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Effects of motivational conflicts on visually elicited saccades in monkeys

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Abstract The prospect of reward evoked by external stimuli is a central element of goal-oriented behavior. To elucidate behavioral effects of reward expectation on saccade latency, we employed a visually guided saccade task with asymmetrical reward schedule. The monkey had to make an immediate saccade to a peripheral visual target in every trial, but was rewarded for a correct saccade to only one of four possible target positions. Reward availability was predictable on the basis of the spatial position of the target throughout a daily session. Compared with the condition where all positions were rewarded with a smaller amount, the mean saccade latency in the asymmetrical reward schedule was significantly shorter when the saccade was made toward the position associated with reward than when it was directed to no-reward positions. Furthermore, a divergence-point analysis on cumulative latency distributions showed that the expectation of reward facilitated saccades at all latency ranges. In contrast, the expected lack of reward delayed the initiation of saccades with latencies longer than about 200 ms, irrespective of whether the saccade was made to a position orthogonal or opposite to the

reward position. For saccades with latencies of more than approximately 240 ms, an additional delay was observed when the saccade was made to a position opposite, as compared to orthogonal, to the reward position. These results suggest that the facilitation by predictive reward is mediated by a preparatory process that is location-specific, whereas the inhibition by the absence of reward takes about 200 ms after the target onset to become effective and is initially location nonspecific but turns location-specific over time.

Keywords Saccade · Latency · Reward · Conflict · Monkey

Introduction

Animals constantly face conflicts. Some conflicts originate from the presence of multiple sensory and/or cognitive tasks (sensory/cognitive conflict). Others come from disparities between cognitive demand (i.e., what to do) and motivational demand (i.e., what the animal wants to do; motivational conflict). The effects of sensory/cognitive conflicts on simple motor responses have been investigated in detail in both humans and nonhuman primates. Although there are cases when a response with conflicting information does not appear to result in speed and/or accuracy changes (Hanes and Carpenter 1999; Hanes and Schall 1995; Logan and Cowan 1984; Logan 1994; but see Colonius et al. 2001), a sensory/cognitive conflict leads to inferior performances of a required response. For example, when two visual stimuli are presented closely and simultaneously, a first saccade often directs the gaze to an intermediate location between stimuli (saccadic averaging or global effect; Becker and Jürgens 1979; Chou et al. 1999; Findlay 1982; Ottes et al. 1984; Watanabe 2001). A similar effect occurs in a manual pointing task in humans (Sailer et al. 2002). When the separation of two stimuli is large, saccade latency increases, while the saccade metrics do not change (distracter effect; Walker et al. 1997). Another example

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of sensory/cognitive conflicts, the Stroop effect, involves a behavioral cost when relevant information of a stimulus appears in conflict with irrelevant information from the same stimulus (Stroop 1935/1992). Manual and oculomotor responses are executed more slowly and less accurately when a response associated with relevant information is incongruent with a response associated with irrelevant information (MacLeod 1991; Nakamura et al. 2002; Washburn 1994; Lauwereyns et al. 2000). In summary, the presence of sensory/cognitive conflicts generally produces delays and errors in required manual or oculomotor responses.

In contrast to sensory/cognitive conflicts, the study of behavioral effects of motivational conflicts in primates is still in its infancy. Only recently, studies in nonhuman primates have started showing that manual responses tend to be quicker when reward is expected after responses than when reward is not expected (Bowman et al. 1996; Schultz et al. 1992; Shidara et al. 1998; Shidara and Richmond 2002; Trembray and Schultz 2000; Watanabe et al. 2001). It has been demonstrated that the facilitation by reward can also be observed in oculomotor behaviors (Takikawa et al. 2002b). A saccadic eye movement is likely to occur earlier with higher velocity and higher accuracy when it is directed toward a position associated with reward. Thus, the effects of motivational conflicts seem to have some commonalities with those of sensory/cognitive conflicts.

Most of previous studies on motivational conflicts, however, used delayed-response tasks; subjects withhold a motor response until the “go” instruction occurs (Watanabe et al. 2001; Takikawa et al. 2002b). Therefore, the required response and reward gain in a particular trial were fully known to subjects, which significantly reduces the uncertainty and urgency in motor response. Therefore, it inevitably reduces the variation in response latency, which may preclude possibly delicate effects of predictive reward outcome and motivational conflict. Additionally, in a delayed-response situation, measures cannot reflect the decision process but only the decision outcome (MacLeod 1991). Measures such as latency will therefore not only be more sensitive in a speeded version of the task, they will tap into qualitatively different aspects of the behavior. In order to elucidate the behavioral effects of prospect of reward on saccade latency, the present study employed a visually guided saccade task with an asymmetric reward schedule (Lauwereyns et al. 2002b; Watanabe et al. 2002). We anticipated that the uncertainty and urgency of required response in the visually guided saccade task would result in larger variations of saccade latency and provide insights into the underlying mechanism for translation of reward expectation into oculomotor behavior.

Materials and methods

Subjects

We used two adult male Japanese monkeys (*Macaca fuscata*; monkeys R and H, body weight 6.0–7.5 kg). A head-holding device and a scleral search coil were implanted. The monkeys were initially sedated with ketamine (4.6–6.0 mg/kg) and xylazine (1.8–2.4 mg/kg) given intramuscularly. A head-holding device and a scleral search coil were then implanted under general anesthesia induced by intravenous injection of pentobarbital (4.5–6.0 mg/kg per hour) with butorphanol tartrate (0.02 mg/kg per hour). All surgical procedures were performed under aseptic conditions in an operating room. They received antibiotics (sodium ampicillin 25–40 mg/kg intramuscularly each day) after the operation. The monkeys were kept in individual primate cages in an air-conditioned room, where dry pellets were always available. Small amounts of fresh fruit or vegetable were given daily as treats. During periods of training and experiments, monkeys' access to water in the cage was controlled and monitored. Water was freely available for each weekend. Their health conditions were checked daily. All surgical and experimental procedures conformed to the NIH Principles of Laboratory Animal Care (NIH publication no. 86–23, revised 1985) and were approved by the Juntendo University Animal Care and Use Committee.

Behavioral tasks

The monkey sat in a primate chair inside a sound-attenuated dark room with his head fixed. Visual stimuli were small red spots (subtending 0.2° in diameter) back-projected onto a tangent screen (30 cm from the monkey's face) by LED projectors. All trials began with the presentation of a central fixation spot. After the monkey maintained his gaze at the fixation spot for a variable delay (1.0–1.5 s), the fixation spot disappeared and another target spot appeared at one of four positions (left, right, up, down; Fig. 1) pseudorandomly. A session consisted of a sequence of blocks. Each block contained 20 trials, which were evenly distributed for the four positions (5 trials for each position). The sequence of trials was shuffled within each block. Note that there was no break between blocks that the monkey could notice. The pseudorandom presentation of the target ensured that the number of saccades would be close to equal for all four positions. The eccentricity of the target was 20° . The monkey had to make a saccade within 500 ms to within 5° from the target position. An auditory feedback (900-Hz rectangular wave form) immediately followed each correct trial. If the monkey made an error (breaking fixation or making an incorrect saccade), the same trial was repeated. Two types of reward schedule were used. In the all-directions-reward (ADR) schedule, the monkey was rewarded by a drop of water for each single correct saccade. In the one-direction-reward (IDR) schedule, only correct saccades made to one particular position were rewarded. The amount of reward in the IDR schedule was 4 times larger than that in the ADR schedule. In a single daily session (about 300–600 trials), the reward position was fixed. The position of the reward target in IDR was counterbalanced among the four possible positions. Thus, the number of IDR daily sessions was always a multiple of 4 (see Results). This procedure prevented results from being distorted by direction-dependent differences in saccade parameters that could be general or subject-specific. Both monkeys were trained extensively over eight months before collecting behavioral data reported in the present study.

Eye movement recording and analysis

Eye position was measured with a standard magnetic search-coil technique (MEL-25, Enzanshi-Kogyo; Judge et al. 1980; Robinson 1963), digitized at 500 Hz, and stored with event times on computer disk for offline analysis. An eye movement was considered as candidate of a saccade if its instantaneous velocity rose above $30^\circ/\text{s}$

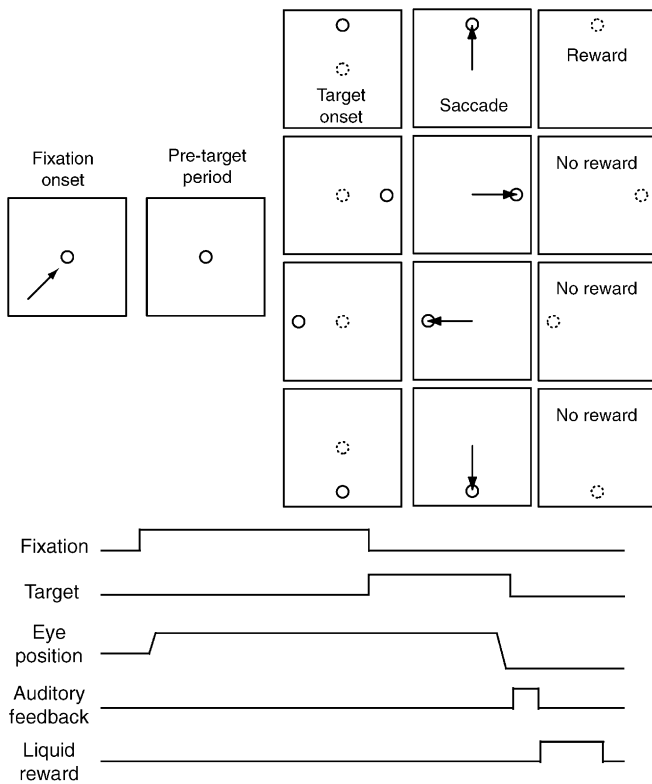


Fig. 1 Visually guided saccade task in one-direction-reward (1DR) condition. In 1DR, only one position (e.g., upward) was rewarded throughout a daily session

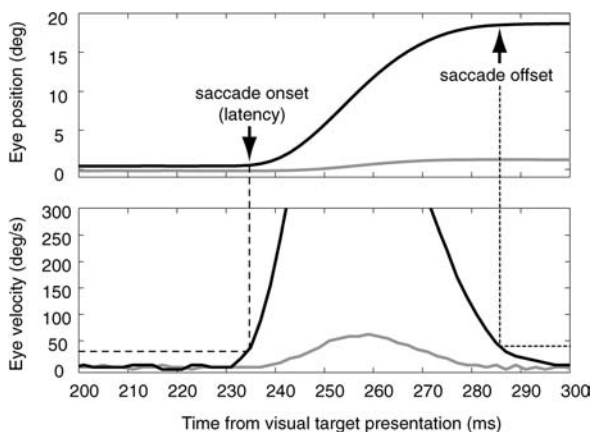


Fig. 2 Example of eye movement trace. In this particular trial (monkey R), the visual target was presented at the left position in the all-directions-reward (ADR) condition. *Black lines* and *gray lines* represent horizontal and vertical components, respectively. A saccade was detected when velocity exceeded $30^\circ/\text{s}$ after the visual target onset. The saccade offset was determined when the velocity fell to less than $40^\circ/\text{s}$

after the visual target onset. The end of the eye movement was determined when the velocity fell lower than $40^\circ/\text{s}$. The eye movement was then accepted as a saccade if the velocity was higher than $45^\circ/\text{s}$ at least for 10 ms and the total duration was longer than 30 ms (Fig. 2).

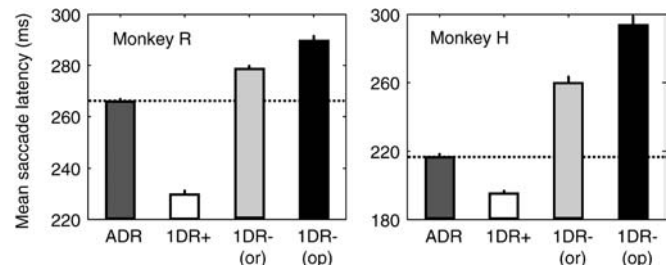


Fig. 3 Effects of reward expectation on latency of visually guided saccades. Mean saccade latencies are shown with *bars*, indicating 1 SE. For both monkeys, the mean saccade latencies in reward trials of 1DR (1DR+) were shorter than those in ADR. In no-reward trials (1DR-or and 1DR-op) the initiation of a saccade was delayed as compared to that in ADR. There was an additional delay when the target was presented in a position opposite to reward position (1DR-op) as compared to when it was presented orthogonal positions (1DR-or)

Results

Monkeys R and H completed 17 (ADR = 5, 1DR = 12) and 6 (ADR = 2, 1DR = 4) daily sessions, respectively. Based on the criteria for saccade detection and after excluding erroneous trials, we collected 7,299 trials from monkey R (ADR 3,081; 1DR 4,218) and 1,793 trials from monkey H (ADR 661; 1DR 1,182). Error trials (less than 0.9% mostly from monkey H) were not analyzed. Thus, a total of 9,092 correct saccades constituted the data for the following analyses.

The saccade latencies, averaged within subject, are shown in Fig. 3. For both monkeys, the mean saccade latency in reward trials of the 1DR schedule (1DR+) was shorter than those in the ADR schedule. The mean saccade latency in no-reward trials of the 1DR schedule (1DR-) was longer than those in the ADR schedule. Among the no-reward trials, the mean saccade latency was significantly longer when saccades were made to the direction opposite to the reward position (1DR-op) than to the direction orthogonal to the reward position (1DR-or). These effects of the reward expectation on saccade latency were significant in both monkeys (Kruskal-Wallis, $\chi^2=828.84$, $P<0.001$ for monkey R; $\chi^2=432.98$, $P<0.001$ for monkey H). Post-hoc comparisons showed that saccade latencies in all conditions were different from each other (Bonferroni, $P<0.05$).

Figure 4 shows the cumulative probability distributions of saccade latency in each condition. The distributions confirmed the modulation of saccade latency by reward expectation. The saccade latencies in 1DR+ were shorter than those in ADR. In 1DR-or and 1DR-op trials, saccades were delayed. However, the ways in which the reward expectation changed the saccade distribution were different between 1DR+ and 1DR- conditions. The 1DR+ condition shifted the overall latency distribution toward earlier saccades. In contrast, the 1DR- conditions produced elongated long-latency trials by delaying only the initiation of saccades with longer latencies. In other

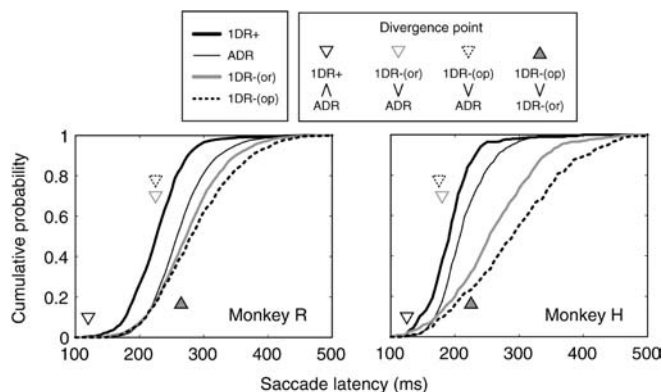


Fig. 4 Cumulative probability distributions of saccade latency. To find out at which point in time the frequency of saccades in one condition became significantly different from that in another condition (divergence point), the Fisher exact probability was computed for each 5-ms bin (see Results for details). The calculated divergence points are shown as *triangles*. Note that the 1DR-or and 1DR-op conditions diverge from ADR at about the same time

words, saccades with shorter latencies were not affected by the absence of reward.

In order to examine at which point in time these distributions (cumulative curves) diverge, cumulative frequencies of saccade latency were divided into 5-ms bins. We then computed the Fisher exact probability (Agresti 1990) for each bin-pair (1DR+ vs ADR, ADR vs 1DR-or, ADR vs 1DR-op, and 1DR-or vs 1DR-op) from shorter to longer latency bin. A divergence point was determined when the Fisher exact probability became less than 0.05 and stayed less for 10 consecutive bins (i.e., 50 ms). Triangles in Fig. 4 indicate the calculated divergence points. Compared with ADR, the probability of saccade occurrence in 1DR+ became significantly higher as early as 120 ms for monkey R and at 125 ms for monkey H. The saccade probability in 1DR-or became statistically less than that in ADR at 225 ms for monkey R and 180 ms for monkey H. Similarly, the 1DR-op condition diverged from the ADR condition at 225 ms for monkey R and 175 ms for monkey H. Finally, the 1DR-op condition deviated from the 1DR-or condition at 265 ms for monkey R and at 225 ms for monkey H.

Figure 5a shows that mean saccade landing positions with 3 standard deviations (SD); long axes of ellipses indicate the first components of principal component analysis and short axes indicate the second, orthogonal components. At first glance, there appears no systematic difference in landing position among reward schedules and reward gains (i.e., among ADR, 1DR+, 1DR-or, and 1DR-op). However, statistical analysis indicated small but significant changes in mean absolute amplitude (Fig. 5b). Amplitude was largest when a saccade was made toward a reward position, whereas the other conditions produced more hypometric saccades (Fig. 5b; Kruskal-Wallis; $\chi^2=432.98$, $P<0.001$ for monkey R; $\chi^2=59.02$, $P<0.001$ for monkey H). For monkey R, the 1DR+ condition produced saccades with larger amplitude than the other

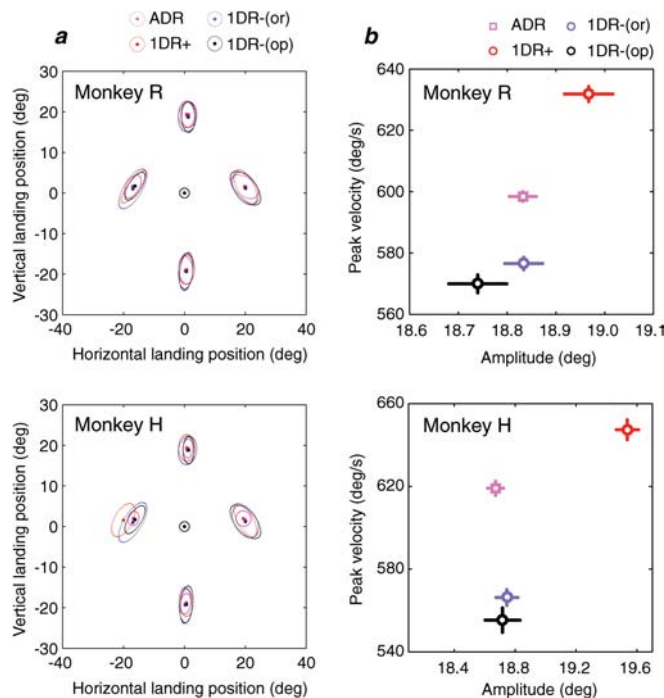


Fig. 5a, b Effects of reward expectation on velocity and amplitude of visually guided saccades. **a** Mean saccade landing positions with 3 standard deviations; long axes of ellipses indicate the first components of principal component analysis, and short axes indicate the second, orthogonal components. **b** Mean peak saccade velocity as a function of mean saccade amplitude. The bars indicate 1 SE. Qualitatively, there is a positive relation between saccade amplitude and saccade peak velocity

three conditions (post-hoc Bonferroni, $P<0.05$). The 1DR-op condition reduced saccade amplitude, as compared to the 1DR+ condition and the ADR condition ($P<0.05$). No other comparison reached significance. For monkey H, the saccade amplitude in the 1DR+ condition stood out while those in the other three conditions were not different from each other ($P<0.05$).

Peak velocity was also modulated by reward schedule and reward gain (Fig. 5b; Kruskal-Wallis; $\chi^2=344.81$, $P<0.001$ for monkey R; $\chi^2=222.09$, $P<0.001$ for monkey H). It was highest in the 1DR+ condition for both monkeys (post-hoc Bonferroni, $P<0.05$). The two 1DR-conditions resulted in lower velocity of saccades than the others ($P<0.05$), while no statistical difference was found between the two. The peak velocity in ADR was between those of 1DR+ and 1DR- conditions, and significantly different from them ($P<0.05$). Despite the differences between subjects, there was a qualitative positive relation between saccade amplitude and peak saccade velocity.

Discussion

The results of the present study demonstrate that the latency of visually guided saccades is influenced by the prospect of reward. This result complements the facilitation of the saccade initiation observed in the previous

study using the memory-guided saccade task (Takikawa et al. 2002b). Yet, the magnitude of the effect was larger and, more importantly, the larger variations in saccade latency allowed us to inspect the resulting latency distributions more prudently.

Effects of reward expectation on velocity and amplitude of visually guided saccades

In the present study, both saccade amplitude and saccade peak velocity were increased by the expected presence of reward. This shows a clear contrast with the result obtained by using the memory-guided saccade task (Takikawa et al. 2002b). In the memory-guided saccade task, the expected reward gain increased the peak velocity, whereas no systematic modulation of saccade amplitude was observed. One interpretation is that the increase in saccade peak velocity might not be a genuine increase but a natural consequence of an increase in saccade amplitude. It is well known that peak velocity and amplitude are positively correlated among normal saccades. This relationship, which is called the main sequence (Bahill et al. 1975), is directly determined by the firing rate and firing duration of the brainstem motor neurons that control ocular muscles (Moschovakis and Highstein 1994). Therefore, our result could be a manifestation of the main sequence of saccade. However, the positive relationship between amplitude and velocity observed in the present study was still qualitative. To fully explain the results in terms of the main sequence, further experiments are warranted, in which the eccentricity of a target is systematically manipulated.

Effects of reward expectation on latency of visually guided saccades

The expectation of reward facilitated saccades in general. The overall distribution in 1DR+ was shifted to earlier saccades as compared to that in ADR. The occurrence of saccades for 1DR+ was already higher at 120 ms for monkey R and 125 ms for monkey H; this was in the range of earliest saccades (i.e., left-most trials in the latency distributions) in ADR. Also, the facilitation of saccades appears to be fairly constant across latency distributions. These observations suggest that the latency facilitation of a saccade to a reward position is caused by a preparatory mechanism that operates before the appearance of the visual target. Note that the preparatory mechanism should be location-specific and driven by reward-oriented bias (Lauwereyns et al. 2002b). In the 1DR schedule, monkeys do not know the position of an upcoming target and hence there is no rational motive to prepare a saccade to a particular direction. However, since they know saccades toward a particular direction lead to reward, it is natural for them to want to make and prepare for a saccade to the rewarded position. This may be achieved by enhancement of visual processing for the

reward-associated stimulus. Single-unit recording studies have shown changes of visual responses by the expectation of reward in many brain areas (Apicella et al. 1992; Hikosaka et al. 1989b; Kawagoe et al. 1998; Kobayashi et al. 2002; Leon and Shadlen 1999; Platt and Glimcher 1999; Schultz et al. 1992; Tremblay and Schultz 2000; Watanabe 1996). For example, Kobayashi et al. (2002) showed that spatial information carried in visual responses in dorsolateral prefrontal cortex (DLPF) and frontal eye field (FEF) is improved in reward trials as compared to nonreward trials. Alternatively, the oculomotor system may set a response bias toward a reward position before the target appears. Since the reward position was fixed in a daily session, the monkey had an opportunity to develop a response bias and to prepare a saccade in a particular direction associated with reward. Our recent studies have shown that this type of reward-based response-bias may be implemented in the basal ganglia, particularly the caudate nucleus, of monkeys (Lauwereyns et al. 2002b).

In contrast to the expectation of reward, the expected lack of reward seems to have differential effects on early and late saccades. When the monkeys made saccades to no-reward positions, the saccades with latencies longer than about 200 ms (225 ms for monkey R, 180 ms for monkey H) were delayed, whereas the earlier saccades were not affected. Notably, within individual subjects, the divergence points were about the same for 1DR-or and 1DR-op, and the saccade probabilities in 1DR-or and 1DR-op were not significantly different for about 40 ms after those divergence points (up to 265 ms for monkey R and at 225 ms for monkey H). Then, the 1DR-op condition diverged from the 1DR-or condition: saccades in the direction opposite to the reward position were delayed further. These results indicate that saccades to no-reward positions are initially inhibited by a nonspatial mechanism, or a mechanism uniform across the sampled space, with a certain delay from the appearance of the visual target. Saccades to a position opposite to a reward position are further slowed down by a (broadly tuned) location-specific mechanism with an additional delay. This is because, otherwise, 1DR-or and 1DR-op should diverge from each other around the time that they diverge from ADR (i.e., about 200 ms).

Parallel processes for cognitive and motivational demands

Numerous cortical and subcortical neurons in primates show activities related to the expectation of reward (see Schultz 2000 for review). Many of them coexist with neurons that code the preparation or execution of eye or body movements, whose activities are modulated by the expectation of reward (Bowman et al. 1996; Handel and Glimcher 2000; Hassani et al. 2000; Hikosaka et al. 1989a, 1989b, 1989c; Hollerman et al. 1998; Kawagoe et al. 1998; Lauwereyns et al. 2002a, 2002b; Leon and Shadlen 1999; Sato and Hikosaka 2002; Schultz et al. 1992; Shidara et al. 1998; Shidara and Richmond 2002; Takikawa et al. 2002a; Tremblay and Schultz 2000;

Watanabe 1996). Among the brain structures that show reward-related activity, the basal ganglia play a pivotal role in translating motivational context into oculomotor behavior (Hikosaka et al. 2000).

We propose that the saccades observed in the present study were generated by two main parallel corticocollicular streams. The intermediate layers of the superior colliculus (SC) receive direct convergent input from the FEF, DLPF, supplementary eye field (SEF), and lateral intraparietal area (LIP; for review, see Schall 1997). In addition to these direct corticocollicular pathways, there exists another indirect pathway via the basal ganglia. The FEF, SEF, and DLPF all project to the caudate nucleus (CD), which sends inhibitory projections to the substantia nigra pars reticulata (SNr), which in turn sends inhibitory projections to the intermediate SC (Hikosaka and Wurtz 1988; Hikosaka et al. 2000). This CD-SNr-SC disinhibition mechanism has a net effect of facilitation on the intermediate layers of the SC.

There is some evidence for the conjecture that positive and negative motivational contexts are attached to motor signals by the pathway through the basal ganglia (Hikosaka et al. 2000). The initiation of a saccade can be facilitated by preparatory activity in the SC (Dorris et al. 1997; Paré and Munoz 1996) in advance of the target appearance. In the asymmetrical reward schedule, this could be achieved by the reward-based anticipatory activity in the caudate nucleus, facilitating oculomotor activity at a particular location of the SC through the CD-SNr-SC serial inhibitions (Ikeda et al. 2001; Lauwereyns et al. 2002b; Sato and Hikosaka 2002; Takikawa et al. 2002a). Since the anticipatory activity starts before the target presentation (Lauwereyns et al. 2002b), any saccade that is directed toward a reward position can be affected by the reward-based anticipatory activity.

Within the basal ganglia, in parallel with the CD-SNr-SC serial inhibitions, there are other pathways that are relatively independent of the CD-SNr-SC pathway (Hikosaka and Wurtz 1988). They are mediated by the external segment of the globus pallidum (GPe) and/or subthalamic nucleus (STN). The effects of the CD-GPe/STN-SC pathways are opposite to that of the CD-SNr-SC pathway (i.e., inhibition of the SC). Additionally, GPe and STN neurons are less spatially selective than CD neurons (Kato and Hikosaka 1995; Matumura et al. 1992), presumably due to the divergent CD-GPe connection (Kincaid et al. 1998). Therefore, it fits well with the idea of initially location-nonspecific inhibition for nonrewarded saccades. We speculate that the initiation of inhibitory processes through this pathway requires the registration of the visual target (in some other areas of the brain), which produces a delay for the inhibitory process to affect the SC. As a result, populations of saccades that are generated early can be free from the effect of the negative motivational context. But movement signals for slower saccades may interact with the inhibitory signals from the CD-GPe/STN-SC pathways of the basal ganglia.

The location-nonspecific inhibition seems to be followed by an inhibitory process that is location-specific.

This location-specific inhibitory process seems to start later, about 240 ms after the target appearance. Currently we do not know the underlying neurophysiological mechanism for the late location-specific inhibitory process. Further investigations are necessary to address this issue.

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