatic movements such as reaching of the arm, saccades are too fast for visual feedback to guide their trajectory. Saccades must therefore be preprogrammed in advance of their execution, and in this sense are under open-loop control. The saccadic system possesses an off-line error correction mechanism, called saccadic adaptation, that recalibrates the saccadic gain (saccade amplitude / target eccentricity) constantly and thus ensures movement accuracy in the face, for example, of altered plant mechanics (Hopp and Fuchs, 2004; Optican and Robinson, 1980). If saccades consistently fall short of the target, as may result from damage to an extraocular muscle, their amplitude gradually increases until the target is acquired again with a single movement. Similarly, if saccades consistently overshoot the target, they gradually become smaller to reduce the error that must be corrected after the primary movement.

Saccadic adaptation can be induced experimentally with a paradigm that creates a visual error by stepping the target during saccades (McLaughlin, 1967). This intrasaccadic step (ISS) paradigm has been used successfully to reveal several important characteristics of adaptation. First, adaptation elicited by the ISS paradigm has a roughly exponential course with a rate constant of 100-800 saccades in monkeys (Scudder et al., 1998; Straube et al., 1997) and 30-60 saccades in humans (Albano, 1996; Deubel et al., 1986, 1987; Frens and van Opstal, 1994). The amount and rate of adaptation are highly variable across subjects and also across experiments in the same subject (Fuchs et al., 1996; Straube et al., 1997). Second, a visual error present in a short period immediately after saccades has been shown to be a crucial stimulus for the induction of adaptation in both human and nonhuman primates (Fujita et al., 2002; Noto

and Robinson, 2001; Shafer et al., 2000; Wallman and Fuchs, 1998). Third, adaptation is fairly specific to the amplitude and direction of adapted saccades and does not generalize fully to those with different vectors in monkeys (Noto et al., 1999; Straube et al., 1997; Wallman and Fuchs, 1998; Watanabe et al., 2000) as well as in humans (Albano, 1996; Frens and van Opstal, 1994; Miller et al., 1981; Semmlow et al., 1989). The specificity of saccadic adaptation has an important implication as to the site of plasticity and is thought to indicate that adaptation occurs before saccadic signals are broken into horizontal and vertical components (Deubel, 1987). Finally, repeated exposures to the same paradigm over days (i.e., practice) do not cause faster or greater changes in saccade amplitude (Straube et al., 1997).

It is known that eye blink conditioning, another example of motor learning, exhibits a phenomenon called savings. Re-exposure to paired stimuli after extinction induces reacquisition that is much faster than original acquisition (Frey and Ross, 1968; Napier et al., 1992), indicating that a memory of learning is formed to facilitate subsequent learning. I wondered whether the saccadic system indeed lacks such a memory mechanism. One factor that might have masked possible effects of practice in saccadic adaptation is large day-to-day variability in its speed and magnitude (Fuchs et al., 1996; Straube et al., 1997).

In the study that will be described in chapter 1, I attempted to clarify whether repeated induction of adaptation within single experimental sessions affects the course of learning. I addressed this question by using the double reversal paradigm, a series of three alternating gain changes, which eliminates part of the complications related to the variability. Results show that saccadic adaptation occurs faster when repeated within single experiments, suggesting the storage of learning history. This chapter also gives some insights into the erasure process of this memory of adaptation.

The study in chapter 1 only examined adaptation of saccades in a horizontal direction. It is unknown whether adaptation of saccades in one direction exerts any

influence on subsequent adaptation of saccades in a different direction. Clarifying spatial properties of the facilitating effect of adaptation might give us a clue to how adaptation is facilitated, just as the characteristics of adaptation fields have provided insight into the adaptation mechanism.

In the study described in chapter 2, I examined the effects of adaptation of horizontal or vertical saccades on subsequent adaptation of oblique saccades, as well as the amount of transfer of the original adaptation to oblique saccades. The relative rate of adaptation of the horizontal and vertical components was found to depend on the direction of saccades in the original adaptation.

Methods

Surgery

Two rhesus monkeys (*Macaca mulatta*, male) were prepared for eye movement recording by the magnetic search coil method (Fuchs and Robinson, 1966). Anesthesia was introduced with ketamine hydrochloride (15-20 mg/kg, i.m.) and maintained by inhalation of isoflurane. A coil of Teflon-coated stainless steel wire was implanted beneath the insertions of the four recti of one eye to measure eye movements. Stainless steel tubes were attached to the skull with bone screws and dental acrylic. During experiments, rigid metal rods were inserted to the tubes for painless immobilization of the animal's head. After surgery, antibiotics were given intramuscularly for 5 days to prevent infection. After recovery from the surgery, the monkeys were trained to follow a small jumping target (a red spot displayed on a video monitor) with the eye. All surgical and experimental protocols were approved by the Animal Care and Use Committee at the University of Tsukuba.

During recording sessions, the monkey sat in a primate chair in a darkened booth with its head restrained (Fig. 1). The animal was required to make saccades toward a target spot ($\sim 0.3^\circ$) presented on a monitor screen, which was 35.5 cm from its eyes. Whenever the monkey maintained its eye position within 1.5° of the target continuously for 0.8-1.0 sec, the target jumped to another position and the animal was rewarded with a small amount of apple juice. The animal followed the target spot reliably for several thousand trials in a single experiment, which lasted 1-1.5 hours.

Behavioral paradigms

Adaptive changes in saccade amplitude were induced by a conventional intrasaccadic target step paradigm (McLaughlin, 1967) (Fig. 2). The animal was exposed to a target that jumped along the horizontal meridian and then, during the

saccade, stepped backward or forward by a fixed percentage of the initial step (intrasaccadic step, ISS). This created a visual error at the end of the movement as if the saccade had been too large or too small, requiring the animal to make a corrective saccade to catch the target. This procedure, when repeated over several hundreds of movements, gradually decreased or increased the saccade gain (movement size / target eccentricity) (Fig. 3, Fig. 4). I adapted saccades that were elicited by horizontal 10° steps of the target. Only saccades in one direction (either left or right) were adapted in each experiment. The target stepped pseudorandomly in either direction within a movement range of 40° (within 20° of the straight ahead position).

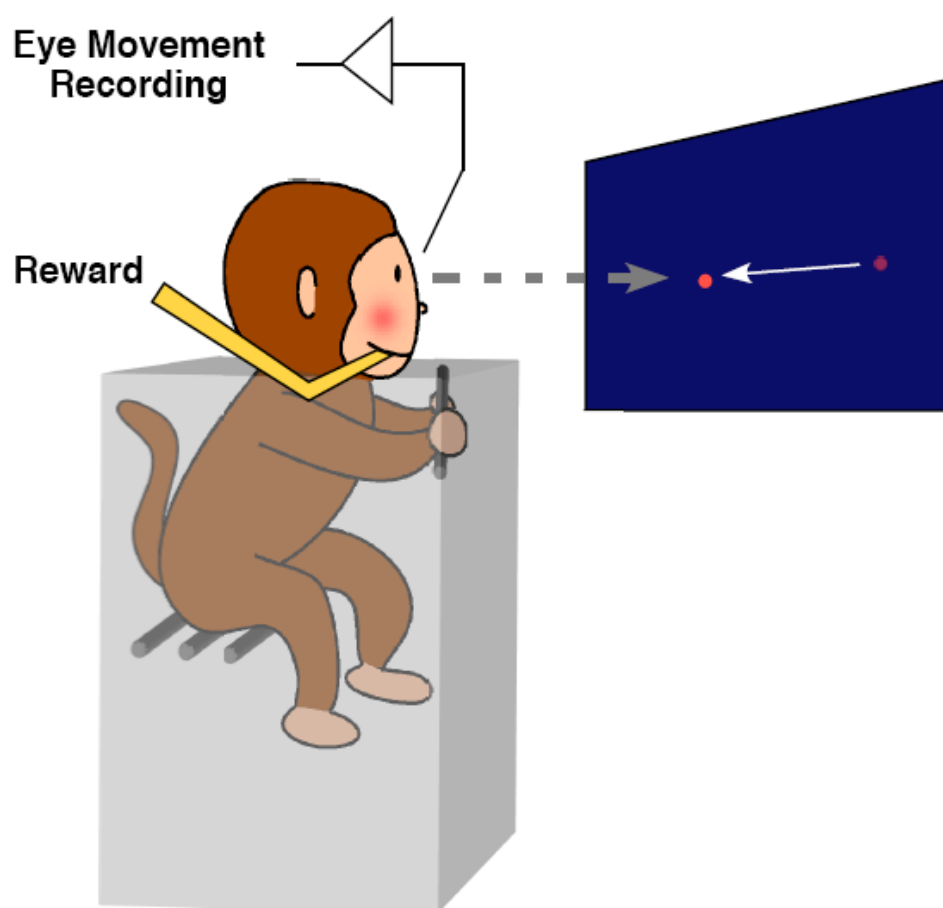


Figure 1

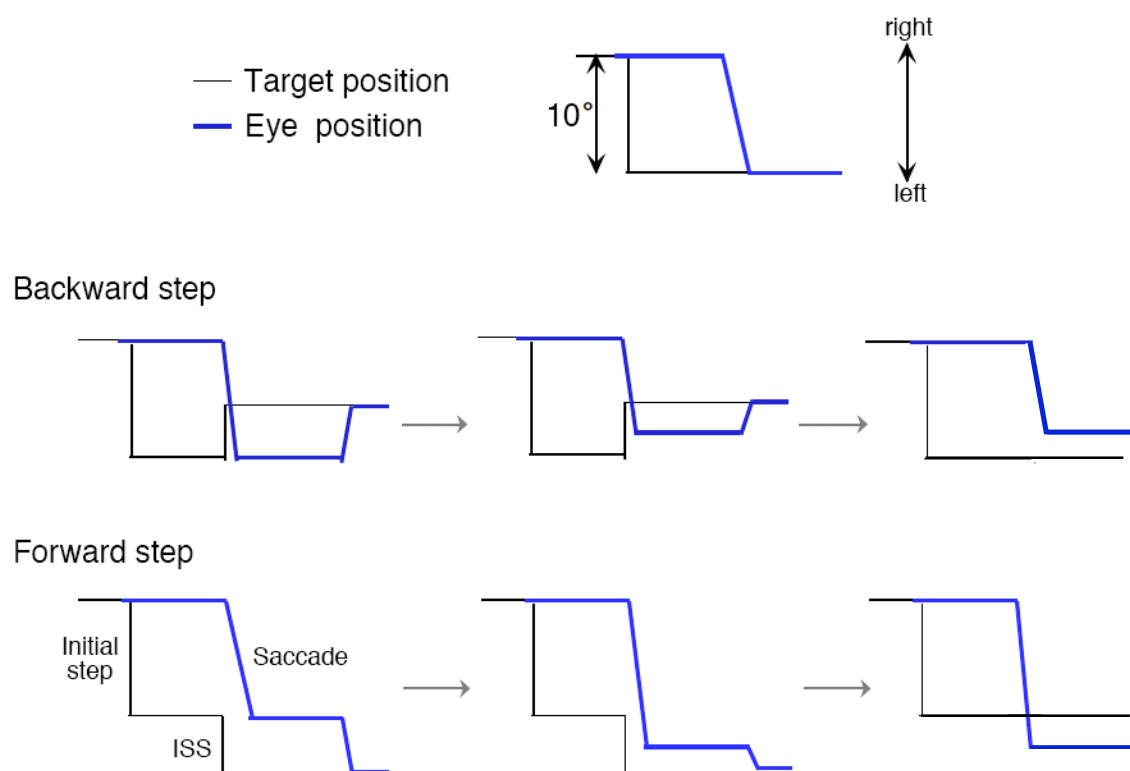
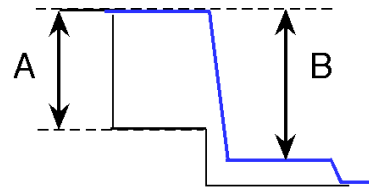


Figure 2



$$\text{Saccadic Gain} = \frac{B}{A}$$

A: Target eccentricity

B: saccade amplitude

Figure 3

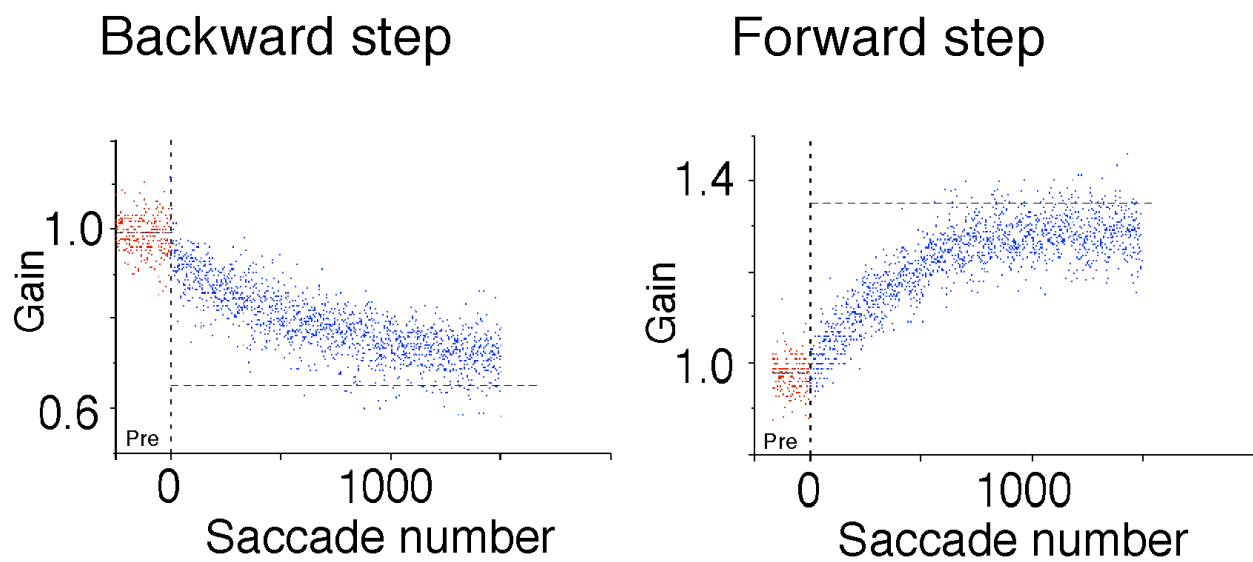


Figure 4

Chapter 1

Memory of Learning Facilitates Saccadic Adaptation in the Monkey.

Abstract

A motor learning mechanism, called saccadic adaptation, ensures accuracy of saccades throughout life in spite of growth, aging and some pathologies of the oculomotor plant or nervous system. The present study investigates effects of preceding adaptation on the speed of subsequent adaptation during single experiments. Adaptive changes in gain (movement size / target eccentricity) were induced by intrasaccadic step (ISS) of the target. After the gain was altered (control block), I reversed the direction of ISS to bring the gain back to ~ 1.0 (recovery). I then reversed ISS direction again to induce another adaptation (test block). Analyses revealed that the gain changed at a higher rate in the early part of test adaptation than in the corresponding part of control. At ~ 100 - 300 th saccade in the test block, adaptation slowed down. The gain value at which adaptation slowed was correlated with the gain achieved in the control. I further examined effects of a 30-min intervention, inserted between recovery and test blocks. When zero-visual-error trials (~ 700 saccades) were repeated during this period, the rate of test adaptation was similar to that of control. In contrast, when the animal was deprived of visual inputs during this period, test adaptation was still influenced by preceding learning. I conclude that a memory of previous learning remains during recovery to facilitate subsequent adaptation and that such a memory does not disappear merely with time but is erased actively by repeated zero-error movements. Our results, which cannot be explained by a single mechanism, suggest that the saccadic system is equipped with more than one plasticity processes.

Introduction

Saccades are rapid eye movements that shift the direction of gaze. They are so fast, and therefore brief, that visual feedback cannot be used to guide their trajectory. Therefore, without some error correcting mechanism, alterations of mechanical properties of the oculomotor plant, for example, would inevitably lead to the generation of inaccurate saccades. In reality, saccades remain accurate throughout life in spite of growth, aging and some pathologies of the plant or the nervous system. This is because the saccadic gain (saccade amplitude/target eccentricity) is constantly recalibrated by a learning mechanism called saccadic adaptation (Hopp and Fuchs, 2004 for review). If saccades consistently overshoot the target, their amplitude gradually decreases. If they consistently fall short, their size gradually increases. There is good evidence that saccadic adaptation is a form of motor learning driven by visual error immediately after the end of saccades (Wallman and Fuchs, 1998; Shafer et al., 2000; Noto and Robinson, 2001).

Characteristics of saccadic adaptation in the monkey, as well as in humans, have been studied extensively. Adaptation elicited by an intrasaccadic step of the target (McLaughlin, 1967) has a roughly exponential course with a rate constant of 100-800 saccades (Straube et al., 1997; Scudder et al., 1998). The amount and rate of adaptation are highly variable across animals and also across experiments in the same animal (Fuchs et al., 1996; Straube et al., 1997). Adaptation is fairly specific to the amplitude and direction of adapted saccades and does not generalize fully to those with different vectors (Straube et al., 1997; Wallman and Fuchs, 1998; Noto et al., 1999; Watanabe et al., 2000). Finally, repeated exposures to the same paradigm over days, i.e., practice, do not cause faster or greater changes in saccade amplitude (Straube et al., 1997).

It is known that eye blink conditioning, another example of motor learning,

exhibits a phenomenon called savings. Reexposure to paired stimuli after extinction induces reacquisition that is much faster than original acquisition (Frey and Ross, 1968; Napier et al., 1992), indicating that a memory of learning is formed to facilitate subsequent learning. I wondered if the saccadic system indeed lacks such a memory mechanism. One factor that might have masked possible effects of practice in saccadic adaptation is large day-to-day variability in its speed and magnitude (Fuchs et al., 1996; Straube et al., 1997). In the present study, I attempted to clarify whether repeated induction of adaptation within single experimental sessions affects the course of learning. I addressed this question by employing the double reversal paradigm, a series of three alternating gain changes, which eliminates part of the complications related to the variability. Results show that saccadic adaptation occurs faster when repeated within single experiments, suggesting the storage of learning history. The present study also gives some insights into the erasure process of this memory of adaptation. Preliminary accounts of the present study have appeared elsewhere (Kojima et al., 2002, 2003a, b).

Materials and Methods

Surgery

Two rhesus monkeys (*Macaca mulatta*, male, 4.5 and 6.8 kg) were prepared for eye movement recording by the magnetic search coil method (Fuchs and Robinson, 1966). Anesthesia was introduced with ketamine hydrochloride (15-20 mg/kg, i.m.) and maintained by inhalation of isoflurane. A coil of Teflon-coated stainless steel wire was implanted beneath the insertions of the four recti of one eye to measure eye movements. Stainless steel tubes were attached to the skull with bone screws and dental acrylic. During experiments, rigid metal rods were inserted to the tubes for painless immobilization of the animal's head. After surgery, antibiotics were given intramuscularly for 5 days to prevent infection. After recovery from the surgery, the monkeys were trained to follow a small jumping target (a red spot displayed on a video monitor) with the eye. All surgical and experimental protocols were approved by the Animal Care and Use Committee at the University of Tsukuba.

During recording sessions, the monkey sat in a primate chair in a darkened booth with its head restrained. The animal was required to make saccades toward a target spot ($\sim 0.3^\circ$) presented on a monitor screen, which was 35.5 cm from its eyes. Whenever the monkey maintained its eye position within 1.5° of the target continuously for 0.8-1.0 sec, the target jumped to another position and the animal was rewarded with a small amount of apple juice. The animal followed the target spot reliably for several thousand trials in a single experiment, which lasted 1-1.5 hours.

Behavioral paradigms

Induction of saccadic amplitude adaptation Adaptive changes in saccade amplitude were induced by a conventional intrasaccadic target step paradigm (McLaughlin, 1967). The animal was exposed to a target that jumped along the horizontal meridian and then,

during the saccade, stepped backward or forward by a fixed percentage of the initial step (intrasaccadic step, ISS). This created a visual error at the end of the movement as if the saccade had been too large or too small, requiring the animal to make a corrective saccade to catch the target. This procedure, when repeated over several hundreds of movements, gradually decreased or increased the saccade amplitude. I adapted saccades that were elicited by horizontal 10° steps of the target. Only saccades in one direction (either left or right) were adapted in each experiment. The target stepped pseudorandomly in either direction within a movement range of 40° (within 20° of the straight ahead position).

Double reversal paradigm In 30 experiments, I induced a series of three alternating gain changes by reversing the polarity of visual error twice during on-going adaptation. After collecting 100-400 preadaptation saccades to horizontal steps of the target, I started the first block of adaptation session by subjecting the animal to 35% forward or backward ISS (control block). When the gain was altered by ~ 0.1 - 0.2 after 400-800 saccades, the direction of ISS was reversed to bring the gain back to the preadaptation value, i. e., ~ 1.0 (recovery block). Then I reversed the ISS direction again and induced a gain change using the ISS of the same size as in the control block. This last block of the session (test block) contained a larger number of saccades than the control block. Figure 1 schematically illustrates these procedures for gain increase (A) and gain decrease (B) adaptation. These paradigms will be called the *standard gain-increase* or *gain-decrease paradigms* as opposed to their modifications described below.

Modified paradigms In 44 experiments, I subjected the animal to one of 5 modified versions of the standard paradigm. In the *zero-error paradigm*, I discontinued the ISS of the target when the gain returned to ~ 1.0 at the end of recovery block and required the animal to continue to track the target for 30 min. During this period, saccadic gain was kept at ~ 1.0 , with the average end point error nearly zero. I then resumed the ISS with the same size and direction (test block) as in the control adaptation. In the *dark*

paradigm, I placed the animal in the dark by gently covering its head and the upper portion of the primate chair with a large piece of black cloth. I kept the animal alert by making noises or tapping the booth and continuously monitored our monkey's eye movements. After 30 min, I removed the cloth and subjected the monkey again to the ISS with the same size and direction as in the control adaptation. In 5 gain-increase experiments, I employed what I call *dark no-ISS paradigm*, in which target steps were not followed by ISS during the test block. The 7 paradigms used in the present study are summarized in Figure 1C.

Analysis

Horizontal and vertical components of eye position and target position were digitized on line at 1 kHz and stored in a hard disk with an interface (Micro1401, CED). Data were analyzed off-line on a computer (Power Macintosh G4, Apple) using homemade programs that ran on a software (Spike2, CED). Saccade onset and end were defined by an eye velocity threshold criterion of $20^\circ/\text{s}$. Targeting saccades elicited by an initial (not intrasaccadic) target step were selected for analysis. The computer stored parameters of saccades and target steps, i.e., positions, timings, and peak eye velocities. These parameters were exported to statistics programs (StatView or JMP, SAS inc.) to calculate other saccade characteristics. The *target eccentricity* was defined as the difference between the target and the eye positions at the saccade onset. The *gain* of a saccade is defined as the ratio of the horizontal saccade size to the horizontal target eccentricity. Saccades with latencies less than 60 ms were regarded as anticipatory and removed. I also removed saccades with gains > 2.0 or < 0.35 . The number of these eliminated saccades was ~20-30, less than 2% of the total number of saccades (> 2500) in the relevant direction. For each experiment, I plotted the saccadic gain as a function of the accumulated number of saccades during which the target was stepped. The rate of adaptation in the control and test blocks was estimated by the slope of linear

regression line fitted for 150 consecutive saccades.

Results

Data were collected in a total of 74 experiments using two animals. In 30, I employed standard double reversal paradigms (see Methods) to compare the courses of control and test adaptations. The *start gain difference* had a mean of 0.012 ± 0.047 ($n = 30$), indicating that the two adaptations started with similar gains. In the remaining 44 experiments, I subjected the monkeys to either the zero-error paradigm or dark paradigm.

Standard double reversal paradigms

Faster learning in the initial part of test adaptation In many experiments, the initial portion of test adaptation appeared to exhibit a faster gain change than that of control adaptation. Figure 2A shows the gain change profile of a standard gain-increase experiment, in which the gain was increased to ~ 1.2 , decreased to ~ 1.0 , and then increased again with 35% ISS. Note that gain changes faster in the initial part of the test block than in the initial part of the control block. I observed similar accelerated adaptation also in gain-decrease experiments, an example of which is shown in Figure 2B. Here, the gain was decreased to ~ 0.85 , brought back to ~ 1.0 , and decreased again with 35% ISS. The initial fall of the saccadic gain in the test is steeper than that in the control adaptation.

To test statistically whether there is a significant difference in the rate of adaptation between the test and control blocks, I wanted to choose the appropriate number of data points that could be used for all experiments and also was adequate for estimation of the adaptation rate. For this, I had to make a compromise. The faster gain change appeared to occur over the initial ~ 100 -300 saccades in the test block. To estimate the adaptation rate in this facilitated portion of test adaptation, therefore, it is desirable to take a small number of saccades. On the other hand, because of

saccade-to-saccade variability in gain, estimation would be more reliable for increasing number of saccades. I plotted the slope of the linear regression line as a function of the number of data points (20-300) for each experiment. In many experiments, variation in the slope increased markedly as the number of saccades decreased below ~100, suggesting that reliable estimation of the rate of adaptation requires more data points. Based on these considerations, I regarded the gain change rate obtained for the initial 150 saccades as a representative value for each block.

For estimation of the rate of adaptation, linear regression lines are fitted for the control and test blocks in Fig. 2A. Test adaptation shows a larger slope (6.9×10^{-4} /saccade) than the control (4.0×10^{-4} /saccade). Figure 2C shows gain change rates for all gain-increase experiments in monkey K ($n = 6$) and monkey I ($n = 8$). In both animals, the test adaptation had a significantly larger rate than the control adaptation (Wilcoxon signed rank test, $p < 0.05$). The ratio of adaptation rate, the test rate divided by the control rate, had a mean of 1.56 ± 0.32 and 1.59 ± 0.62 for monkeys K and I, respectively. This is an average increase of ~60% over the control rate. An example of the fitted regression lines for gain-decrease experiments is shown in Figure 2B, the slope being -8.9×10^{-4} /saccade and -5.0×10^{-4} /saccade in the test and control, respectively. Figure 2D summarizes the results of gain-decrease experiments. In monkey K (Fig. 2D, left), the absolute value of the gain change rate in the test was significantly larger than that in the control adaptation (Wilcoxon signed rank test, $p < 0.05$). The ratio of adaptation rate had a mean of 1.68 ± 0.85 ($n = 9$), indicating an average increase in adaptation rate of 70% over the control rate. In monkey I (Fig. 2D, right), there was no significant difference in gain change rate between the test and control ($p = 0.50$). However, the ratio of adaptation rate exhibited a mean of 1.42 ± 0.73 ($n = 7$).

The size of the increase in adaptation rate was variable across experiments as seen in Figure 2C, D. The test-control difference in the absolute value of rate of

adaptation ranged widely from -2.26 to 5.19 ($\times 10^{-4}$ /saccade) with a mean of 1.62 ± 1.81 ($\times 10^{-4}$ /saccade) ($n=30$, positive values indicating faster test adaptation). Test adaptation was faster than control adaptation in 25 experiments and slower in the remaining 5 experiments. The test-control ratio of adaptation rates ranged from 0.61 to 3.61 with a mean of 1.57 ± 0.66 ($n = 30$).

Slowing of adaptation The results described above indicate that adaptation occurs faster when repeated at a short interval. This increased adaptation rate was observed only over the initial ~100-300 saccades and did not continue throughout test adaptation. The saccade number at which this facilitation ended appeared to vary across experiments. I wondered what might determine or influence the end of the faster adaptation. To visualize the course of adaptation, I fit data points with a variable span smoother (Supersmoother, StatView). In several experiments, the facilitated portion appeared to end so abruptly as to exhibit an inflection on the smoothed curve, as exemplified by two gain-increase experiments in Figure 3A (arrows). The control adaptation resulted in a higher gain in Figure 3A-a than in 3A-b. Correspondingly, the inflection in the test adaptation occurred at a higher gain in Figure 3A-a than it did in 3A-b. This suggested a possibility that the gain at the end of facilitation (*facilitation end gain*) was positively correlated to the gain at the end of control adaptation (*control final gain*).

To test this possibility, I had to define the control final gain and facilitation end gain. I calculated the *control final gain* as the average of gains of the last 50 saccades in the control block. To calculate the facilitation end gain, I used the following procedures. As a measure of "instantaneous" rate of adaptation, I set a window of 150 saccades and calculated the slope of the linear regression line for the window. I started with the 1st to 150th saccades and assigned the slope of a line fit to these saccades to the 75th saccade. I then moved the window by one saccade,

calculated the slope for the next 150 points (2nd to 151st), and assigned it to the 76th saccade. This procedure was repeated until a slope value was assigned to the 300th saccade. I then compared such slope profiles of the control and test adaptations. Figure 3B (top) shows an example of slope profiles calculated for a gain-increase experiment. At the beginning of the block, the test adaptation (black) has a larger slope than the control adaptation (gray). The slope of the test adaptation then gradually decreases to cross the control profile between the 218th and 219th saccades. I regarded this crossing point, where the rate of test adaptation fell below that of control adaptation, as the facilitation end. The *facilitation end gain* for this particular experiment was then obtained as an average of gains of 50 consecutive saccades distributed equally before and after the facilitation end (i. e., 194th to 243rd). As shown in Figure 3B (bottom), the crossed trace method appears to pick a reasonable, if not unique, point that is not too deviated from the inflection on the smoothing curve (black).

I performed a similar analysis for experiments in which the slope for the initial 150 saccades of the test block was steeper than that of the control block (see Fig. 2C, D). In all such experiments (13 of 14 gain-increase and 11 of 16 gain-decrease), the slope profile of test adaptation decreased below that of control adaptation. After its initial high rate, test adaptation proceeded at a rate lower than that of the control adaptation. The saccade number at which the two curves crossed ranged from 82 to 291 (mean = 141.1 ± 45.8) in gain-increase experiments and 82 to 331 (mean = 213.0 ± 89.7) in gain-decrease experiments. Finally, I plotted the *facilitation end gain*, calculated as described above, against *control final gain* (Fig. 3C). There was a significant positive correlation between the two parameters both for gain-increase and gain-decrease adaptations in each monkey ($p < 0.05$).

Modified double reversal paradigms

To further characterize the facilitated learning described above, I investigated the course of adaptation in zero-error and dark paradigms (Methods). For the ease of description, results obtained in gain-decrease experiments are presented first.

Gain-decrease experiments with zero-error paradigm In 9 gain-decrease experiments, I subjected the animal to 10° target steps not coupled with ISS when the saccadic gain returned to ~1.0 by the recovery adaptation. Figure 4A shows the result of one experiment. The gain was first reduced to ~0.85 by backward ISS and brought back to ~1.0 by forward ISS. I then discontinued the ISS and required the monkey to make normometric saccades in the adapted direction for 30 min (~790 saccades). After this zero-error block, the gain was again decreased by backward ISS. As shown by the regression lines in Figure 4A, their slopes were similar for the test and control (-5.7×10^{-4} /saccade and -6.1×10^{-4} /saccade, respectively). Figure 4B shows the results of all the 9 experiments for the two monkeys. The length of the zero-error block was fixed at 30 min across these experiments. The number of "zero-error" saccades made in the relevant direction during this block ranged from 574 to 877. There was no significant difference in gain change rate between the test and control for each animal as well as for the two animals combined (Wilcoxon signed rank test, $p = 0.70$, $n = 5$ in monkey K; $p = 0.50$, $n = 4$ in monkey I; $p = 0.44$, $n = 9$ in both animals). The results indicate that the test adaptation is not accelerated after hundreds of normometric saccades.

Gain-decrease experiments with dark paradigm I then examined the effect of deprivation of visual inputs on the subsequent adaptation. Figure 5A shows the result of a gain-decrease experiment, in which the animal was placed in the dark for 30 min after the gain returned to ~1.0 at the end of the recovery block. I continuously

monitored the animal's eye movements during this "dark" block. The monkey was kept alert and made saccades of a variety of size and direction. It was, however, unable to hold the eye at any location and showed continuous drift of the eye (not shown). I therefore assumed that during the dark block there were no visual targets to which the monkey could make saccades. After 30 min period in the dark, test adaptation still occurred at a higher rate than control adaptation (Fig. 5A). This was confirmed quantitatively by a steeper slope of the regression line for the test adaptation than that of the control adaptation (-7.2×10^{-4} /saccade and -3.5×10^{-4} /saccade, respectively). Figure 5B summarizes the results of 14 experiments conducted with the dark gain-decrease paradigm. In monkey K (Fig. 5B, left), the test block showed a significantly faster gain change than the control block ($p < 0.01$, $n = 9$), a similar result to that in the standard experiments (see Fig. 2D, left). The ratio of adaptation rates had a mean of 1.44 ± 0.41 , indicating an average increase by $\sim 40\%$. In monkey I, although the test-control difference did not reach a significant level ($p = 0.07$), the test block exhibited faster adaptation in all 4 experiments (Fig. 5B, right). The ratio of the test rate to the control rate exhibited a mean of 2.47 ± 0.96 , showing an average increase by $\sim 150\%$.

I examined whether, in this dark paradigm, the initial faster gain change was followed by slower gain change as in the standard paradigm. Figure 5C shows a smoothed function fitted to the same data in Figure 5A. It is clear that adaptation suddenly slowed down and resulted in an inflection on the smoothed curve (arrow). As in standard paradigms, I analyzed the course of the rate of adaptation for experiments in which the initial slope of the test block was steeper than that of the control block. Again, in all such experiments (7 and 4 for monkeys K and I, respectively), the slope profile of the test adaptation decreased to cross that of the control adaptation. The saccade number at the crossing point ranged from 103 to 281 (mean = 179.4 ± 65.2 , $n=11$). Figure 5D shows the relation between the

facilitation end gain and the control final gain. In monkey K, the two parameters were found to be significantly correlated in this dark gain-decrease paradigm (Fig. 5D, left, $p < 0.01$) as was the case with the standard paradigm. The data in monkey I was consistent with such a correlation but not significant. (Fig. 5D, right, $p = 0.1$).

Gain-increase experiments with zero-error paradigm The effect of zero-error saccades in gain-increase experiments was similar to that in gain-decrease experiments. Figure 6A illustrates the result of one experiment. After the gain returned to ~ 1.0 , the animal was required to make saccades to target steps not followed by ISS for 30 min (~ 780 saccades in the relevant direction). The regression lines fitted for the initial 150 data points in the control and test blocks had similar slopes, 4.4×10^{-4} and 4.2×10^{-4} /saccade, respectively. Figure 6B summarizes the results of 8 experiments. The number of zero-error saccades made in the relevant direction during the 30-min zero-error block ranged from 574 to 877. There was no significant difference in gain change rate between the test and control for each animal as well as for the two animals combined (Wilcoxon signed rank test, $p = 0.50$, $n = 4$ in monkey K; $p = 0.50$, $n = 4$ in monkey I; $p = 0.99$, $n = 8$ in both animals). The result indicate that the gain-increase adaptation is not accelerated after hundreds of normometric saccades, as was the case with gain-decrease adaptation (cf. Fig.4).

Gain-increase experiments with dark paradigm The result of this paradigm was not a simple mirror image of gain-decrease adaptation. Figure 7A-a shows a gain change profile for one experiment in monkey K. As indicated by a vertical open arrow, the test adaptation started with a gain that was clearly higher than the gain at the end of the recovery block. The average gain of the initial 50 saccades in the test block was higher than that of the last 50 saccades in the recovery block by 0.08. Such discrepancies in gain, or apparent "jumps" in gain as I call them below, were more

pronounced in the other animal. In one experiment in monkey I, the jump in gain was as large as 0.16 (Fig. 7A-b). However, similar jumps in gain might also be present in other paradigms. In fact, the standard gain-increase experiment shown in Figure 3A-b, for example, appears to exhibit some jump in gain at the beginning of test adaptation. I therefore tested quantitatively whether the jump in gain in the dark gain-increase paradigm is indeed larger than that in other paradigms. For standard and dark paradigms, the jump in gain was estimated by the same method as described above. For zero-error paradigms, I used the average gain of the last 50 saccades of the zero-error block for that of the recovery block. Figure 7C shows the jump in gain calculated for each paradigm. All paradigms showed positive jumps, i. e., changes in gain in the same direction as the ISS. The jump in gain in the dark gain-increase paradigm was significantly larger than that in any other paradigm in both animals (MANOVA Scheffé, $p < 0.05$). There was no significant difference between any two of the remaining paradigms. The large, apparent gain jump at the beginning of the test adaptation was thus specific to the dark gain-increase paradigm.

Observing this apparent increase in gain, one might suspect that the gain of the saccadic system gradually increased from ~ 1.0 to a higher value during the dark block. To test this possibility, I required the animal in the test block to make saccades to target steps not followed by ISS. If the above explanation were true, I should observe an increased gain at the beginning and a subsequent recovery toward 1.0. This, however, did not happen. The gain remained constant at ~ 1.0 throughout this no-ISS test block as if the gain had been held constant during the dark block (Fig. 7B). The results of 5 dark no-ISS experiments confirmed the reproducibility of this phenomenon (double hatched bars in Figure 7C). The jump in gain in the dark no-ISS paradigm was significantly smaller than that in the dark gain-increase paradigm (MANOVA Scheffé, $p < 0.05$) and similar to those in other paradigms.

Discussion

Our data provided evidence for the storage of learning history during saccadic amplitude adaptation. First, test adaptation occurred faster than control adaptation. In standard paradigms, the gain was brought back close to the preadaptation gain before test adaptation. If the saccadic system, too, had returned to the pre-learning state, test adaptation would have occurred in the same fashion as control adaptation. Clearly, this was not the case. Furthermore, this accelerated learning did not continue throughout test adaptation but ended in relation to the final gain of control adaptation. Our results thus suggest that learning history is stored during adaptation and that this memory facilitates subsequent adaptation.

A previous study on the characteristics of saccadic adaptation has reported that repeated induction did not result in faster adaptation on different days (Straube et al., 1997). The gain change rate in control adaptation in our study, too, did not show any obvious increase over different experiments (unpublished observation). Our study, however, showed a facilitatory effect of repetition within single experiments. If learning history is retained, as I concluded above, why does it not affect the next adaptation on a different day? The results of our zero-error paradigm may explain, at least partly, this apparent discrepancy. After making ~700 nearly normometric saccades, test adaptation was no longer faster. This suggests that the memory of adaptation lost its facilitatory action on subsequent learning, most likely because it was erased. Presumably, in our study as well as in the study by Straube et al. (1997), erasure of memory may have occurred after recovery, where saccades were accompanied by no consistent visual error.

The faster adaptation was followed by slowing (Fig. 3). Analysis of the rate of adaptation indicated that, after facilitation end, test adaptation was slower than control adaptation. These results, together with a linear relationship between

facilitation end gain and control final gain, suggest that the physiological function of the memory of adaptation may not merely to increase the rate of learning. Rather, the memory might be regarded as a mechanism to bring the gain quickly to that achieved in preceding adaptation and hold the gain at that level.

Erasure and retention of the memory of adaptation

The results of our modified paradigms provide clues to the nature of the process underlying the accelerated motor learning. In zero-error paradigms, the memory of learning clearly did not fade away merely with time, because gain-decrease adaptation was accelerated after the animal was placed in the dark. The memory thus appeared to be erased actively as the animal made normometric saccades. Exposures to visual errors whose sizes were nearly zero may have played a key role in this erasure process. Such visual stimuli could signal disappearance of the need for adaptation, resetting the saccadic system to the preadaptation state. Alternatively, maintaining the gain at a pre-learning value (~ 1.0) for hundreds of saccades, rather than the exposure to zero visual error, might have been more important in promoting the erasure. If I could somehow maintain the gain at ~ 1.0 while exposing the animal to consistent visual error, the memory of adaptation might still be erased. It requires further studies to discriminate between these possibilities.

The memory of previous adaptation did not remain after 30 min of zero-error block, during which the animal made several hundred saccades. It might seem surprising that only 30 minutes of zero-error saccades can erase previous learning. Note, however, that only saccades to horizontal 10° target steps were adapted, recovered, and readapted in the present experiment. Previous studies have shown that adaptation is relatively specific to the size and direction of target eccentricity (Deubel et al., 1987; Semmlow et al., 1989; Frens and van Opstal, 1994; Straube et al., 1997; Noto et al., 1999; Watanabe et al., 2000). It has been demonstrated that adaptation progresses

more slowly when the subject is exposed to adapting target steps of a variety of sizes and directions in humans (Miller et al. 1981) and monkeys (Scudder et al. 1998). This, as these authors pointed out, is a direct consequence of the spatial specificity of adaptation. Saccades to a particular target eccentricity could be influenced only by saccades to similar target eccentricities. Thus, far more trials are needed to adapt movements to many different target eccentricities than those to a single, fixed eccentricity. With the same logic, if the facilitation of adaptation also had similar specificity, the erasure of the memory of adaptation for target eccentricities of a variety of vectors, as may occur in physiological situations, would require a greater number of normometric saccades and therefore a longer time than in the present experiment.

Our data suggest that the memory of forward adaptation was not merely retained but processed further during the dark block in gain-increase paradigm. Instead of accelerated adaptation, staying in the dark produced a jump-like increase in gain that was significantly larger than that in any other paradigm (Fig. 7C). Furthermore, the gain did not show such a large increase when tested with no ISS (Fig. 7B). Two explanations may be possible for this apparent increase in gain. The first assumes that the gain was held constant near 1.0 during darkness. Facilitatory effects of the memory, nevertheless, were enhanced to such an extent during darkness that it produced in the test block an extremely fast adaptation that was completed within a very small number of saccades. To test this possibility, I calculated average gains of the first 5, 10 and 20 saccades. They were significantly higher than those of the same number of saccades at the recovery end (Wilcoxon signed rank test, $p < 0.01$, $n = 9$) by similar amounts, 0.089, 0.091 and 0.096, respectively. The average course of gain change (means across 9 experiments) suggested that the gain did not change rapidly from ~ 1.0 but jumped at the very start of the test block. These results make the first possibility unlikely. Alternatively, the saccadic system created a gain state of > 1.0 during the dark block while simultaneously retaining the gain state of 1.0. The system

could then switch between the two states depending on visual errors it encountered at the beginning of the test block. Whatever the mechanism, it seems likely that consolidation-like processing of the memory takes place during darkness in a time-dependent manner. This contrasts with the erasure process, discussed above, which appeared to depend on the number of trials rather than time. Finally, it should be noted that only gain-increase, not gain-decrease, adaptation exhibited the jump in gain, for which I currently do not have any plausible explanation.

Possible mechanisms of accelerated learning in saccades

I will speculate below where and how saccadic adaptation might be facilitated on the basis of recent findings including those on other forms of cerebellar-dependent motor learning. The oculomotor vermis and the fastigial oculomotor region (FOR) of the cerebellum have been shown to be a key player in saccadic adaptation (Optican and Robinson, 1980; Takagi et al., 1998; Barash et al., 1999; Scudder, 2002; Inaba et al., 2003; Scudder and McGee, 2003). A recent study has further demonstrated that adaptation occurs upstream of the FOR (Robinson et al., 2002). I suggest here two general schemes for the accelerated learning in saccades. The first scheme is similar to that proposed for savings in eye blink conditioning. Medina et al. (2001) have suggested that plastic changes occur not only in the cerebellar cortex but also in the cerebellar nucleus during initial acquisition. The nuclear plasticity survives extinction and can later contribute to fast reacquisition. For saccadic adaptation, our first scheme assumes that a plasticity mechanism like long-term potentiation is activated gradually during control adaptation in the cerebellar nucleus, in addition to the one such as long-term depression (LTD) in the cortex (Fig. 8A-a). In the subsequent recovery block, the cortical plasticity decreases back to and possibly beyond the preadaptation level, as has been suggested for the extinction of eye blink conditioning (Medina et al., 2001), but the nuclear plasticity remains potentiated. Test adaptation then progresses

faster because the effect of cortical plasticity is now augmented by the residual plasticity downstream in the nucleus.

The second scheme assumes oppositely-directed plastic processes that could enhance each other. Blocking nitric oxide signaling in the goldfish cerebellum (Li et al., 1995) and use of a novel behavioral paradigm in mice (Boyden and Raymond, 2003) have both suggested separate plasticity mechanisms for increases and decreases in VOR gain. Similarly, the second scheme for saccadic adaptation assumes separate plasticity mechanisms in the cerebellar cortex for increases and decreases in gain (Fig. 8A-b). Figure 8B-a, taking our gain-decrease paradigm as an example, illustrates how such dual processes might combine to accelerate saccadic motor learning. In the control block, gain change (black solid line) is achieved only by activation of gain-decrease mechanism (broken line). During recovery, gain-increase mechanism (gray solid line) begins to be activated and, simultaneously, gain-decrease mechanism (broken line) now recovers toward the initial baseline level. At the beginning of test adaptation, the net gain change is zero because of equal contributions of two mechanisms. In the early part of the test block, reactivation of gain-decrease mechanism and recovery of gain-increase mechanism work together to accelerate gain decrease (facilitation). Because deactivation of gain-increase mechanism stops when it recovers to baseline, the slowing of adaptation will result, showing an inflection on the gain profile (black solid line). In this scenario, results of zero-error and dark paradigms, too, can be explained, respectively, by return of two mechanisms to baseline (Fig. 8B-b) and by retention of partial activation of both mechanisms at the end of the recovery block (Fig. 8B-c). The deactivation of plasticity mechanisms that does not progress beyond baseline that I postulate is not pure speculation. Recent results describe a previously unrecognized form of long-term potentiation in the cerebellar cortex (Lev-Ram et al., 2002) and a synaptic depotentiation in the hippocampus (Montgomery and Madison, 2002). Similar mechanisms could underlie the saccadic adaptation. Recently, a specific

mechanism for acceleration and slowing of saccadic adaptation has been proposed in a theoretical model (Fujita, 2003a, b), which postulates a map of visual error in the cerebellar cortex. It can explain our results by LTD and its deactivation (de-LTD) occurring simultaneously at different sites in the oculomotor vermis.

It should be noted that neither model explains the jump-like increase in gain observed in the dark gain-increase experiment. Note also that the present study does not rule out other possibilities, including extra-cerebellar mechanisms. Nevertheless, our results strongly suggest that the saccadic adaptation system can recruit more than one plasticity processes when the need arises, enabling previous learning to affect subsequent learning.

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Figure and figure Legends

Figure 1. A, B: Illustration of standard double reversal paradigm for gain-increase adaptation (A) and gain-decrease adaptation (B). First, adaptation was induced by 35% forward (A) or 35% backward (B) ISS (control block). The direction of ISS was reversed to bring the gain back to ~ 1.0 (recovery block). Then I reversed the ISS direction again and induced a gain change (test block) using the ISS of the same size and direction as in the control block. I adapted saccades elicited by horizontal 10° target steps in one direction. C: Summary of 7 paradigms used in the present study.

Figure 2. A: Gain change profile of a gain-increase experiment with linear regression lines fitted for the first 150 saccades of control and test blocks. The slope of test adaptation was larger than that of control. B: Gain change profile of a gain-decrease experiment with similar regression lines. Note the steeper slope of test adaptation. C, D: Summaries of gain change rate for gain-increase experiments (C) and gain-decrease experiments (D). Test adaptation has a significantly higher rate than control adaptation except for gain-decrease experiments in monkey I. Data shown in A and B are indicated by small horizontal arrows in C and D, respectively.

Figure 3. Slowing of adaptation. A: Gain change profiles for two gain-increase experiments, in which accelerated adaptation appears to end abruptly to produce inflections (arrows) on the fitted curves (Supersmoother, StatView). Control adaptation in A-a exhibits a higher gain than that in A-b. Correspondingly, the gain at facilitation end in test adaptation in A-a is higher than in A-b. B: Estimation of facilitation end gain for the experiment in A-a. Profile of instantaneous rate of gain change, slopes of linear regression line for 150-saccade moving window plotted as a

function of saccade number (top). Slope of test adaptation (black) was initially larger but decreases beyond that of control adaptation (gray). The crossing point was regarded as facilitation end. Facilitation end gain was calculated as the average gain of 50 saccades distributed about facilitation end (bottom). C: Relation between facilitation end gain and control final gain. There was a significant positive correlation between the two parameters both in gain-increase adaptation (left) with $p < 0.05$, $r = 0.86$, $n = 6$ for monkey K, $p < 0.05$, $r = 0.77$, $n = 7$ for monkey I and in gain-decrease adaptation (right) with $p < 0.05$, $r = 0.76$, $n = 7$ for monkey K, $p < 0.01$, $r = 1.00$, $n = 4$ for monkey I. Data shown in A-a and A-b are indicated by small horizontal arrows (labeled a and b, respectively) in C.

Figure 4. A: Gain change profile of a zero-error gain-decrease experiment with linear regression lines fitted for the first 150 saccades of the control and test blocks. B: Summary of all experiments with this paradigm in two monkeys. There was no significant difference in gain change rate between the test and control. Data shown in A is indicated by a small horizontal arrow in B, monkey K.

Figure 5. A: Gain change profile of a dark gain-decrease experiment with linear regression lines fitted for the first 150 saccades of the control and test blocks. The slope of test adaptation is steeper than that of control. B: Summary of all experiments with this paradigm in two monkeys. Test adaptation has a significantly larger rate than control adaptation. Data shown in A is indicated by a small horizontal arrow in B, monkey K. C: Slowing of test adaptation seen as an inflection (arrow) on the fitting curve (Supersmoother, StatView). D: Relation between facilitation end gain and control final gain. The facilitation end gain was calculated by the same method as for standard paradigm data (see Fig. 3B). There was a significant positive correlation between the two parameters in monkey K (left, $p < 0.01$, $r = 0.88$, $n = 7$). The relation

did not reach a significant level in monkey I (right, $p = 0.1$, $r = 0.90$, $n = 4$). Data shown in C is indicated by a small horizontal arrow in D, monkey K.

Figure 6. A: Gain change profile of a zero-error gain-increase experiment with linear regression lines fitted for the first 150 saccades of the control and test blocks. B: Summary of all experiments with this paradigm in two monkeys. There was no significant difference in gain change rate between the test and control. Data shown in A is indicated by a small horizontal arrow in B, monkey K.

Figure 7. A: Gain change profiles of dark gain-increase experiments in monkey K (A-a) and monkey I (A-b). Test adaptation starts with a gain that is higher than the gain at recovery end. Height of open arrows indicates this jump in gain, which is 0.08 and 0.16 for A-a and A-b, respectively. B: Gain change profile of a dark No-ISS experiment. In contrast to A, the No-ISS test block starts with a gain that is similar to the gain at recovery end. C: Jump in gain shown as a bar chart with SD for each paradigm in the two monkeys. Positive values represent gain changes in the same direction as the ISS. The jump in the dark gain-increase paradigm (asterisk) was significantly larger than that in any other paradigm in both animals.

Figure 8. Possible mechanisms for facilitated adaptation. A: Postulated sites of plasticity in two general schemes. a. A memory of learning forms in the cerebellar nucleus during control adaptation and remains during recovery. During test adaptation, this memory amplifies the effect of plasticity process occurring in the cerebellar cortex, resulting in accelerated adaptation. b. Increases and decreases in gain depend on separate plasticity mechanisms in the cerebellar cortex. B: Schematic illustrations of how the two oppositely-directed mechanisms, assumed in A-b, might produce acceleration and subsequent slowing of adaptation observed in the present study. a.

Standard gain-decrease paradigm. In the early phase of test adaptation, reactivation of gain-decrease process (broken line) combined with deactivation of gain increase process (gray solid line) produces accelerated gain change (black solid line). When gain increase process recovers fully to baseline, it stops being deactivated and can no longer contribute to overall gain change, resulting in slowing of adaptation (inflection on the gain curve). b. Zero-error paradigm. Erasure of memory is realized by simultaneous deactivation of the two mechanisms to baseline. c. Dark paradigm. Both mechanisms remain partially activated during the dark block, exhibiting acceleration and slowing in the test block.

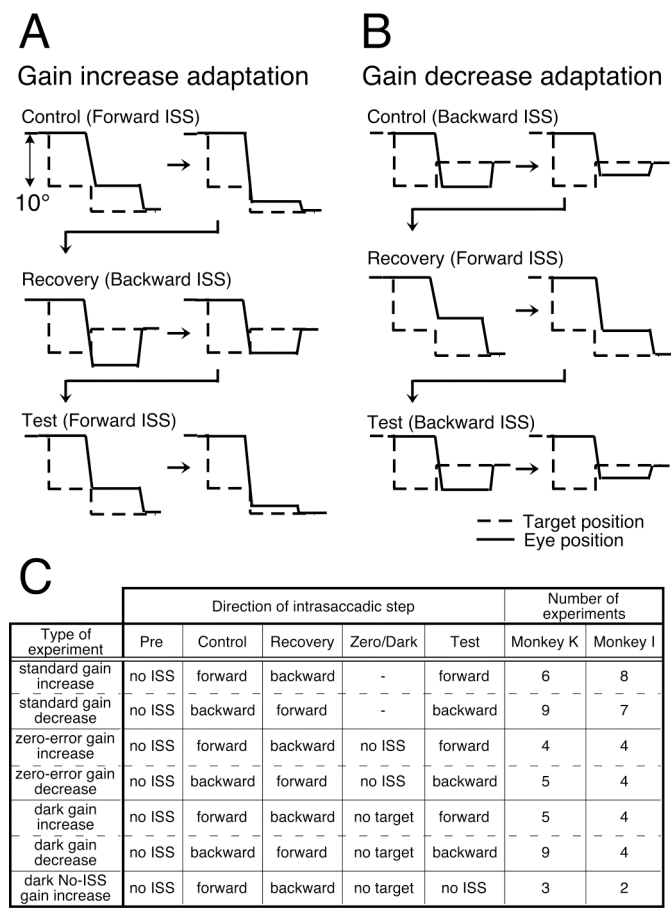


Figure 1

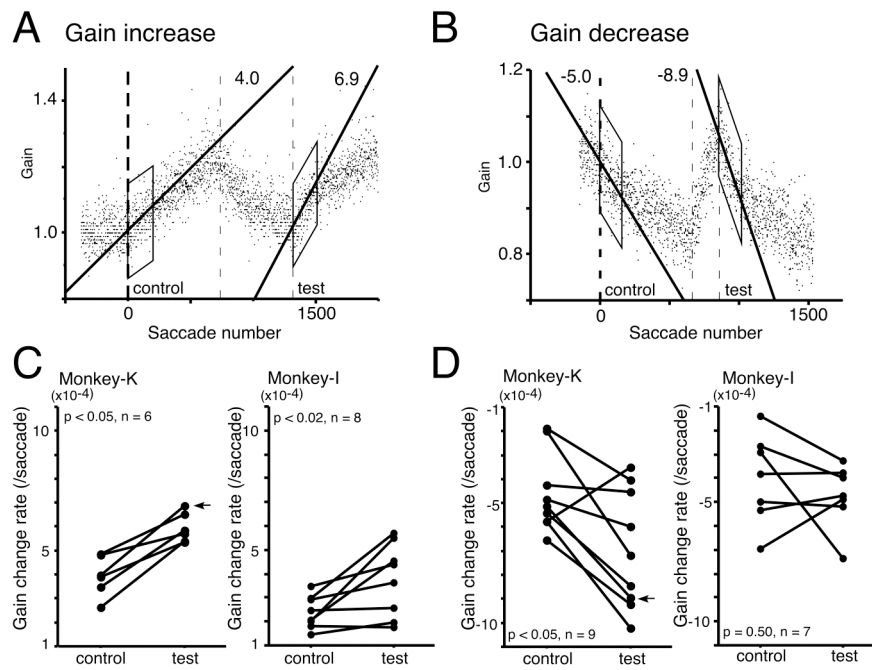


Figure 2

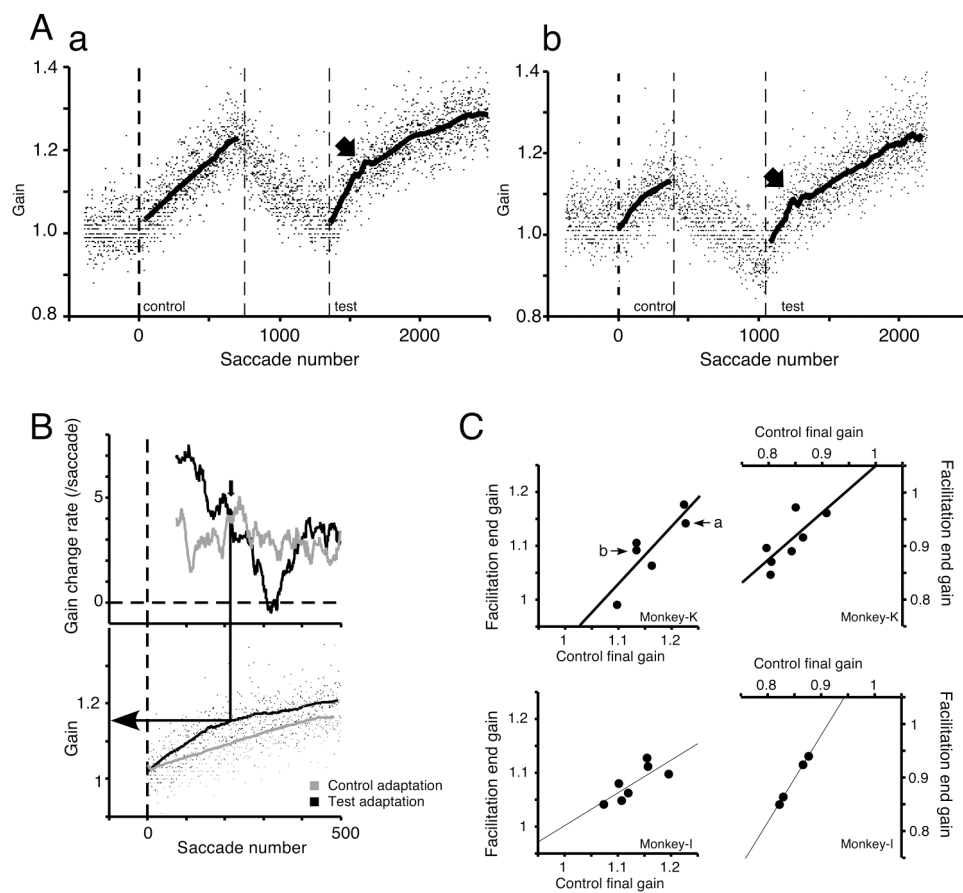


Figure 3

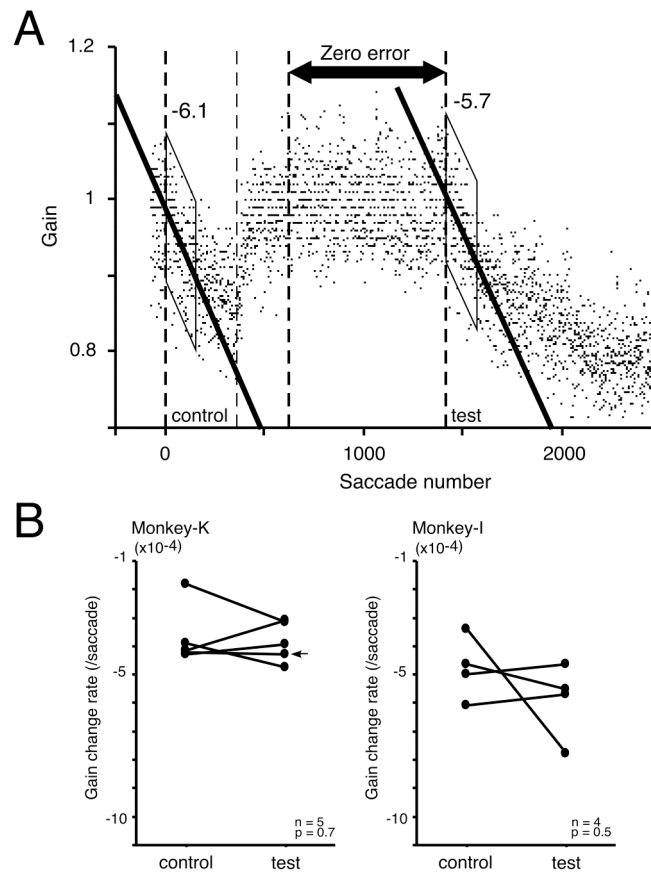


Figure 4

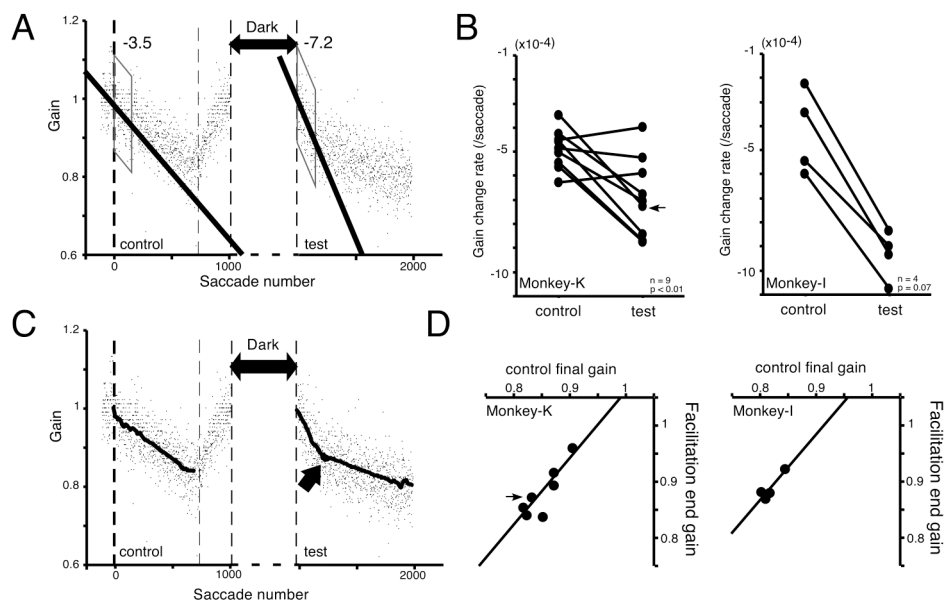


Figure 5

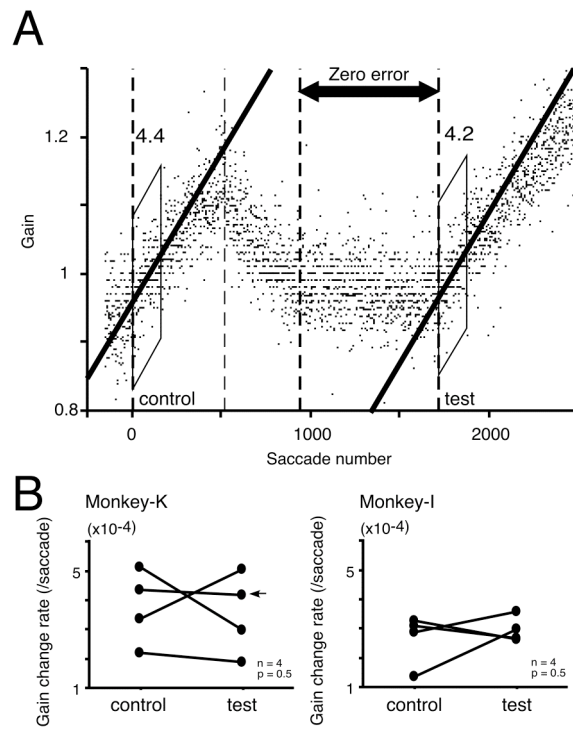


Figure 6

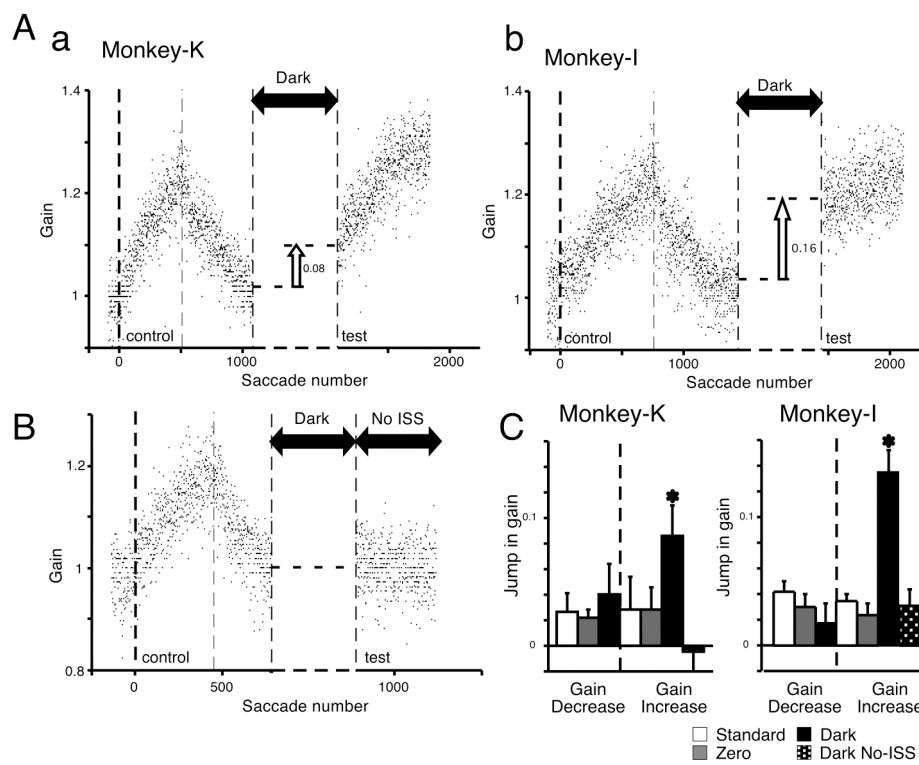


Figure 7

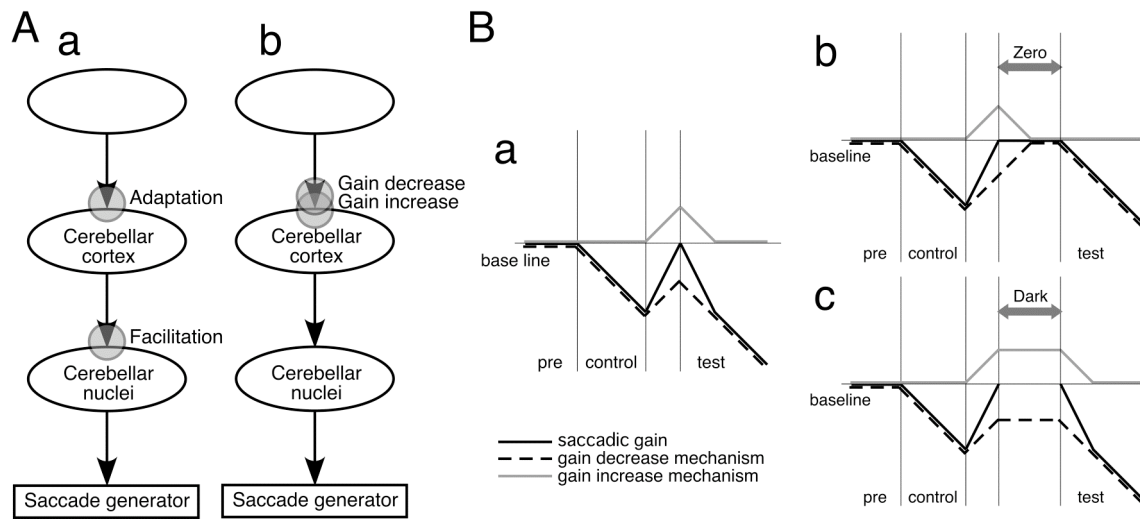


Figure 8

Chapter 2

Effect of saccadic amplitude adaptation on subsequent adaptation of saccades in different directions.

Abstract

I have shown previously that adaptation of horizontal saccades exerts facilitating effects on subsequent adaptation of saccades in the same direction. Now I investigated the effect on saccades in different directions. A series of three alternating gain changes was induced by intrasaccadic step (ISS) of the target in two monkeys. The gain of saccades to horizontal or vertical target steps was decreased by backward ISS (conditioning). Then, I used forward ISS to increase their gain back to ~ 1.0 . Finally, I induced a gain decrease for saccades to oblique target steps with backward ISS. I analyzed dependency of test adaptation rates on the direction of conditioning saccades. The rate of adaptation of the horizontal component of oblique saccades was significantly larger when conditioned with horizontal saccade adaptation than with vertical saccade adaptation. The rate for the vertical component did not show such differences. Following horizontal saccade adaptation, the horizontal component adapted faster than the vertical component. After vertical saccade adaptation, the vertical component tended to adapt at higher rates. Taken together, the results indicate that horizontal saccade adaptation exerts a facilitating effect on subsequent adaptation of the horizontal component of oblique saccades.

Introduction

Saccades, rapid shifts in the direction of gaze, enable the primate to acquire a visual target with the fovea. Because of the small size of the fovea, efficient collection of visual information depends heavily on the accuracy of saccades. Unlike somatic movements such as reaching of the arm, saccades are too fast for visual feedback to guide their trajectory. Saccades must therefore be preprogrammed in advance of their execution, and in this sense are under open-loop control. The saccadic system possesses an off-line error correction mechanism, called saccadic adaptation, that recalibrates the saccadic gain (saccade amplitude / target eccentricity) constantly and thus ensures movement accuracy in the face, for example, of altered plant mechanics (Hopp and Fuchs, 2004; Optican and Robinson, 1980). If saccades consistently fall short of the target, as may result from damage to an extraocular muscle, their amplitude gradually increases until the target is acquired again with a single movement. Similarly, if saccades consistently overshoot the target, they gradually become smaller to reduce the error that must be corrected after the primary movement.

Saccadic adaptation can be induced experimentally with a paradigm that creates a visual error by stepping the target during saccades (McLaughlin, 1967). This intrasaccadic step (ISS) paradigm has been used successfully to reveal several important characteristics of adaptation. First, adaptation elicited by the ISS paradigm has a roughly exponential course with a rate constant of 100-800 saccades in monkeys (Scudder et al., 1998; Straube et al., 1997) and 30-60 saccades in humans (Albano, 1996; Deubel et al., 1986, 1987; Frens and van Opstal, 1994). The amount and rate of adaptation are highly variable across subjects and also across experiments in the same subject (Fuchs et al., 1996; Straube et al., 1997). Second, a visual error present in a short period immediately after saccades has been shown to be a crucial stimulus for the induction of adaptation in both human and nonhuman primates (Fujita et al., 2002; Noto

and Robinson, 2001; Shafer et al., 2000; Wallman and Fuchs, 1998). Third, adaptation is fairly specific to the amplitude and direction of adapted saccades and does not generalize fully to those with different vectors in monkeys (Noto et al., 1999; Straube et al., 1997; Wallman and Fuchs, 1998; Watanabe et al., 2000) as well as in humans (Albano, 1996; Frens and van Opstal, 1994; Miller et al., 1981; Semmlow et al., 1989). The specificity of saccadic adaptation has an important implication as to the site of plasticity and is thought to indicate that adaptation occurs before saccadic signals are broken into horizontal and vertical components (Deubel, 1987).

Recently, an interesting temporal characteristic of saccadic adaptation was revealed by subjecting the monkey to an adaptation paradigm twice within one experiment. Kojima et al. (2004a) altered the saccadic gain, brought the gain back to ~ 1.0 , and then induced a second gain change using the same ISS as the first one. They found that the gain changed at a higher rate in the early part of the second adaptation than in the corresponding part of the first adaptation. The facilitating effect was observed when the animal was placed in the dark before the second adaptation. These results indicate that some form of memory of the first adaptation remains and modifies the subsequent adaptation. The memory manifests itself as facilitation of the second adaptation.

Because Kojima et al. (2004a) only examined adaptation of saccades in a horizontal direction, it is unknown whether adaptation of saccades in one direction exerts any influence on subsequent adaptation of saccades in a different direction. Clarifying spatial properties of the facilitating effect of adaptation might give us a clue to how adaptation is facilitated, just as the characteristics of adaptation fields have provided insight into the adaptation mechanism.

In the present study, I examined the effects of adaptation of horizontal or vertical saccades on subsequent adaptation of oblique saccades, as well as the amount of transfer of the original adaptation to oblique saccades. The relative rate of adaptation

of the horizontal and vertical components was found to depend on the direction of saccades in the original adaptation. A preliminary account of this study has appeared elsewhere (Iwamoto et al., 2004; Kojima et al., 2004b).

Materials and Methods

Surgery

Two rhesus monkeys (*Macaca mulatta*, male, 4.5 and 6.8 kg) were prepared for eye movement recording by the magnetic search coil method (Fuchs and Robinson, 1966). Anesthesia was introduced with ketamine hydrochloride (15-20 mg/kg, i.m.) and maintained by inhalation of isoflurane. Electrocardiogram and blood oxygen level were monitored. A coil of Teflon-coated stainless steel wire was implanted beneath the insertions of the four recti of one eye to measure eye movements. Stainless steel tubes were attached to the skull with bone screws and dental acrylic. During experiments, rigid metal rods were inserted into the tubes for painless immobilization of the animal's head. After surgery, antibiotics were given intramuscularly for 3 days to prevent infection. After recovery from the surgery, the monkeys were trained to follow a small jumping target with the eye. All surgical and experimental protocols were approved by the Animal Care and Use Committee at the University of Tsukuba.

During recording sessions, the monkey sat in a primate chair in a darkened booth with its head restrained. The animal was required to make saccades toward a target spot ($\sim 0.3^\circ$) presented on a monitor screen, which was 35.5 cm from its eyes. Whenever the monkey maintained its eye position within 1.5° of the target continuously for 0.8-1.0 sec, the target jumped to another position and the animal was rewarded with a small amount of apple juice. The animal followed the target spot reliably for several thousand trials in a single experiment, which lasted 1-1.5 hours.

Behavioral paradigms

Induction of saccadic amplitude adaptation Adaptive changes in saccade amplitude were induced by a conventional intrasaccadic target step paradigm (McLaughlin, 1967). The target jumped along the horizontal meridian, vertical meridian or oblique line

directed 45° away from horizontal, and then, during the saccade, stepped backward by a fixed percentage of the initial step. This intrasaccadic step (ISS) created a visual error at the end of the movement as if the saccade had been too large, requiring the animal to make a corrective saccade to catch the target. This procedure, when repeated over several hundreds of movements, gradually decreased the saccade amplitude. I adapted saccades that were elicited by 10° steps of the target. The target stepped pseudo-randomly in either direction in a movement range of 30° (within 15° of the straight ahead position).

Experimental paradigm I induced a series of three alternating gain changes by reversing the polarity of visual error twice during ongoing adaptation. The basic design of the paradigm was similar to the double reversal paradigm used in a previous study (Kojima et al., 2004a). In the present study, I performed two types of experiment as summarized in Table 1. In the “horizontal-to-oblique” experiments (Hor-to-Obl), after collecting 100-400 preadaptation saccades to 10° oblique and horizontal steps of the target, I first decreased the gain of saccades to horizontal target steps with 35% backward ISS (conditioning adaptation). When the gain was altered by ~ 0.1 - 0.2 after 400-800 saccades, I stopped ISS and measured the gain of ~ 30 saccades elicited by oblique target steps to examine the transfer of adaptation of horizontal saccades (transfer test). The gain of horizontal saccades was then increased back to ~ 1.0 with 20% forward ISS (recovery). I then induced a gain decrease for saccades to oblique target steps (test adaptation). In “vertical-to-oblique” experiments (Ver-to-Obl), saccades to 10° upward target steps were adapted with 35% backward ISS in conditioning adaptation. Saccades to either 10° right-up or left-up oblique target steps were examined in transfer test. After the gain of upward saccades was brought back to ~ 1.0 , I induced a gain-decrease for the oblique saccades in test adaptation.

Analysis

Horizontal and vertical components of eye position and target position were digitized on line at 1 kHz and stored in a hard disk with an interface (Micro1401, CED). Data were analyzed off-line on a computer (Power Macintosh G4, Apple) using homemade programs that ran on an analysis software (Spike2, CED). Saccade onset and end were defined by an eye velocity threshold criterion of $20^\circ/\text{s}$. Targeting saccades elicited by an initial (not intrasaccadic) target step were selected for analysis. Saccades with latencies less than 60 ms were regarded as anticipatory and removed. Parameters of saccades and target steps, i.e., positions, timings, and peak eye velocities, were exported to statistics programs (StatView or JMP, SAS inc.) to calculate other saccade characteristics. The *target eccentricity* was defined as the difference between the target and the eye positions at saccade onset. The *gain* of a saccade to a target step in a specific direction (horizontal, vertical, or oblique) was defined as the ratio of the saccade size to the target eccentricity in that direction. For example, the *gain* of a saccade to an upward target step was defined as the ratio of the saccade's upward component to that of the target eccentricity. The *gain of the horizontal or vertical component* of oblique saccades was obtained by dividing the respective component of saccade size by that of target eccentricity, which was $\sim 7.5^\circ$.

The gain change achieved in the conditioning block (horizontal or vertical saccades) was estimated by the difference in average gain between the last 20 saccades in the conditioning block and the last 20 horizontal or vertical saccades in the preadaptation block. The gain change for oblique saccades in the transfer test block was calculated as a difference in average gain between the initial 20 saccades in the transfer test block and the last 20 oblique saccades in the preadaptation block. Numerical data, such as gains, are presented as a mean \pm SD.

Results

Data were collected in a total of 22 experiments using two animals. In 11, I decreased the gain of saccades to horizontal (either left or right) target steps in conditioning adaptation and the gain of saccades to oblique (left-up or right-up) target steps in test adaptation. In 11 other experiments, I decreased the gain of saccades to upward target steps in conditioning adaptation and the gain of saccades to oblique target steps in test adaptation. In 18 of these 22 experiments, I also examined transfer of conditioning adaptation to oblique saccades (Table 1).

Preadaptation gain of saccades

The gains of saccades collected in the preadaptation block are summarized as follows. In horizontal-to-oblique experiments ($n = 11$), the average preadaptation gain of horizontal saccades in individual experiments had a mean of 1.014 ± 0.034 whereas that of oblique saccades was slightly smaller, having a mean of 0.955 ± 0.060 .

Horizontal and vertical components of the oblique saccades exhibited similar means, 0.963 ± 0.054 and 0.947 ± 0.069 , respectively. In vertical-to-oblique experiments ($n = 11$), the preadaptation gain of upward saccades had a mean of 0.985 ± 0.031 .

Although oblique saccades showed a slightly smaller gain (mean = 0.953 ± 0.052), their horizontal and vertical components again exhibited similar gains, 0.966 ± 0.048 and 0.941 ± 0.063 , respectively. Thus in both types of experiments, the preadaptation gain and therefore the imposed gain change, one factor that could affect the rate or transfer of adaptation, were similar for both components.

Effects of conditioning adaptation of horizontal or vertical saccades on subsequent adaptation of oblique saccades

I examined adaptation of oblique saccades that was induced after conditioning adaptation. Figure 1Aa shows an example of the courses of adaptation in

horizontal-to-oblique experiments. The gain of rightward saccades was decreased to ~ 0.8 (conditioning adaptation), increased to ~ 1.0 , and then the gain of right-up saccades was decreased (test adaptation). As reported previously (Straube et al. 1997, Kojima et al. 2004a), the gain of individual saccades varied across saccades but showed a clear change as the saccade number increased. The gain of oblique saccades exhibited similar variability. For estimation of the rate of adaptation, linear regression lines were fitted for the initial 150 saccades in the conditioning and test adaptation blocks. Test adaptation showed a larger slope (8.4×10^{-4} /saccade) than the conditioning (6.5×10^{-4} /saccade). Figure 1Ab summarizes the results of this and 10 other experiments in which adaptation of horizontal saccades preceded that of oblique saccades (8 in Monkey I, 3 in Monkey K). Oblique saccades adapted faster than the conditioning horizontal saccades in all experiments. The adaptation rate for oblique saccades, $9.58 \pm 2.23 \times 10^{-4}$ /saccade, was significantly higher than that for horizontal saccades in conditioning adaptation, $5.57 \pm 0.98 \times 10^{-4}$ /saccade (Wilcoxon signed rank test, $p < 0.005$).

An example of vertical-to-oblique experiments is shown in Fig. 1Ba. The gain of upward saccades was decreased with an initial rate of 7.1×10^{-4} /saccade in conditioning adaptation. The gain of oblique (right-up) saccades decreased with a similar rate, 7.7×10^{-4} /saccade in the subsequent test adaptation. The gains of upward and oblique saccades appeared to show saccade-to-saccade variability that was similar to that for the horizontal saccades (Fig. 1Aa). Figure 1Bb summarizes the results of this and 10 other experiments in which adaptation of upward saccades preceded that of oblique saccades (6 in Monkey I, 5 in Monkey K). The adaptation rate for conditioning upward saccades varied greatly and had a mean of $7.83 \pm 2.40 \times 10^{-4}$ /saccade, which was larger than that for conditioning horizontal saccades (cf. Fig 1Ab). The initial rate of test adaptation of oblique saccades, $7.82 \pm 1.58 \times 10^{-4}$ /saccade, was not significantly different than that of conditioning adaptation of upward saccades (Wilcoxon signed rank test).

To examine whether conditioning adaptation produces different effects on adaptation of horizontal and vertical components of oblique saccades, I compared the initial rates of gain change calculated separately for the horizontal and vertical components. Figure 2Aa shows the course of test adaptation for the two components in a horizontal-to-oblique experiment (same experiment as in Fig. 1A). The horizontal component changed its gain with an initial rate of 11.6×10^{-4} /saccade, far faster than did the vertical component (4.7×10^{-4} /saccade). For the 11 experiments in which adaptation of horizontal saccades preceded that of oblique saccades, the gain change rate for the horizontal component, $10.64 \pm 2.31 \times 10^{-4}$ /saccade, was significantly larger than that for the vertical component, $8.47 \pm 2.98 \times 10^{-4}$ /saccade (Fig. 2Ab; Wilcoxon signed rank test, $p < 0.05$). I next compared the adaptation rates for conditioning saccades with those for the component of oblique saccades in the same direction as the conditioning saccades. In horizontal-to-oblique experiments, the rate of adaptation of the horizontal component was significantly larger than the rate of conditioning adaptation of horizontal saccades, $5.57 \pm 0.98 \times 10^{-4}$ /saccade (cf. Fig. 1Ab left, Fig. 2Ab left; Wilcoxon signed rank test, $p < 0.005$).

Analyses of the rate for the components were performed on the data obtained in vertical-to-oblique experiments as well. The course of adaptation of the components in one experiment was shown in Figure 2Ba (same experiment as in Fig. 1B). The vertical component of oblique saccades adapted at a rate of 8.8×10^{-4} /saccade and the horizontal component at a rate of 6.6×10^{-4} /saccade. For the 11 experiments in which adaptation of upward saccades preceded that of oblique saccades, the initial adaptation rate of the vertical component had a larger mean, $8.42 \pm 1.91 \times 10^{-4}$ /saccade, than that of the horizontal component, $7.25 \pm 1.69 \times 10^{-4}$ /saccade (Fig. 2Bb). The difference, however, did not reach a significance level of 0.05 (Wilcoxon signed rank test, $p = 0.06$). Then I compared the rate of adaptation of the vertical component with the rate of conditioning adaptation of vertical saccades. There was not a

significant difference between the two variables (cf. Fig. 1Bb left, Fig. 2Bb right; Wilcoxon signed rank test).

The analyses described above focused on the comparison of the gain change rates within each type of experiments, either horizontal-to-oblique or vertical-to-oblique. To examine more directly the dependency of test adaptation on the direction of saccades used in conditioning adaptation, I next compared the gain change rates between the two types of experiments. I first tested whether the adaptation rate for each component of oblique saccades differed depending on the direction of conditioning saccades. The adaptation rate for the *horizontal* component of oblique saccades with conditioning adaptation of horizontal saccades, $10.64 \pm 2.31 \times 10^{-4}$ /saccade, was significantly larger than that with conditioning adaptation of vertical saccades, $7.25 \pm 1.69 \times 10^{-4}$ /saccade (cf. Fig. 2Ab left, Fig. 2Bb left; ANOVA, $p < 0.001$). On the other hand, there was no significant difference in the adaptation rate for the *vertical* component between horizontal-to-oblique experiments and vertical-to-oblique experiments, $8.47 \pm 2.98 \times 10^{-4}$ /saccade and $8.42 \pm 1.91 \times 10^{-4}$ /saccade, respectively (cf. Fig. 2Ab right, Fig. 2Bb right; $p = 0.97$).

Finally, I tested directly whether the *relative* rate of adaptation of the two components differed between the horizontal and vertical conditioning directions, as might be expected from the comparison of Figure 2Ab and 2Bb. As an index for statistical evaluation, I calculated a difference in the rate between the horizontal and vertical components for each experiment. It indicates how much larger the gain change rate for the horizontal component is compared with that for the vertical component. The index may be less susceptible to variability across experiments than the actual rates and would be useful to examine how the two components behave against each other. Statistical tests indicated that this index of the relative component rate was significantly different between the horizontal conditioning direction (mean = 1.2 ± 1.7) and the vertical conditioning direction (mean = -2.2 ± 2.6) (ANOVA; $p <$

0.005).

To summarize, the analyses of the gain change rates produced different pictures for the horizontal and vertical conditioning directions. I will discuss these results in relation to facilitating effects of adaptation later in Discussion.

Transfer of horizontal and vertical adaptation to oblique saccades

To compare spatial characteristics of adaptation transfer and those of facilitating effect on subsequent adaptation, I quantified the transfer of conditioning adaptation to oblique saccades in 18 of the 22 experiments. Figure 3Aa shows an example of transfer of adaptation of horizontal saccades to oblique saccades. Saccade end points relative to the initial target location are represented in two dimensions for preadaptation (red dots) and postadaptation (blue dots). Adaptation resulted in a clear shift of the end points of rightward saccades (red to blue dots along the horizontal broken line). To test whether this gain decrease of rightward saccades transferred to oblique (right-up) saccades, I compared the end points (relative to the initial target position) of oblique saccades after adaptation with those before adaptation. As shown in Figure 3Ab (left panel), the horizontal component of the end points for oblique saccades after adaptation was significantly smaller than that before adaptation (ANOVA; $p < 0.001$). Meanwhile, the vertical component of the end points did not show a significant difference (Fig. 3Ab right panel, $p = 0.68$). A similar analysis, using the gains of individual saccades, indicated that the gain of the horizontal component of oblique saccades changed significantly ($p < 0.01$) whereas the gain of the vertical component did not ($p = 0.13$). To estimate the amount of gain decrease, I calculated the difference between average gains of 20 saccades collected before and after adaptation. The gain decrease for horizontal saccades was 0.232 and that for the horizontal component of oblique saccades was 0.081, indicating an adaptation transfer of 35%.

I performed similar analyses in a total of 8 of 11 experiments. In 6 of 8 experiments, the horizontal component of the end points relative to the initial target position showed a significant decrease ($p < 0.01$). The vertical component showed no significant change in the 8 experiments ($p > 0.01$). Thus there is a tendency for the horizontal component of end points of oblique saccades to decrease its size in association with amplitude-decreasing adaptation of horizontal saccades. As expected, an analysis of the saccadic gain produced similar results. The gain of the horizontal component of oblique saccades decreased significantly in 6 of 8 experiments ($p < 0.01$). There was no significant difference in the gain of the vertical component of oblique saccades between pre- and postadaptation ($p > 0.01$). For the above 6 experiments, the estimated gain change for the horizontal component of oblique saccades had a mean of 0.065 ± 0.014 (range: 0.031 to 0.082) and that for horizontal saccades in conditioning adaptation 0.188 ± 0.048 (range: 0.128 to 0.238).

I tested transfer of adaptation of vertical saccades to oblique saccades. Figure 3Ba shows for one experiment saccade end points relative to the initial target location plotted in the same format as in Fig. 3Aa. Adaptation resulted in a downward shift of end points of upward saccades (red to blue dots along the vertical broken line). I compared the end points of oblique (left-up) saccades after adaptation (blue dots) with those before adaptation (red dots). The horizontal component of end points after adaptation was not significantly different than that before adaptation (Fig. 3Bb left panel, $p = 0.25$). On the other hand, the upward component of end points after adaptation was significantly smaller than that before adaptation ($p < 0.0001$, Fig. 3Bb right panel). Analyses based on the gains of individual saccades agreed with these findings; the gain of the upward component of oblique saccades showed a significant change ($p < 0.0001$) and that of the horizontal component did not ($p = 0.39$). The gain decrease for upward saccades was 0.201 whereas that for the upward component of oblique saccades was 0.068. There was thus a 33.8 % transfer of adaptation from

upward saccades to the upward component of oblique saccades.

I performed similar analyses in a total of 10 experiments. The vertical component of the end points of oblique saccades relative to the initial target position exhibited a significant decrease in 8 of 10 experiments ($p < 0.01$). In 5 of these 8 experiments, horizontal component showed no significant decrease. In the remaining 3 of the 8 experiments, the horizontal component also showed a significant decrease, though the decrease was smaller than that of the vertical component. An analysis of the saccadic gain produced essentially the same results. For the 8 experiments that showed significant decreases in the gain of the upward component of oblique saccades, the estimated gain change for the upward component of oblique saccades had a mean of 0.086 ± 0.020 (range: 0.068 to 0.111) and that for upward saccades was 0.223 ± 0.024 (range: 0.186 to 0.263).

To summarize the results on transfer, adaptations of both horizontal and vertical saccades transferred to oblique saccades the direction of which was 45° away from the adapted saccades. The transfer occurred mainly to the component that was in the same direction as the adapted saccades. These data on transfer of adaptation agreed well with the previous reports (Deubel 1987; Noto et al. 1999) as will be discussed later. Thus, unlike the effect of conditioning adaptation on test adaptation, transfer of adaptation of horizontal saccades and that of vertical saccades were qualitatively similar.

The results on the effect of conditioning adaptation on test adaptation, described in a previous section, suggested that the horizontal saccade adaptation exerted a facilitating effect on subsequent adaptation of the horizontal component of oblique saccades (Discussion). I compared the degree of facilitation of test adaptation and the amount of transfer of conditioning adaptation for the horizontal-to-oblique experiments ($n = 8$). As a measure of the degree of facilitation for each experiment, I first obtained a ratio of the adaptation rate for the horizontal component of oblique saccades to the

rate of conditioning adaptation of horizontal saccades. The %facilitation was calculated by subtracting 1 from this ratio and multiplying by 100. The %transfer of conditioning adaptation to the horizontal component of oblique saccades was obtained as a percentage of the gain change for the horizontal component of oblique saccades (transfer test) to the gain change attained in conditioning adaptation of horizontal saccades. The %facilitation ranged from 45.4 to 122.9 with a mean of 77.9 ± 28.6 . The %transfer had a lower mean, 33.6 ± 15.7 , ranging between 18.6 to 64.1. Then I examined whether these two variables were correlated. A regression analysis indicated that there was no significant correlation between %facilitation and %transfer ($p = 0.45$).

Discussion

Interaction of adaptations of saccades in different directions

The present study examined the effects of adaptation of saccades in one direction on subsequent adaptation of saccades in a different direction. Specifically, I compared conditioning adaptation of horizontal or vertical saccades with subsequent test adaptation of oblique saccades. Analyses of the gain change rates have provided following results. First, when preceded by horizontal saccade adaptation, oblique saccades adapted at significantly higher rates than the conditioning horizontal saccades in all 11 experiments. Second, the horizontal component of oblique saccades exhibited a higher adaptation rate than conditioning horizontal saccades. The average rate for the former was roughly twice that for the latter. Third, the gain change rates for the *horizontal* component in horizontal-to-oblique experiments were significantly larger than those in vertical-to-oblique experiments. Meanwhile, the gain change rates for the *vertical* component did not show a significant difference between the two types of experiments. Finally, the relative rate of adaptation of the horizontal and vertical components, as estimated by the difference in the rate between the horizontal and vertical components, differed significantly depending on the direction of saccades in conditioning adaptation. Taken together, these results are most consistent with an interpretation that conditioning adaptation of horizontal saccades had a facilitating effect on adaptation of the horizontal component of oblique saccades. The present study indicates that the facilitating effect on subsequent adaptation is dependent on the direction of saccades in the original adaptation.

I have previously suggested that adaptation history is retained as a memory, which exhibits facilitating influence on subsequent adaptation (Kojima et al., 2004a). However, it is generally possible that some nonspecific processes could increase the rate

of motor learning irrespective of movement direction. For example, it is possible that varying degrees of general enhancing mechanisms might contribute to the high variability in the rate of adaptation across experiments, as observed in previous studies (Straube et al., 1997; Hopp and Fuchs, 2004) as well as this study. The observed directional dependency of facilitation makes a general process, such as alertness, attention or motivation, unlikely, and argues for a plastic change at a specific site in the saccadic circuitry. The present study has added further evidence that the facilitation of subsequent adaptation does reflect the memory of the original adaptation by showing that the memory includes information about the direction of saccades.

The present data did not provide evidence that adaptation of the vertical component of oblique saccades was facilitated by preceding adaptation of vertical saccades. Following vertical saccade adaptation, the vertical component did not adapt at different rates than the original vertical saccades. The gain change rates of the vertical component were similar in horizontal-to-oblique and vertical-to-oblique experiments. However, these results do not necessarily indicate that the vertical saccadic system lacks a mechanism that facilitates the next adaptation. For example, a larger variability and a higher average of the adaptation rate for conditioning vertical saccades than for conditioning horizontal saccades (cf. Fig. 1Ab left, Bb left), for which I do not have any plausible explanation, might have masked a facilitating effect on the vertical component. An analysis of the relative rates of the two components, which are probably less vulnerable to variability across experiments than the actual rates, seems compatible with this possibility; the vertical component tended to adapt faster than the horizontal component (Fig. 2Bb), an opposite tendency to that observed in horizontal-to-oblique experiments. Note also that I compared adaptations of saccades whose directions were $\sim 45^\circ$ apart. It is possible that the vertical system is equipped with a similar but less efficient facilitation mechanism that could not influence adaptation of movements over such a large directional difference. Effects on

adaptation of saccades in a more adjacent direction must be investigated to verify this possibility.

Transfer of adaptation and facilitation of subsequent adaptation

Besides the interaction between adaptations of saccades in different directions, I examined in the same experiments how adaptation of horizontal or vertical saccades transferred to oblique saccades whose direction was deviated by $\sim 45^\circ$ from that of adapted saccades. As might be expected from previous reports (Deubel 1989; Deubel et al. 1987; Noto et al. 1999; Wallman and Fuchs 1998), the amount of transfer to these oblique saccades was relatively small, the average of percent transfer being $\sim 18\%$ for horizontal saccades and $\sim 25\%$ for vertical saccades. Adaptation of horizontal saccades transferred almost exclusively to the horizontal component with virtually no transfer to the vertical component. After adaptation of vertical saccades, significant transfer was observed mainly for the vertical component. Our data confirmed previous reports that adaptation of horizontal and vertical saccades changed the gain of oblique saccades (Deubel 1987; Noto et al. 1999). The preferential transfer of adaptation of horizontal and vertical saccades to the respective components, observed in our study, also confirms observations by Deubel (1987), who examined transfer of adaptation of saccades in one direction to saccades in a variety of adjacent directions and reported that the direction of the induced *changes* in adjacent saccade vectors was similar to the direction of the *change* in adapted saccades. Recently, a theory of saccadic adaptation has been proposed by Fujita (2005), who postulates that the visual error at the end of saccades, equivalent to the vector of impending corrective saccades, is place-coded in the site of adaptation and that a signal for a given saccade is widely distributed in that site. The theory predicts that the induced change for tested saccades has the same direction as that for adapted saccades. Our data on adaptation transfer, like those of Deubel (1987), are consistent with this prediction.

How do the spatial characteristics of adaptation transfer compare those of the facilitating effect of adaptation? While the adaptation transfer from horizontal and vertical saccades occurred in a roughly symmetrical fashion, i. e., mainly to their respective component, a facilitating effect was observed only on adaptation of the horizontal component of oblique saccades. This is one clear difference in results between transfer and facilitation. However, the data from horizontal-to-oblique experiments indicate that transfer and facilitation have qualitatively similar directional preferences; both occur mainly to the component that has the same direction as the original adapted saccades. In the light of Deubel's report (1987) described above, I may restate that the facilitating effect on subsequent adaptation is exerted in the direction of the change in saccade vector induced in the original adaptation. At least for the horizontal system, the similarity in directional preference is compatible with an idea that adaptation and its facilitation may have a common site of plasticity. I have proposed a possibility that two plasticity mechanisms for gain increases and gain decreases, respectively, exist for saccadic adaptation, as proposed for adaptation of the vestibuloocular reflex (Boyden and Raymond, 2003; Li et al., 1995) and that the simultaneous activation of one and deactivation of the other produces a faster gain change in the second adaptation (Kojima et al., 2004a). Our results are consistent with this possibility.

It should be pointed out that for the horizontal conditioning direction there may be some quantitative differences between transfer of adaptation and its facilitating effect. The %facilitation was on the average more than twice the %transfer although no correlation was found between the two. I currently do not have an explanation for this apparent discrepancy and am reluctant to conclude that facilitating effect of horizontal saccade adaptation *transfers* more widely than adaptation itself for the same directional difference of 45°. Further experiments are needed to clarify this issue.

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Figure and figure Legends

Table 1. Direction of target step used in two types of experiments. In “Hor-to-Obl” and “Ver-to-Obl” experiments, horizontal and vertical saccades, respectively, were adapted in conditioning adaptation, and oblique saccades were examined in transfer test and test adaptation. The number of experiments for each monkey was shown in the far-right column with the number of experiments that included transfer tests in parentheses.

Fig. 1. Effects of adaptation of horizontal saccades (A) and vertical saccades (B) on subsequent adaptation of oblique saccades. Aa: Course of adaptation in a “Hor-to-Obl” experiment. Ab: Summary of gain change rates for 11 experiments. Arrows indicates the experiment shown in Aa. Ba: Course of adaptation in a “Ver-to-Obl” experiment. Bb: Summary of gain change rates for 11 experiments. Arrows indicates the experiment shown in Ba.

Fig. 2. Course of test adaptation of the horizontal and vertical components. Aa: Course of component adaptation in a “Hor-to-Obl” experiment (same experiment as Fig. 1Aa). Ab: Summary of adaptation rates for 11 experiments. Arrows indicate the experiment shown in Aa. Ba: Course of component adaptation in a “Ver-to-Obl” experiment (same experiment as Fig. 1Ba). Bb: Summary of adaptation rates for 11 experiments. Arrows indicate the experiment shown in Ba.

Fig. 3. Examples of adaptation transfer from horizontal to oblique saccades (A) and vertical to oblique saccades (B). a: Saccade end points relative to the initial target location represented in two dimensions. Red and blue dots indicate pre- and postadaptation saccades, respectively. Blue dots along horizontal (A) and vertical (B)

broken lines indicate last 20 saccades in conditioning adaptation. Blue dots along oblique (A, B) broken lines indicate first 20 saccades in transfer test. b: Pre-post comparison for the horizontal (left panel) and vertical component (right panel) of end points of oblique saccades. Positive values indicate right or up.

Type of experiment	Pre		Conditioning	Transfer test	Recovery	Test	Number of Experiments
	no-ISS		35% backward	no-ISS	20% forward	35% backward	
Hor-to-Obl	Right-Up	Right	Right	Right-Up	Right	Right-Up	I : 8 (6)
	Left-Up	Left	Left	Left-Up	Left	Left-Up	K : 3 (2)
Ver-to-Obl	Right-Up	Up	Up	Right-Up	Up	Right-Up	I : 6 (6)
	Left-Up			Left-Up		Left-Up	K : 5 (4)

Table 1

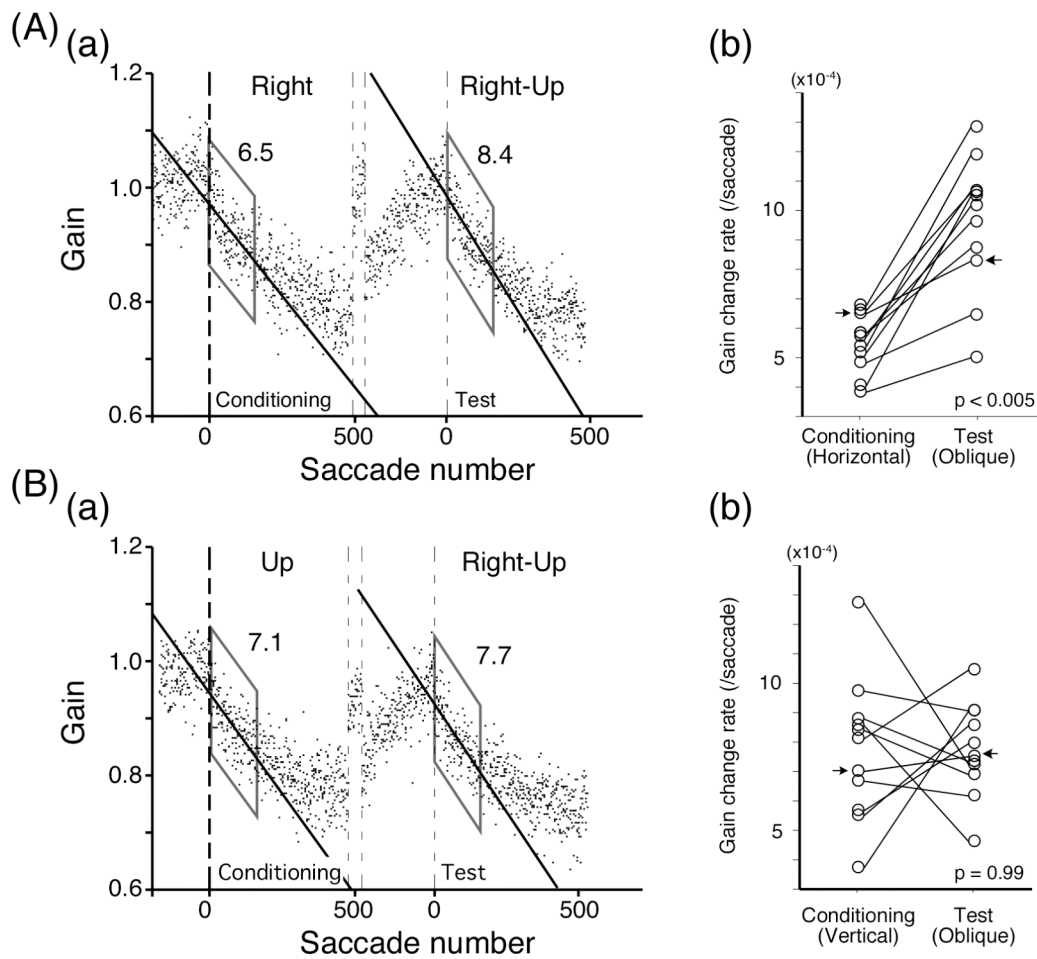


Fig. 1

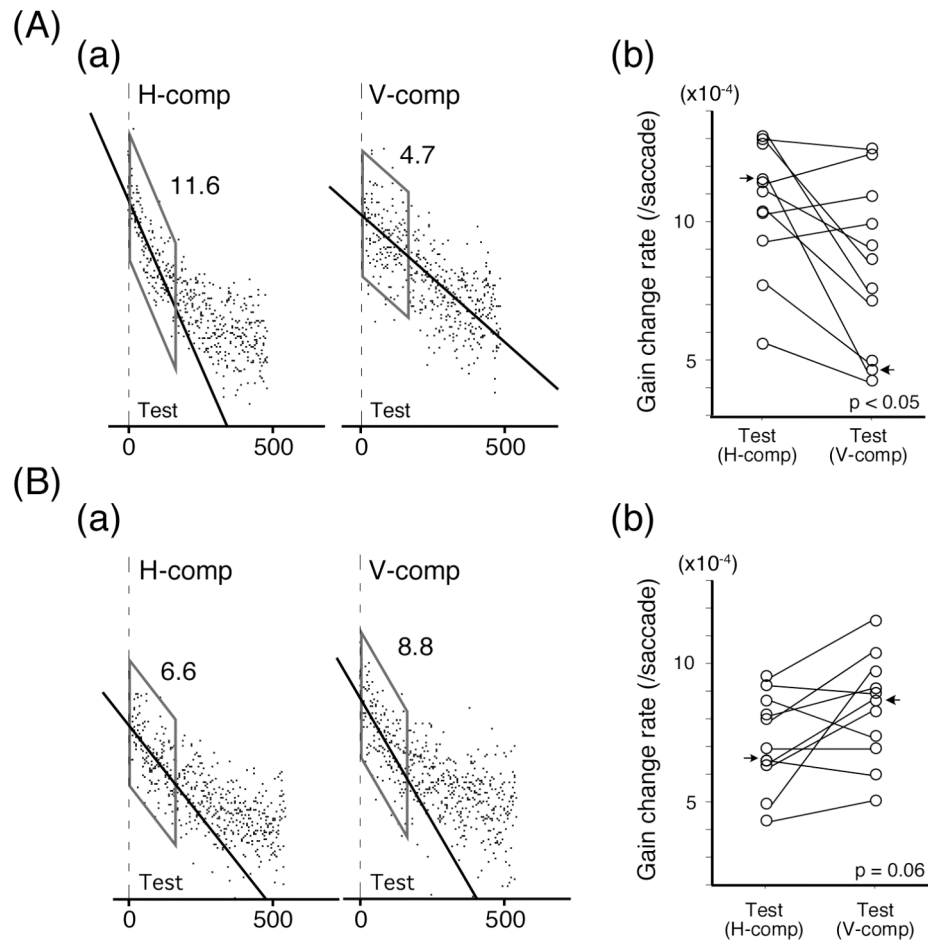


Fig. 2

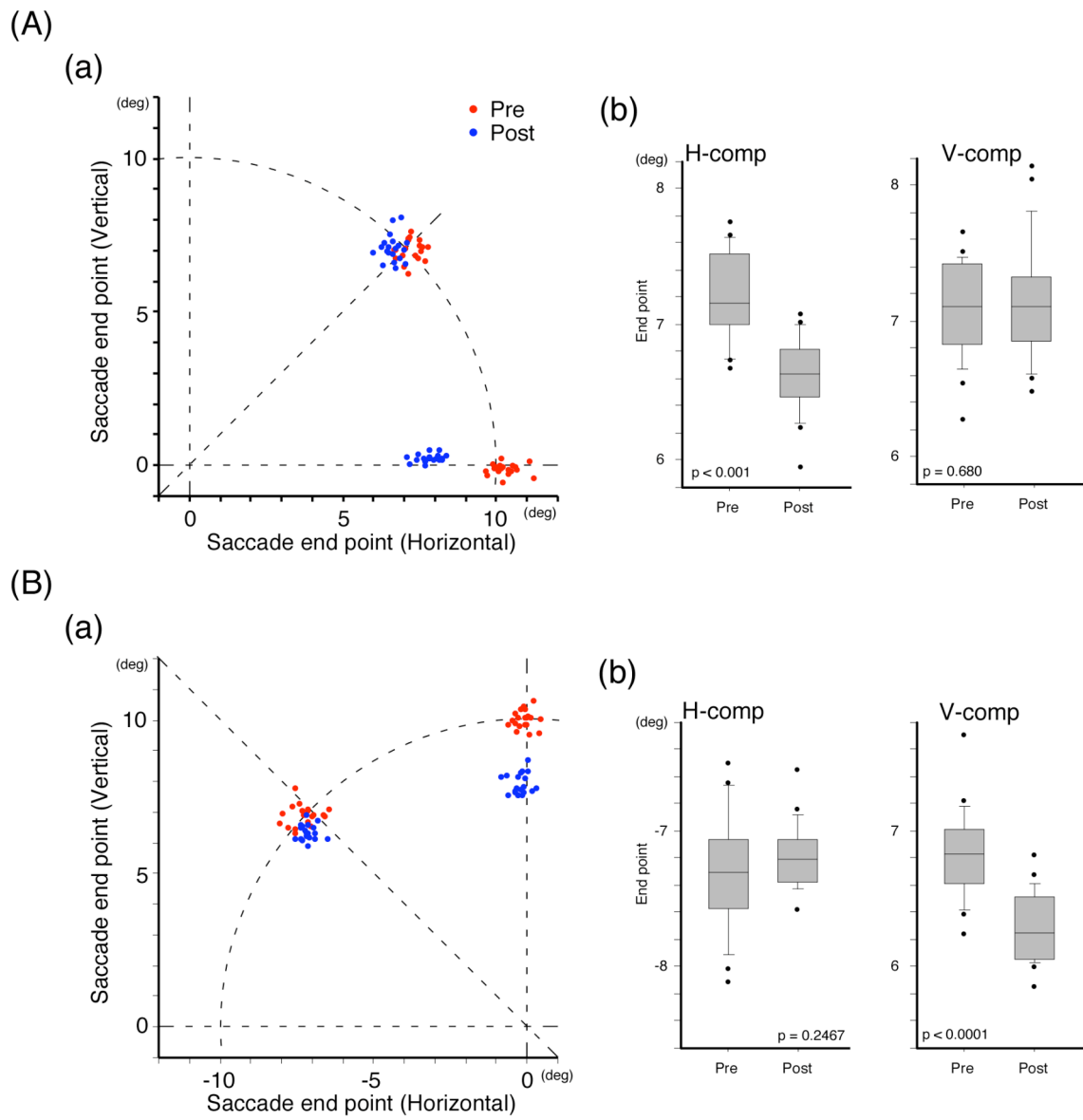


Fig. 3

Summary and conclusions

In the present study, I first provided evidence for the storage of learning history during saccadic amplitude adaptation. I altered the saccadic gain, brought the gain back to ~ 1.0 , and then induced a second gain change using the same ISS as the first one. The gain changed at a higher rate in the early part of the second adaptation than in the corresponding part of the first adaptation. The facilitating effect was observed when the animal was placed in the dark before the second adaptation. These results indicate that some form of memory of the first adaptation remains and modifies the subsequent adaptation. The memory manifests itself as facilitation of the second adaptation. To provide a clue to how adaptation is facilitated, I next clarified spatial properties of the facilitating effect of adaptation. To this end, I examined the effects of adaptation of saccades in one direction on subsequent adaptation of saccades in a different direction. The results indicated that the facilitating effect on subsequent adaptation is dependent on the direction of saccades in the original adaptation. To compare spatial characteristics of adaptation transfer and those of facilitating effect on subsequent adaptation, I quantified the transfer of conditioning adaptation to oblique saccades. The transfer occurred mainly to the component that was in the same direction as the adapted saccades. The similarity in directional preference is compatible with an idea that adaptation and its facilitation may have a common site of plasticity.

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