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Temporal Development of Asymmetric Reward-Induced Bias in Macaques

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Ding L, Hikosaka O. Temporal development of asymmetric reward-induced bias in macaques. *J Neurophysiol* 97: 57–61, 2007. First published October 4, 2006; doi:10.1152/jn.00902.2006. Time and expected outcome are two ubiquitous factors contributing to decision-making. However, it is unclear how they interact to influence motor responses. When two differential reward outcomes are expected at the end of a waiting period, behavioral bias is consistently induced, manifested as shorter latencies for motor responses associated with the preferred reward. To examine how this bias develops in time during the waiting period, we manipulated the duration of the waiting period in an asymmetric reward saccade task in monkeys. We found that the bias increases with the duration of waiting period. Surprisingly, the bias resulted from gradual suppression of saccades to nonpreferred targets rather than from facilitation of saccades to preferred targets. These results have important implications on the neural correlates of reward-induced bias.

INTRODUCTION

Time and expected outcome are two ubiquitous factors influencing decision-making. When the final actions are differentially linked to expected outcome of different values, behavioral bias is often induced toward the more preferred outcome. Such behavioral bias reflects the output of the internal decision-making process and provides a basis for identifying neural correlates of decision-making. Despite the ubiquitous presence of temporal factors, its influences on behavioral bias is poorly understood. The best studied interaction between time and behavioral bias is the phenomenon of temporal discounting. When a fixed reward is expected but with variable delays, the subjective value of the same reward decreases as a function of delay, such that an immediate small reward is preferred over a large reward with long delay (Green and Myerson 2004; Mazur 1984; Richards et al. 1997; Rodriguez and Logue 1988). This phenomenon indicates that time can modulate behavioral bias by affecting directly the value of the expected outcome. However, it is unknown whether temporal factors have additional effects.

In an asymmetric reward saccade task (Fig. 1A), monkeys make saccades to targets associated with preferred reward with shorter latency than to targets associated with nonpreferred reward (Fig. 1B) (Lauwereyns et al. 2002b; Watanabe et al. 2003a,b). In this task, monkeys were trained to maintain fixation of a central point for a constant waiting period. At the end of the waiting period, a target was presented, and monkeys were required to make saccades to the target. The expected reward associated with each target is stable over a block of trials, i.e., the reward asymmetry is known to the monkeys throughout a block of trials, but the actual reward in a given trial is unknown to the monkeys until target presentation. This

design raises several possibilities about how the reward asymmetry information is used over time to result in the final behavioral bias (Fig. 1C). In the first scenario, because the reward asymmetry is always known, behavioral bias toward the preferred target may be present at the beginning of the trial and constant throughout. In the second scenario, the subjective values of reward decreases with time, following a hyperbolic function that is multiplicative to the actual reward magnitude (Fig. 1C, inset) (Mazur 1984). Because the temporal discounting function is independent of reward magnitude (Green et al. 2004; Richards et al. 1997), the difference in the subjective values of the asymmetric rewards decreases in time, giving rise to a decreasing bias. In the third scenario, although the reward asymmetry information is always available, it is only gradually taken into account as time approaches the expected time of target presentation (i.e., the end of the waiting period). Accordingly, an increasing bias may be expected, especially in light of previous results of gradually increasing anticipatory neural activities in asymmetric reward tasks (Coe et al. 2002; Ikeda and Hikosaka 2003; Lauwereyns et al. 2002a,b; Sato and Hikosaka 2002; Takikawa et al. 2002), temporal modulation of attention allocation-related neural signals (Ghose and Maunsell 2002), and effects of time estimation on motor preparation (Janssen and Shadlen 2005).

To test which of these possibilities is valid, we trained two monkeys on the asymmetric reward task using a 2.1-s control waiting period and various probe waiting periods. We found that the behavioral bias increased over time. The increase in the bias resulted primarily from a gradual suppression of saccades toward the nonpreferred target.

METHODS

Two male rhesus monkeys (*Macaca mulatta*; monkey L, 5.3 kg; monkey D, 8–9 kg) were used. All animal care and experimental procedures were approved by the Institute Animal Care and Use Committee and complied with Public Health Service Policy on the humane care and use of laboratory animals. A QNX-based real-time data acquisition system (REX, LSR/NEI/National Institutes of Health, Bethesda, MD) was used for stimulus presentation and data collection. Visual stimuli were rear-projected by an active matrix LCD projector (PJ550, ViewSonic). Water reward was delivered through a spigot under the control of a solenoid valve (Crist Instrument, Hagerstown, MD).

Behavioral tasks

In the visually guided saccade task (Fig. 1A), a trial began with the onset of a central point (diameter: 0.6°). Once the monkey's eye entered the fixation window (3° for monkey D and 4° for monkey L), an

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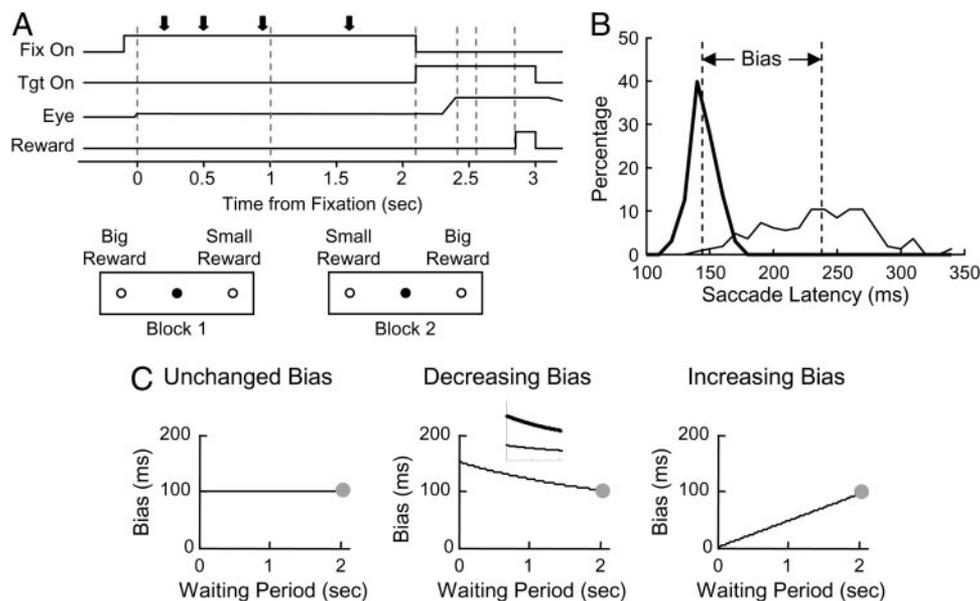


FIG. 1. *A*: asymmetric reward task. Monkeys fixated on a central point for a fixed waiting period of 2.1 s. A peripheral target (left or right) was presented simultaneously with disappearance of fixation point. Monkeys made visually guided saccades to the target to obtain water reward. In one block of trials, large reward is paired with left target and small reward is paired with right target. In the next block, reward association is reversed. In probe trials, fixation point was turned off and target turned on at 200, 500, 950, or 1,600 ms after initial fixation (black arrows). *B*: example distributions of saccade latency in regular trials in one session (monkey D, right target). Thick line, large reward trials; thin line, small reward trials. Dashed vertical lines indicate median values. *C*: 3 predictions of temporal development of asymmetric reward-induced bias. A 100-ms bias at the end of the 2.1-s waiting period was used for illustration purposes (gray circles). “Decreasing bias” was based on a temporal discounting function, $S_{\text{rew}} = \lambda R / (1 + \gamma D)$, where S_{rew} was the subjective value, R was the reward magnitude, γ was the discount factor, D was the length of waiting period in milliseconds, and λ was a constant. For illustration, reward magnitudes were 4 and 1 for large and small rewards, respectively. *Inset*: time-course of subjective values of large (thick line) and small rewards (thin line). $\text{Bias} = (S_{\text{large}} - S_{\text{small}}) \times 1 \text{ ms}$. $\gamma = 0.00025 \text{ ms}^{-1}$; $\lambda = 50.83$. These 2 parameters are arbitrarily chosen to show an ~ 50 -ms decrease in bias over the 2.1-s waiting period and a 100-ms bias at the end. “Increasing bias” is shown as a linear increase in bias.

auditory click signaled the beginning of the waiting period. The monkey was required to maintain its eye within the fixation window until the end of the waiting period, when the fixation point was turned off and a peripheral target was turned on simultaneously. Targets were presented at 20° left or right to the fixation point. The monkey made saccades to the target to obtain water reward. In regular trials ($\sim 85\%$ of all trials), the waiting period was 2.1 s. In probe trials ($\sim 15\%$ of all trials), the waiting period was one of four possible values: 200, 500, 950, and 1,600 ms. Whether a trial is a regular or probe trial was determined randomly except for the following constraints: 1) the first three trials after a block change were always regular trials; 2) probe trials were not presented consecutively; and 3) if an error occurred, regular trials, but not probe trials, were repeated. Error trials consisted of mainly fixation breaks, defined as eyes leaving the fixation window before fixation point disappearance, occasionally two-step saccades, consisting of incorrect initial saccades toward the large reward target followed by corrective saccades to the small reward target, and rarely premature saccades, defined as eyes leaving the fixation window within 100 ms after fixation point disappearance. Error trials were followed by an auditory buzz and penalized by 1- to 1.5-s extension of the intertrial interval. Intertrial interval after a correct trial was 1.5 s.

We explored two schemes of selecting the probe waiting period duration. In the first scheme, probe waiting period duration was pseudorandomly chosen from the four possible values. This value was used in all probe trials for the entire session. An example session consisted of 85% of trials with 2.1 s and 15% trials with 500 ms waiting period. In the second scheme, probe waiting period duration was randomly chosen for every probe trial. An example session consisted of $\sim 84\%$ of trials with 2.1 s and $\sim 4\%$ each with a 200-, 500-, 950-, and 1,600-ms waiting period. The first scheme has the advantage of generating a larger number of probe trials in every target-reward combination, thus facilitating estimation of saccade latency distribution. However, it has the drawback of potential vari-

ability in baseline motivation. The second scheme offers uniform baseline motivation for comparison among different probe waiting period durations, but with smaller numbers of saccades for every condition. Preliminary data suggest that saccade latency was modulated by time in a similar fashion in the two schemes. For this study, we primarily used the first scheme and presented example data using the second scheme in Fig. 2*C* for comparison. Note that, although the first scheme used two discrete periods, it was fundamentally different from the previously used bimodal timing distributions (Ghose and Maunsell 2002; Janssen and Shadlen 2005). In these previous studies, monkeys were extensively exposed to the bimodal distribution to form a stable expectation of events at different timings. In our task, on the other hand, monkeys had extensive experience only with the fixed regular waiting period before this study. In addition, during experiments, probe trials served as “catch trials” and only consisted of $\sim 15\%$ of all trials, thus limiting the possibility that monkey might form stable expectations of bimodal event timings. In addition, the required saccade, of two possible directions, was not known to the monkey until target onset.

In the asymmetric reward task, reward magnitude was differentially associated with the left and right target. In one block of trials (30–35 trials), the left target was associated with large reward (0.3 ml), and the right target was associated with small reward (0.075 ml). The reward association was reversed in the next block and alternated throughout an experimental session. In the equal reward task, reward magnitude was kept constant in a block of trials (50 \sim 100 trials) and could be small (0.075 ml) or large (0.3 ml). Block changes were indicated to monkeys by a prolonged intertrial interval (>5 s).

Data analysis

For analysis, only correct trials were included. Saccade onset latency was determined using standard velocity and acceleration

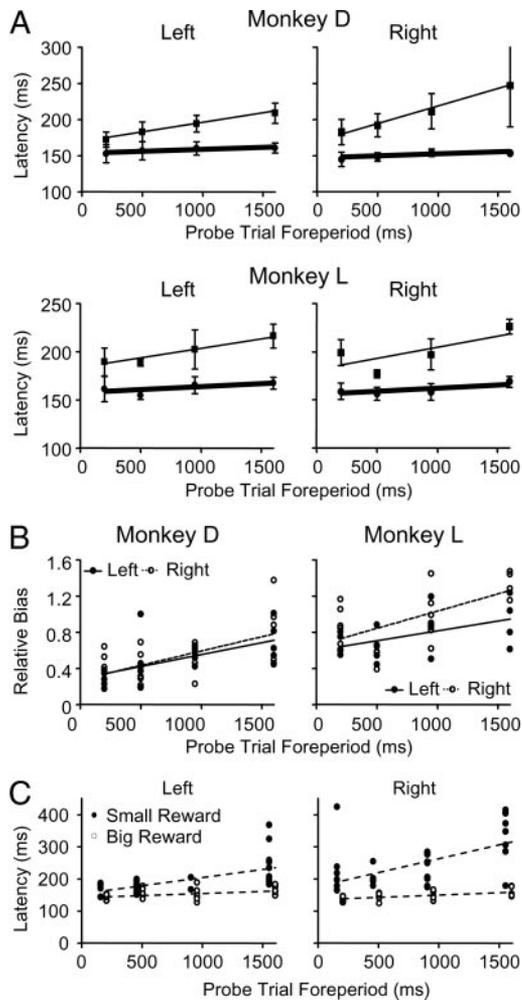


FIG. 2. Bias increases with time in probe trials. *A*: median saccade latency (mean \pm SD) as a function of probe waiting period duration. Latency in large reward trials (circles and thick lines) did not vary with waiting period duration. Latency in small reward trials (squares and thin lines) increased with waiting period duration. Lines represent results from linear regression. *B*: relative bias increased as a function of probe waiting period duration. *C*: saccade latency in probe trials in 1 experiment, in which probe waiting period was selected randomly from 4 values in each trial. Data points for small reward trials were displaced horizontally for better visualization. Dashed lines represent linear regression results.

threshold-crossing algorithms. Examples of saccade latency distribution in regular trials in one experiment session are shown in Fig. 1*B*. Median saccade latency was calculated for every target-reward combination in both regular and probe trials. Behavioral bias was calculated as the difference in median latency between small and large reward trials with the same target. Relative bias was calculated as the ratio of probe trial bias to regular trial bias in the same experimental session. Linear regression and statistical tests were performed on median saccade latency, before averaging for figure presentations, using internal functions in GraphPad Prism 4.01 (GraphPad Software, San Diego, CA).

RESULTS

Consistent with previous reports, behavioral bias was induced in the asymmetric reward task. It is reflected as longer saccade latency in small reward trials than in large reward trials for saccades to the same target (Fig. 1*B*). In probe trials, when the target instructed a saccade with small reward (Fig. 2*A*),

median latency increased significantly as a function of the waiting period duration (linear regression: monkey D: $r^2 = 0.5581$ and 0.3908 , $P < 0.0001$ and $P = 0.0024$ for left and right saccades, respectively; monkey L: $r^2 = 0.3694$ and 0.338 , $P = 0.0075$ and $P = 0.0114$, for left and right saccades, respectively). When the target instructed a saccade with large reward (Fig. 2*A*, black circles, thick lines), median latency showed no significant change with the waiting period duration (linear regression: $r^2 < 0.17$, $P > 0.05$). As a result, behavioral bias, defined as the difference in median latency between small and large reward trials, increased with the waiting period duration. To control for daily variability in baseline motivation, relative bias was computed as bias in the probe trials normalized by bias in the regular trials (Fig. 2*B*). Relative bias showed significant increase with the duration of probe trial waiting period (linear regression: monkey D: $r^2 = 0.3687$ and 0.3311 , $P = 0.0035$ and $P = 0.0063$ for left and right saccades, respectively; monkey L: $r^2 = 0.2617$ and 0.3571 , $P = 0.03$ and $P = 0.0088$, for left and right saccades, respectively). These results indicate that behavioral bias develops in time, even when the same reward asymmetry information is available and constant throughout a block. Saccade latency in regular trials in the same experiments did not vary with the probe waiting period duration (linear regression: $r^2 < 0.05$, $P > 0.38$ and for all target-reward combinations in both monkeys), indicating that the temporal modulation of behavioral bias did not result from changes in baseline motivation or general behavioral strategy. Furthermore, similar temporal development of saccade latency was observed when probe duration was randomly selected for each probe trial (Fig. 2*C*, 2nd scheme). Thus this phenomenon is independent of the actual distribution of probe waiting period, consistent with our assumption that monkeys maintained a stable expectation of a single 2.1-s waiting period distribution rather than forming expectation of bi- or multimodal distributions.

The temporal build-up of behavioral bias resulted from a constant saccade latency in large reward trials and an increasing saccade latency in small reward trials. However, some studies on human subjects have shown that reaction time in simple detection tasks increases with waiting period duration (Foley 1959; Green and Luce 1971; Karlin 1959; Nickerson and Burnham 1969; Sanders and Wertheim 1973). Therefore an alternative hypothesis is conceivable. In the alternative scenario, there is a reward-independent increase in saccade latency as a function of the waiting period duration. In large reward trials, this increase is compensated for by large reward-induced facilitation of saccades, thereby giving rise to apparently stable saccade latency. In small reward trials, this increase is unchanged or augmented by additional small reward-induced suppression of saccades, thereby giving rise to increasing saccade latency. To test the validity of this alternative hypothesis, we characterized the relationship between saccade latencies and waiting period duration in the same monkeys in an equal reward task, with identical timing arrangements as the asymmetric reward task.

As seen in Fig. 3, two main observations argued against a significant reward-independent increase in saccade latency. The first observation was that the median latency in equal reward trials (black data points and lines) followed that in large reward trials in the asymmetric reward task (dashed lines). The estimated slopes were not different between the two conditions

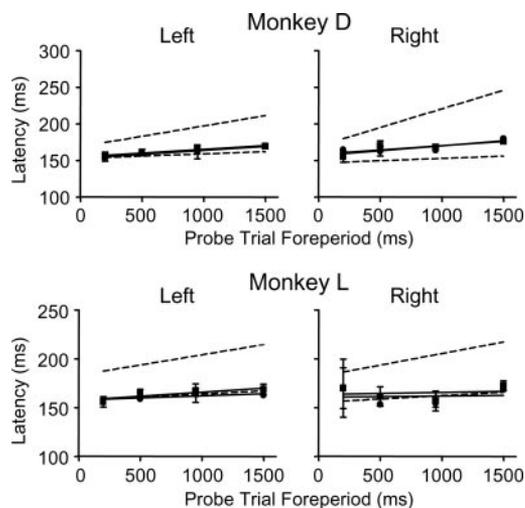


FIG. 3. Median saccade latency (mean \pm SD) in probe trials in equal reward task. Circle, large reward trials; square, small reward trials. Lines represent results from linear regression. Note that median latency was almost indistinguishable between large and small reward trials in equal reward condition. Dashed lines were duplicates of linear regressions data from Fig. 2A, obtained in asymmetric reward task.

($P > 0.3$ for both saccades in both monkeys). The estimated intercepts were also not different between the two conditions in three of four cases ($P = 0.2131$ for left saccades in monkey D; $P > 0.6$ for both saccades in monkey L). The only exception was for right saccades in monkey D. However, even in this exception, median latency in the equal reward task was closer in value to large reward than to small reward trials in the asymmetric reward task. The second observation was that the data points and regression lines for trials with different reward magnitudes were almost identical in the equal reward task (Fig. 3, squares and circles). The estimates of both slopes and intercepts were not significantly different between two reward conditions (slope: $P > 0.35$ for both saccades in both monkeys; intercepts: $P > 0.18$ for both saccades in both monkeys). This indicates that, when there is no reward bias, as in the equal reward task, reward magnitude has little effect on saccade latency. Collectively, these observations indicate that the temporal build-up of the bias seen in the asymmetric reward task resulted mainly from gradually increased suppression of saccades to the small reward target.

DISCUSSION

To summarize, we found that 1) the behavioral bias increased as a function of waiting period duration in monkeys performing in an asymmetric reward saccade task and 2) the increase in the bias resulted primarily from a gradual suppression of saccades toward the nonpreferred target. The first result showed a new form of temporal modulation of behavioral bias, in addition to the phenomenon of temporal discounting. The second result was, to our knowledge, the first demonstration of differential effects of time on actions linked with different outcomes. Furthermore, these results have important implications on the neural mechanisms underlying behavioral bias.

The gradual suppression of small reward saccades without substantial facilitation of large reward saccades suggests that the behavioral bias cannot be fully accounted for by preferential saccade preparation toward large reward targets or by

preferential attention allocation to large reward target positions. It has been shown that when the saccade target is known and the waiting period is variable, saccade latency is inversely correlated to the hazard function based on the subjective estimation of the waiting period distribution (Janssen and Shadlen 2005). In our experiment, because of the overwhelming exposure to a 2.1-s waiting period compared with the infrequent exposure to shorter probe waiting periods, the hazard function was likely monotonically increasing during the 2.1-s waiting period. Alternatively, monkeys might have learned the underlying timing structure despite the limited experience of short probe waiting periods, in which case the hazard function should follow a multiphasic time-course. If monkeys were merely preparing for saccades toward the known, large reward target position, their saccade latency in large reward trials would mirror the hazard function in time. However, our data indicate that the saccade latency in large reward trials shows little dependence on the probe waiting period, suggesting that saccade preparation toward large reward targets cannot fully account for the behavioral bias.

Because attention and motivation are closely linked, another hypothesis suggests that the reward asymmetry-induced bias may be accounted for by differential attention allocation to target locations associated with large and small rewards (Maunsell 2004). Based on results in attention tasks (Muller and Findlay 1988; Posner 1980), attentional modulation is expected to facilitate saccades toward large reward targets and suppress saccades toward small reward targets. The suppression of saccades to nonpreferred (unattended) targets is similar to what we observed. However, the predicted facilitation of saccades to preferred (attended) targets was not observed, suggesting that attentional modulation cannot fully account for behavioral bias induced by reward asymmetry in our task. Interestingly, in a more complicated asymmetric reward task involving four target locations, facilitation and suppression of rewarded and unrewarded saccades, respectively, were indeed observed (Watanabe et al. 2003a). This discrepancy raises the possibility that attentional mechanisms may have an enhanced contribution to the overall behavioral bias in more difficult tasks. It remains to be determined how saccade facilitation and suppression develop in time in the more complex task and whether a similar time-course is followed in attention tasks.

In addition to these high-level implications, our results also pointed to specific directions to search for the neuronal underpinnings of reward-driven bias. Previous research in our laboratory and others has an emphasis on reward-modulated neural activity that correlates with facilitation of preferred motor responses. For example, using asymmetric reward tasks, our laboratory has shown the reward asymmetry-modulated anticipatory activity observed in the basal ganglia, superior colliculus, and cortical eye fields (Coe et al. 2002; Ding and Hikosaka 2006; Ikeda and Hikosaka 2003; Kobayashi et al. 2006; Lauwereyns et al. 2002b; Sato and Hikosaka 2002; Takikawa et al. 2002). Such anticipatory activity emerged before target presentation and had a tendency to increase gradually in time until target presentation. It is selective for one reward asymmetry condition (e.g., left target-large reward and right target-small reward). In the cortical eye fields and superior colliculus, most instances showed enhanced activity when the contralateral target is rewarded or associated with larger reward and the ipsilateral target is either unrewarded or asso-

ciated with smaller reward. Similar, but weaker, laterality was observed in the basal ganglia. The observed laterality has led to the parsimonious hypothesis that the anticipatory activity mediates the behavioral bias by facilitating desired actions (Hikosaka et al. 2006). Our behavioral data, however, showed that saccade latency changed in time only in the small reward trials in a fashion reminiscent of the time-course of the anticipatory activity. This suggests that the dominant role of the anticipatory activity may be suppression of undesired actions, in addition to its possible role in facilitation of desired actions.

In conclusion, we showed temporal build-up of reward asymmetry-induced behavioral bias in a nonhuman primate model. Because of the ubiquitous presence of temporal factors and the dominance of reward driven tasks in behaving animals, their interactions are crucial aspects of decision-making and deserve further examination.

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GRANTS

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