Primate Antisaccades. I. Behavioral Characteristics

NELLY AMADOR, MADELEINE SCHLAG-REY, AND JOHN SCHLAG

Department of Neurobiology and Brain Research Institute, University of California at Los Angeles School of Medicine, Los Angeles, California 90095-1763

Amador, Nelly, Madeleine Schlag-Rey, and John Schlag. Primate antisaccades. I. Behavioral characteristics. J. Neurophysiol. 80: 1775–1786, 1998. The antisaccade task requires a subject to make a saccade to an unmarked location opposite to a flashed stimulus. This task was originally designed to study saccades made to a goal specified by instructions. Interest for this paradigm surged after the discovery that frontal lobe lesions specifically and severely affect human performance of antisaccades while prosaccades (i.e., saccades directed to the visual stimulus) are facilitated. Training monkeys to perform antisaccades was rarely attempted in the past, and this study is the first one that describes in detail the properties of such antisaccades compared with randomly intermingled prosaccades of varying amplitude in all directions. Such randomization was found essential to force the monkeys to use the instruction cue (prop- or anti-) and the location cue (peripheral stimulus) provided within a trial rather than to direct their saccades to the location of past rewards. Each trial began with the onset of a central fixation target that conveyed by its shape the instruction to make a pro- or an antisaccade to a subsequent peripheral stimulus. In one version of the task, the monkey was allowed to make an immediate saccade to the goal; in a second version, the saccade had to wait for a go signal. Analyses of the accuracy, velocity, and latency of antisaccades compared with prosaccades were performed on a sample of 7,430 pro-/antisaccades in the “immediate saccade” task (delayed saccades suffering from known distortions). Error rates fluctuated ~25%. Results were the same for the two monkeys with respect to accuracy and velocity, but they differed in terms of reaction time. Both monkeys generated antisaccades to stimuli in all directions, at various eccentricities, but antisaccades were significantly less accurate and slower than prosaccades elicited by the same stimuli. Interestingly, saccades to the stimulus could be followed by appropriate antisaccades with no intersaccadic interval. Such instances are here referred to as “turnaround saccades.” Because they occurred sometimes with a long latency, turnaround saccades did not simply reflect the cancellation of an early foveation reflex. Consistent with human data, latencies of one monkey were longer for antisaccades than for prosaccades, but the reverse was true for the other monkey who was trained differently. In summary, this study demonstrates the feasibility of providing a subhuman primate model of antisaccade performance, but at the same time it suggests some irreducible differences between human and monkey performance.

INTRODUCTION

The antisaccade task requires a subject to generate a saccade of equal eccentricity and opposite direction to a peripheral visual stimulus. This is one of several tasks designed by Hallett (1978) to study the properties of human saccades to goals defined by instruction. In this first study, human antisaccades were found to occur with less accuracy, lower velocity, and longer latencies than saccades directed to a visible stimulus. The explanation of their characteristics seems to lie in the indirect visual information supplied about the antisaccade goal and does not seem to require new assumptions about saccadic mechanisms or oculomotor paths (Doma and Hallett 1988; Hallett 1978; Hallett and Adams 1980: but see Smit et al. 1987).

Interest for the mechanism of antisaccade generation was renewed when Guittton et al. (1985) reported that patients affected by frontal lobe lesions could not make antisaccades, although the same individuals could make normal saccades to visual targets. The main problem for these patients was their inability to suppress reflexive glances to sudden visual stimuli. These results were quite provocative in suggesting that antisaccade performance provides means for testing higher oculomotor functions, especially those depending on the integrity of the frontal lobe or its associated forebrain structures. Indeed, subsequent studies of antisaccades in patients affected by prefrontal (Pierrot-Deseilligny et al. 1991) and basal ganglia disorders (Lasker et al. 1987; Tian et al. 1991) showed similar impairments in antisaccade tasks that are now routinely included in clinical neurological studies.

The issue of which oculomotor paths are used in reflexive and voluntary saccades in normal humans was reopened by new experimental research on three fronts: behavioral experiments, cortical potential recordings, and positron emission tomography (PET) studies. First, from the behavioral viewpoint, antisaccades have become a counterpoint to express prosaccades. For instance, antisaccades and prosaccades of normal subjects were compared in the “gap” task, which is known to favor the occurrence of express saccades by disengaging active fixation for a short time before a new target is presented (Fischer and Boch 1983; Fischer and Ramsperger 1984). Using this paradigm, Fischer and Weber (1992) showed that, in contrast to prosaccades, antisaccades are never made with a latency in the range defining express saccades. They interpreted their finding as supporting the hypothesis of a reflexlike pathway connecting the retina to the oculomotor centers in the brain stem—a pathway mediating express saccades—if it is disinhibited at the time of target appearance. More recent studies by the same authors (Fischer and Weber 1997; Weber 1995) analyzed the experimental conditions that govern the occurrence of disallowed glances to the stimulus.

Second, using cortical potential recording, Everling and collaborator (1997, 1998) indicated two cortical oculomotor areas that could play a significant role during the programming of a correct antisaccade. One is the supplementary
eye field (SEF), over which a greater negative potential was found before antisaccades than before prosaccades, in agreement with our finding of greater neuronal discharges before the former than before the latter (Schlag-Rey et al. 1997). The other region implicated by Everling and colleagues is the posterior parietal cortex, over which, during an antisaccade trial, a negative potential shifts from the contralateral to the ipsilateral hemisphere, reflecting the change of planning from a saccade to the stimulus to a saccade to the opposite side. This may be still another type of change of motor planning besides those already associated with neuronal correlates in the lateral intraparietal area (Bracewell et al. 1996; Snyder et al. 1997).

Third PET studies by O’Driscol et al. (1995) and Sweeney et al. (1996), in agreement with cortical potentials and unit studies, demonstrated a pattern of cortical activation that differentiates antisaccades from prosaccades by a comparatively greater activation of the SEF accompanying antisaccades.

To probe the neural substrates of antisaccades it would seem desirable to develop a subhuman primate model of this behavior. Surprisingly, effort in this direction remained scarce thus far (Burman and Bruce 1997; Funahashi et al. 1993; Schlag-Rey et al. 1997). Yet, how monkeys generate saccades to virtual targets is a field of research wide open, not only because human antisaccade experiments multiplied with diverse paradigms but because in principle any question posed about prosaccades may be posed about antisaccades generated in the same condition. Furthermore, from a neurophysiological viewpoint, the antisaccade task is ideal for determining whether the neuronal discharge of a cell is associated with the presentation of the visual stimulus regardless of the subsequent eye movement or the impending eye movement to be made regardless of where the visual stimulus is presented or else with both events (Schlag-Rey et al. 1997).

This is the first of three papers. The current one examines the behavioral characteristics of monkey antisaccades as well as the problems encountered in training subhuman primates. It is the first time that monkey antisaccades are described and analyzed in detail. The next papers are concerned with the neuronal correlates of antisaccades in the SEF and in the primary frontal eye field of the monkeys used in this study.

Our objective here is to evaluate the extent to which monkey antisaccades, instrumentally conditioned, resemble human antisaccades, verbally instructed. In addition, we will compare monkey antisaccades with other types of saccades to invisible goals, such as saccades to remembered targets and saccades to targets of another modality.

Successful performance of antisaccades to goals defined by instruction depends on the conjunction of several abilities: 1) conceptual, understanding the antisaccade instruction; 2) computational, calculating an inverted retinal error vector; 3) inhibitory, repressing reflexive orienting; and 4) motor, self-initiating a saccade to an unmarked location. The question originally posed by Hallett (1978) could be explored in monkeys if the conceptual and computational aspects of the task were preserved, i.e., if we ensured that the monkeys derived their antisaccade goals from the current cues, not from the locus of past rewards. For instance, when antisaccade trials are run in blocks of trials in two directions, a monkey can ignore the instruction and successfully repeat the same saccade until the reward shifts to the other side. Therefore, in adapting the human task for monkeys, we attempted to preserve the conceptual element, by requiring the monkey to interpret a symbolic instruction cue specifying whether a pro- or an antisaccade should be made on a given trial, and the computational element, by forcing the monkey to use a current, unpredictable stimulus, not a reinforced association, for programming the eye movement. Our departure from the two-choice left-right antisaccade paradigm used in human studies was also motivated by the plan to tailor the vector of antisaccades to the particular response field of a cell in subsequent unit recording experiments. (A preliminary analysis of primate antisaccade behavior was made by Sanchez et al. 1994.)

METHODS

Two adult female macaque monkeys (MKA, nemestrina; MKD, rhesus) were implanted with a scleral search coil according to the method described by Judge et al. (1980). The leads of the coil were affixed to a pedestal of dental cement that embedded skull screws and nuts to which a head restraint apparatus was secured during experimental sessions. The surgical procedures, training, and care of the animals followed the guidelines of the National Institute of Health’s Guide for the Care and Use of Laboratory Animals and the instructions of the UCLA Animal Research Committee. During training sessions, the monkey sat in a primate chair with head fixed and facing a tangent screen 132 cm away from the eyes (to minimize the occurrence of converging eye movements). Visual stimuli, positioned by joysticks, were low-intensity (25 mcd/m2) luminous dots or squares (<1") produced by a Tektronix 608 oscilloscope and rear projected through a wide angle lens. Eye position recording methods were previously described (Schlag et al. 1998). The monkey’s facial movements were continuously monitored by an infrared camera. The tasks were performed in a dim red light environment (to permit rapid dark adaptation) or in complete darkness. Drops of apple juice (diluted 50% and sweetened with aspartame) were used as a reward. All stimuli and behavioral events were controlled by a Macintosh Quadra 840AV and stored for off-line analysis. Eye position was sampled at 1 kHz, and saccades were automatically detected. All computer programs were written in MacProbe software.

Tasks

The monkeys were trained to perform interleaved prosaccades and antisaccades in two versions of the task, illustrated in Fig. 1. The two versions are referred to as “immediate” and “delayed” saccade tasks to emphasize a difference consisting in withholding (or not) a prepared saccade rather than a difference in memory load.

In both tasks a trial began with the onset of a central spot of light having the shape of a dot or a small square (<1") until it disappeared. The shape of the fixation target conveyed the instruction to make a prosaccade (●) or an antisaccade (○) to a subsequent peripheral target (always ●), appearing at an unpredictable location. Thus, during initial fixation, the monkey knew what type of saccade (pro- vs. anti-) would be appropriate but did not yet know in what specific direction the movement should be made. In the “immediate saccade condition,” the offset of the fixation point coincided with the onset of a peripheral stimulus (always ●) to which the monkey was required to make a pro- or an antisaccade, depending on the prior instruction cue. In the “delayed saccade condition,” the peripheral target was flashed while the monkey
FIG. 1. Prosaccade and antisaccade tasks. Top and bottom panels: spatial display of stimuli and saccade trajectories in the immediate and delayed saccade tasks, respectively. The traces between the panels indicate the sequence of events. Each trial began with a fixation point stimulus encoding, by its shape, the instruction to make a prosaccade (●) or an antisaccade (○). The disappearance of the fixation point was the go signal for the saccade. An eccentric visual stimulus (always ●) was flashed for 50–100 ms when the fixation point disappeared (immediate saccade task) or at variable times during fixation of the instruction cue (delayed saccade task). The required saccade is indicated by an arrow.
was fixating the central target, and the monkey had to withhold a saccade to it until the fixation target disappeared. In both tasks, the disappearance of the fixation point was the go signal for the eye movement, but no constraint was imposed on the monkey’s reaction time. Stimuli were positioned with a joystick, in directions spanning 360° and eccentricity varying from 5 to 25°. Different stimulus durations, ranging from 10 to 200 ms, were used to test whether short or long durations would facilitate the inhibition of a foveating reflex on antisaccade trials. A short stimulus duration appeared more conducive to the production of antisaccades when no delay was involved; therefore 50 ms became the standard duration. However, this duration was increased to 100 or 200 ms for long delayed saccades (e.g., 900 ms).

An electronic window centered on the peripheral stimulus (prosaccades) or diametrically opposite (antisaccades) served to determine whether the pro- or antisaccade met the criterion accuracy imposed in a particular session. When a one-step pro-/antisaccade terminated in and stayed within the window, a liquid reward was given, simultaneous with a flashed stimulus (dot), indicating the precise location of the saccade goal. No reward was given if a saccade ending in the window was preceded, on the same trial, by a saccade in the wrong direction.

### Training procedure

The two monkeys were trained to the same level of performance but in different ways. After MkA learned the one-step basic prosaccade task, training started on a no-saccade task as a transitional stage. Despite this prior conditioning in suppressing foveation reflexes, MkA appeared unable to suppress them in the immediate antisaccade condition. Antisaccade training was then postponed until she learned to make prosaccades to remembered targets (with delays ≤1 s). She then learned to perform delayed antisaccades and finally immediate antisaccades. Because MkA’s reaction times were found unexpectedly shorter for antisaccades than for prosaccades and because this idiosyncratic behavior was perhaps linked to her prolonged training in saccades to remembered targets, MkD’s training in pro- and antisaccades proceeded on par, first in the immediate condition, second in the delayed condition. After learning the basic prosaccade task, MkD learned to make antisaccades without any detour through a no-saccade task.

To elicit the first antisaccade, for MkA, it was found expedient to present the fixation target encoding the antisaccade instruction at eccentric locations on the screen so that centripetal antisaccades would spontaneously occur and be reinforced. In subsequent trials, the fixation target was gradually returned to the center of the screen. For MkD, no displacement of the fixation target was found necessary; an initially large window was progressively restricted until formal training could begin.

Initially, when pro- and antisaccades were limited to two directions, they were pseudorandomly mixed, but, when new directions were added or a more stringent criterion of accuracy imposed, it was found necessary to run the two types of trials in blocks, even whole sessions. This always boosted the proportion of correct trials, but it also increased the monkey’s tendency to develop a response set impervious to the instruction cue. The correction method consisting of repeating a trial on which an error occurred (to offer the monkey a second chance of performing correctly) was used only in cases of near misses, i.e., when the antisaccade missed the window by a few degrees or failed to stay in the window for the duration prescribed.

Ultimately, antisaccade trials could be pseudorandomly interleaved with prosaccade trials when the peripheral target was presented at a distance varying from 10 to 25° from the fixation point, in one of eight unpredictable directions.

### Data analysis

The time of occurrence and the spatial coordinates of all events pertaining to an experiment were stored in binary files. Such were, for instance, the shape of the fixation point (square or dot), its onset/offset, the location of the visual stimulus, its onset/offset, the timing of reinforcement, the trajectories, and the timing of all saccades made during a trial. Each session was replayed off-line.

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**FIG. 2.** Trajectories of antisaccades made by MkA and MkD to stimuli presented in 8 randomized directions. Arrows were superimposed on the termination points. The location of the stimuli (not shown) was diametrically opposite to the evoked antisaccades. The 2 samples of antisaccades were chosen to illustrate the contrast between antisaccades performed in complete darkness (MkA) and in a dim light environment (MkD).
to delete artifactual detection of saccades. Pro- and antisaccade trajectories were then plotted and quantitatively analyzed. The statistical analysis of the results was made by analysis of variance and $\chi^2$ tests.

RESULTS

Progress during the different phases of training will not be described here, except to note a feature relevant to the interpretation of the results; the learning curves always showed a dramatic regression with every modification of the task. In particular, each novel direction of antisaccade had to be trained anew by successive approximation; there was no evidence of sudden insight in the antisaccade rule, e.g., no immediate transfer of learning from the horizontal to the vertical dimension.

The database consists of 7,430 saccades from pooled sessions in which the percentage of reinforced intermixed pro-and antisaccades fluctuated $\sim 75\%$ with a $\approx 65\%$ for both types of trial. We analyzed the trials on which the instruction differed from that of the preceding trial and found that $71\%$ of these trials were correct. Because in our experiments antisaccades were pseudorandomly interleaved with prosaccades and reinforced with the same criterion window, valid comparisons of the two types of eye movement could be made despite fluctuations in the percentage of correct saccades from session to session. The numbers of correct and incorrect pro- and antisaccades analyzed for each monkey appear in Fig. 7.

With one exception (Fig. 4), data collected during unit recording sessions were excluded because when a cell was isolated the need to map its receptive field and to present stimuli corresponding to its preferred/null vector interfered with the randomization of pro- and antisaccades in all directions.

Quantitative analyses focused on the accuracy, peak velocity, and latency of pro- and antisaccade trajectories aiming toward the goal, in the immediate saccade task, performed in a dim red light environment (delayed saccades and saccades in darkness, whether pro- or anti-, were expectedly less accurate). In addition, latency measurements were made of incorrect trajectories because saccade latency is thought to be a critical parameter for distinguishing voluntary from reflexive eye movements (Fischer and Weber 1992).

Accuracy

Figure 2 documents the ability of the two monkeys to generate antisaccades in eight general directions (underscored by arrows superimposed on the end points of saccades). In addition, Fig. 2 allows one to appreciate, on antisaccade trials, the difference—well known on pro-trials (Gnadt et al. 1991; White et al. 1994)—between saccades generated in complete darkness ($MkA$) and those generated in an illuminated environment ($MkD$). Clearly, a prominent upward drift occurred at the end of antisaccades made by $MkA$ but was absent from antisaccades made by $MkD$. The drift depended on the scotopic condition only not on individual differences between these two monkeys.

When no dark-evoked drift is involved and when fo- veation of the stimulus is successfully inhibited, how accurate are antisaccade trajectories compared with prosaccade trajectories interspersed during the same sessions? Although the criterion for reinforcement (window size) was always the same, varying with sessions but not with the type of saccades, a notable difference in accuracy appeared between the two types of saccades whenever a large window was used to encourage antisaccade behavior. In this case, the end points of prosaccades became relatively more independent of the window size, being more focused than they were required to be. Thus Fig. 3 shows that primary prosaccades (in gray) were much less dispersed than primary antisaccades (in black) around a perfectly aimed saccade vector (direction $0^\circ$ for prosaccades, $180^\circ$ for antisaccades; amplitude ratio 1 for both) within a range of directional disparity.

**FIG. 3.** Distribution of prosaccades (in gray) and antisaccades (in black) terminating in a $30^\circ$ reinforcement window. Abscissa: actual direction disparity with respect to the required direction. Ordinate: amplitude ratio of the actual/required amplitude. The perfectly accurate vector has a direction disparity of $0^\circ$ on prosaccade trials and $180^\circ$ on antisaccade trials, and its amplitude ratio is 1.0 on both types of trial. In this and subsequent illustrations, the database consists of saccades made in the immediate saccade task only. For both monkeys, the results focus on asymptotic performance of this task after they learned to perform delayed antisaccades (i.e., memory training). However, for $MkD$, a comparison is offered with the performance of immediate antisaccades before memory training.
extending to 30°. This finding is reminiscent of the observation made by Groh and Sparks (1996) that the large windows used for reinforcing saccades to visual targets in the same way as saccades to somatosensory targets did not induce the monkeys to relax visuooculomotor accuracy. The difference between pro- and antisaccades visible in the three panels of Fig. 3 was extremely significant in all analyses of direction disparity ($P < 0.0001$), but it was less or not significant in terms of amplitude ratio. Additionally, Fig. 3 (right panel) shows that immediate prosaccades, but not antisaccades, were more accurate after $MkD$ was trained to make delayed saccades, either because this “memory training” was beneficial or simply because later training sessions were involved. However, despite overtraining, no improvement resulted from reducing the criterion window to $< 10°$ for a 20° antisaccade.

Was inaccuracy more pronounced in certain directions? For the two monkeys, angular errors were found minimal for purely horizontal antisaccades, compared with oblique disparities ($P < 0.0001$), but it was less or not significant in terms of amplitude ratio. Additionally, Fig. 3 (right panel) shows that immediate prosaccades, but not antisaccades, included in the training protocol later than horizontal ones, the observed difference may be related to the order of train-

FIG. 4. Six examples of the 5 most accurate trajectories of prosaccades and antisaccades of $MkA$ and $MkD$, elicited by the same target on randomly alternating trials, while recording from cells having their response fields centered on the target ($*$). To avoid obscuring the termination points of the saccade trajectories, the target is represented at a position more eccentric ($\sim 1°$) than it actually was.
However, horizontal antisaccades might be easier to perform accurately because they correspond to a mirror-image symmetry as well as a body symmetry. In fact, when the monkeys failed to make a left-up antisaccade to a right-down stimulus, they eventually produced a right-up antisaccade. Furthermore, a greater difficulty in producing accurate oblique saccades persisted despite overtraining. Training new monkeys first with vertical instead of horizontal antisaccades is needed to dissociate training effects from intrinsic differences between antisaccade directions, such as those observed between horizontal and vertical antisaccades in humans (Goldring and Fischer 1997).

As far as amplitude errors were concerned, there was some tendency toward overshooting when the required antisaccades were small (between 5 and 10°) and undershooting when they were large (similar to the averaging effect in humans, described by Kapoula 1985). However, undershooting was more frequent (Fig. 3). Despite this fact, primary antisaccades were rarely corrected by secondary saccades generated before visual feedback of the antisaccade goal. When secondary antisaccades occurred, they sometimes brought gaze farther from the goal, as was observed for human antisaccades (Hallett 1978). The larger window sizes that were used during training when all directions were mixed may have contributed to a strategy of producing the smallest antisaccades that would terminate within the win-

![Diagram](http://jn.physiology.org/)

**FIG. 5.** A: raw record. B: sample of trajectories of “turnaround saccades” occasionally made by the 2 monkeys on antisaccade trials. The 1st saccade was made by mistake to the visual stimulus and was followed, without pause, by a correct antisaccade. The examples in B illustrate the wide range of latencies from stimulus onset with which turnaround saccades may occur.
down. However, as mentioned above, this strategy was definitely not used for prosaccade. Remarkably, an accurate corrective prosaccade invariably followed visual feedback of antisaccades terminating in the criterion window, although the reward had already been delivered.

Another perspective for evaluating antisaccade accuracy consists in asking, not how the monkeys perform, on average, but what they are capable of doing when they work at their best. This question has practical relevance for single cell studies of antisaccade behavior, which often depend on the reliable production of similar saccade trajectories. An answer is provided in Fig. 4. It illustrates the five most accurate antisaccades and intermixed prosaccades triggered by a particular visual stimulus (*) while recording from cells having different response fields. For graphic clarity, the goal was represented at a distance ~1° farther than it was along its angular axis. The six examples were selected to illustrate a wide-ranging vector selection from files that contained a variable number of trials. In all cases, the best antisaccade trajectories can be seen ending approximately ±5° from each other. Although reasonably good, their aim was definitely less precise, and their velocity conspicuously reduced in comparison with the prosaccades elicited by the same stimulus.

Finally, a radically different and a major source of errors on antisaccade trials was the failure to inhibit reflexive fo- veation of the peripheral stimulus. This reflex was never completely overcome over thousands of trials. A similar observation was made in humans (Fischer and Weber 1992; Fischer et al. 1997).

Interestingly, saccades in the wrong direction could be followed by “turnaround” or back-to-back saccades with extremely short or absent intersaccadic intervals. Such instances, as illustrated in Fig. 5, were never reinforced and therefore remained quite rare (<1% of the current data). Nevertheless, turnaround saccades are worthy of notice because their occurrence on antisaccade trials (94% of the turn-around cases) suggest that the monkey knew where she was supposed to look but could not repress an initial grasp of the stimulus. Indeed, turnaround saccades occurred only after the monkeys learned to some extent the relevance of the instruction cue. They were made at variable latencies, even >250 ms from the stimulus onset (Fig. 5B). As antisaccade performance improved, turnaround saccades tended to be replaced by two distinct saccades, separated by an increasing intersaccadic interval. However, turnarounds reappeared whenever the task difficulty was increased as, for example, by introducing a new stimulus direction.

Velocity

For the two monkeys, correct antisaccades had a signifi- cantly lower peak velocity than correct prosaccades of equal amplitude (P < 0.001). This difference obtained for all saccade amplitudes, as shown in Fig. 6, which graphs main sequences (peak velocity vs. amplitude) for pro- and antisaccades ranging from 5 to 30° amplitude. The curves of Fig. 6 were derived from the same database as the accuracy plots of Fig. 3. Although MkD’s accuracy on prosaccade trials improved after memory training (Fig. 3), her average saccade velocity decreased.

![Fig. 6. Plots of peak velocity vs. amplitude of correct prosaccades (in gray, circles) and antisaccades (in black, triangles) for MkA and MkD (before and after memory training). Means (dots) and SDs (vertical bars) were computed for 5 levels of average amplitude, ranging from 5 to 10° to 25 to 30°.](http://jn.physiology.org/)

Reaction time

The normalized distributions of saccade latency from stimulus onset are shown in Fig. 7 for correct saccades (upward histograms) and incorrect saccades (downward histograms) made during the same sessions. Surprisingly, when MkA was correct, her reaction time was shorter on antisaccade trials than on prosaccade trials (mean = 244 ms for prosaccades and 209 ms for antisaccades; the difference was significant at the P < 0.001 level). This is the opposite of what could have been expected from our knowledge of all human antisaccades. However, consistent with the human literature, MkD had a shorter reaction time for correct prosac- cades (mean = 194 ms for prosaccades and 230 ms for antisaccades; significant difference at P < 0.001). After memory training, MkD’s mean latencies of correct pro- and antisaccades dropped to 188 and 195 ms, respectively (the difference was still significant, P < 0.01). It should be remarked that the average reaction time of the two monkeys was not far apart on antisaccade trials (209 ms for MkA vs. 230–195 ms for MkD). Therefore it is the large difference
FIG. 7. Distributions of saccade latency from stimulus onset for MkA and MkD (before and after memory training). To facilitate the comparison of the different conditions for MkA and MkD, the latency distributions were normalized separately for correct trials (upward histograms) and incorrect trials (downward histograms). The absolute number of trials included in each histogram appears at the right of each plot.

between the prosaccadic reaction times of the monkeys that is responsible for the opposite trend observed when, for each monkey, a comparison is made between reaction times for pro- and antisaccades on correct trials.

On incorrect trials, the reaction times followed a different pattern. They were rather long for prosaccades of both monkeys and for the antisaccades of MkA. For MkD, however, the latency distribution for prosaccades made by mistake on anti-trials shifted toward smaller values and appeared to be bimodal with a first peak ~100 ms. This peak, suggestive of express reflexive errors, was found significant when contrasted to the paucity of correct antisaccades, correct prosaccades, and mistaken antisaccades in the same latency range extending from 70 to 120 ms ($\chi^2 = 5.91, P < 0.05$ before memory training; $\chi^2 = 13.18, P < 0.001$ after memory training).

DISCUSSION

The most important finding of this study is that monkeys can be taught to make antisaccades in any direction, in response to unpredictable stimuli, and that their choice between making an antisaccade versus a prosaccade can be guided by a symbolic instruction cue that alone does not
specify the direction of the saccade to be made. As the monkeys were making antisaccades in all directions, the probability of securing reinforcement by chance or by repetition of the last rewarded saccade became very low. Thus it may be safely concluded that the monkeys came to understand the abstract rule encoded in the instruction cue and that they learned to use it appropriately. This conclusion is further supported by the higher percentage of correct saccades (71%) made on trials in which the instruction differed from that of the previous trial. High error rates in antisaccade tasks are commonly observed in humans and particularly in children (Fischer et al. 1997) with whom—allowing for differences in experimental conditions—our monkeys compare favorably.

The difficulties encountered by our monkeys during training probably reflect more on the poor communication of the object of the task than on the monkey’s ability to perform it. One can only guess how long a human subject would take to discover the rule of correct/incorrect performance without the benefit of prior verbal instructions.

Three characteristics were consistently reported to distinguish antisaccades from prosaccades in human studies: decreased accuracy, longer latency, and slower velocity. We will examine the extent to which the same properties characterize monkeys antisaccades.

**Accuracy**

Antisaccades aiming toward the goal, i.e., a virtual target, were found less accurate than prosaccades to the site of a real target. Both amplitude and angular errors contributed to the inaccurate end points of primary antisaccades. Antisaccade trajectories were rarely corrected by secondary saccades before visual feedback, and when secondary antisaccades eventually occurred they sometimes drove the eyes farther away from the goal. This summary account of monkey antisaccades does not differ from that originally given for human antisaccades by Hallett and colleagues (Doma and Hallett 1988; Hallett 1978; Hallett and Adams 1980). Indeed, these investigators observed that antisaccades differ from prosaccades by a decreased accuracy of primary saccades, not always improved by secondary saccades. They also found that, apart from eliminating unwanted reflexive deviations, antisaccade trajectories could not be improved by further practice.

Inasmuch as antisaccades can be viewed as saccades to an invisible goal, they appear to suffer from the same distortions as eye movements to targets no longer visible (i.e., prosaccades to remembered targets). Such distortions were reported in an early study of human eye movements by Becker and Fuchs (1969), confirmed by later parametric studies (Gnadt et al. 1991; Smit et al. 1987). Comparing saccades with visual targets, saccades to remembered targets, and antisaccades, Smit et al. (1987) found the latter to be the most inaccurate. Comparing human and monkey saccades with remembered targets in the dark, Gnadt and colleagues (1991) demonstrated a systematic hypermetria for upward saccades coupled with hypometria for downward saccades, which we also found evident in the antisaccades of MkA and MkD (Fig. 2).

A more extreme case of saccades to invisible goals is provided by saccades to stimuli of another modality. Groh and Sparks (1996) have shown how difficult it is for humans—and dramatically more so for monkeys—to make accurate saccades to somatosensory targets when the source of the sensory stimulus is invisible.

Taken together, all experimental studies of prosaccades in humans and monkeys indicate that the saccade generator is less efficient when it is somehow deprived of visual information to guide these eye movements. Antisaccades appear similar to prosaccades in this respect.

There is however a profound difference between antisaccades and saccades to remembered targets or other types of prosaccades generated under reduced visual feedback. The difficulty in programming an antisaccade lies not only in the need to compute an accurate virtual goal, derived from a real stimulus, but also in suppressing the powerful grasp reflex that attracts gaze in the direction of that stimulus. This reflex is unopposed when the frontal lobe ceased to be functional (Guitton et al. 1985). Because the gap paradigm favors the occurrence of express saccades thought to be involuntary, Fischer and Weber (1992) used the gap paradigm to show that correct antisaccades—being voluntary—never occur with express latency, in contrast to unwanted fo-veations. They refer to the latter as “direction errors” (equivalent to “mistakes” in Hallett’s terminology). They are, in fact, gross direction errors (~180°) rather than minor deviations from the antisaccade goal. Their occurrence depends on decision and attention mechanisms (Fischer and Weber 1992). For example, with pro- and anti-trials intermixed, Weber (1995) found that the error rate is greatest when the instruction cue mandating a pro or an antisaccade is given at the same time (0-ms lead time) as the visual stimulus indicating the goal (directly or indirectly). In that condition, the type of (gross) direction error is strongly dependent on the type of response made on the previous trial. The influence of the previous trial disappears when the instruction cue lead time exceeds 300 ms, which was always the case in our experiments with monkeys.

Interestingly, human subjects are aware of their mistakes, they simply cannot prevent them (Weber 1995; but see Fischer et al. 1997). This may also be true of monkeys. Otherwise, why would they generate these remarkable turnaround saccades (Fig. 3) as if two motor programs collided? The first program, directing gaze toward the stimulus, may have been generated through a reflexive pathway. Supporting the reflex hypothesis is the fact that some of the mistaken prosaccades made by MkD on anti-trials had express latencies. However, we observed that turnaround saccades can have very long latencies, suggesting that a reflex may be stored or that over time it becomes a voluntary movement.

In any event, the monkeys may have treated the task as a pulse-over/double step task (Becker and Jürgens 1972; Guitton et al. 1985) because, after making an initial saccade to the stimulus, they often generated a large antisaccade to the virtual target, although this correct reaching of the goal was not reinforced (to extinguish the tendency to look first at the stimulus). The latter movement may be subserved by quasi-visual cells (Mays and Sparks 1980) and similar types of cells. This suggests that quasivisual cells could be involved in all antisaccades. They would represent a saccade...
to a virtual stimulus specified by instruction rather than a saccade to a second stimulus impinging on the retina.

**Reaction time**

For MkD, the average reaction time of a correct antisaccade was longer than that of a correct prosaccade, whereas for MkA it was shorter. However, in absolute values, the distributions of antisaccade latencies of the two monkeys were similar and did not include express saccades. However, MkD made some express prosaccades in error on anti-trials. This observation is in line with the majority of results from human studies (Fischer and Weber 1992). As far as MkA’s counterintuitive reaction times are concerned, they might simply attest to individual differences. On the other hand, they may be the product of a prolonged memory training with prosaccades only. If this hypothesis were true, saccade latency appears to depend on different factors than those that affect saccade accuracy and velocity. In any event, it has been shown that, even with a precise determination of the time of target discrimination, the time of saccade initiation cannot be predicted (Thompson et al. 1996).

**Velocity**

The reduced peak velocity of monkey antisaccades compared with prosaccades was the most consistent result in this study, conspicuous in single trials (e.g., in Fig. 4) as well as in the main sequences of the two monkeys (Fig. 6). Slower trajectories were commonly observed in human anti-saccades but not in all subjects. Admittedly, these results were obtained from two monkeys only, but they are unambiguous. Several factors may have contributed to slow down the monkeys’ antisaccades. One, already discussed in relation to their relative inaccuracy, is the uncertainty about the exact location of the antisaccade goal. Another one is an adaptive strategy of slowly approaching the invisible reinforcement window. Still another factor is an ever-present degree of uncertainty about the rules of the game. The latter uncertainty is absent from human experiments because subjects are verbally instructed and do not doubt what they have to do. In contrast, the whole training history of monkeys in complex tasks prepared them for changes in the rules of reward.

In conclusion, this study demonstrates the feasibility of providing a subhuman primate model of antisaccades usable for neurophysiological and other experimental purposes not affordable in human studies. At the same time they suggest that some irreducible differences exist between human and monkey performance of antisaccade tasks.

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REFERENCE


