

## TIME COURSE OF A REPETITION EFFECT ON SACCADIC REACTION TIME IN NON-HUMAN PRIMATES

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### INTRODUCTION

Extensive training in a stimulus-response task can lead to adaptive changes in the performance of the resulting behavior (1, 14). For example, it has been proposed that the previous sequence of trials in a saccade task results in modification of performance, most notably, a decrease in saccadic reaction time (SRT) (4).

It is well documented that task complexity influences mean SRT (2, 3, 12) but recently the focus has shifted to look at the variability that occurs when the task is held constant. Some of this variability is the result of a repetition effect in which monkeys are faster at acquiring a target with a saccade if it was the saccadic target on the previous trial. A neural correlate for this behavioral change in SRT has been found in the pretarget activity of saccade-related neurons in the intermediate layers of the superior colliculus (SC) (4). Although the behavior and the neurophysiology converge in demonstrating that a repetition effect exists, little is known about the parameters of the effect. This study is designed to more fully characterize the time course of this repetition effect and search for neural correlates of this time course in the SC.

The first series of experiments explored the behavioral time course of this effect by varying the inter-trial interval (ITI) systematically and measuring the mean SRT for each ITI. The eccentric targets were placed such that saccades would be directed either to the same location as the previous trial (i.e., compatible) or to a location opposite to the previous trial (i.e., incompatible) (Fig. 1A,B). With this design, we were able to determine the effect that the saccade metrics of the previous trial had on the SRT of the current trial and establish the time course of this repetition effect.

The second experiment was designed to determine how the time course of the behavioral repetition effect was correlated with neuronal activity in the SC. A subset of saccade-related neurons in the intermediate layers of the SC have pretarget buildup activity in advance of eye movements (2, 3, 11) and it has been shown that this early activity is correlated inversely with SRT (2, 3) as well as being correlated with the repetition effect (4). This early activity is thought to signal advanced preparation of saccadic eye movements. In the present study we recorded from this sub-

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set of neurons in the SC in an experiment designed to control the animal's behavior between trials, allowing us to examine the time course and effect that the previous saccade had on excitability in the SC and the SRT for the current saccade.

## MATERIAL AND METHODS

Six male rhesus monkeys (*Macaca mulatta*) weighing between 6 and 13 kg participated in this study. During testing, monkeys were seated in a primate chair with their heads firmly fastened to the chair with a head holder. They faced a tangent screen 86 cm away that spanned  $\pm 35^\circ$  of the central visual field. All testing occurred in a dark room. The behavioral paradigms and storage of eye movement data were under control of a PC computer running a real time data acquisition system (7). Eye position was measured with eye coils (8) using the magnetic search coil technique (6). Single-cell recordings of neurons in the SC were made by lowering microelectrodes through a sterilized recording chamber. Both eye position and single-cell activities were digitized at 500 Hz and all analyses were performed off-line. Monkeys were given liquid rewards and were work to satiation, with additional water and fruit given as necessary. All procedures were approved by the Queen's University Animal Care Committee and complied with the guidelines of the Canadian Council on Animal Care.

We established the time course of the previous history effect by varying the amount of time that elapsed between successive trials. The first series of experiments (Time Course Protocol) was conducted on 4 animals and consisted of four blocks of trials, each one consisting of a different total trial duration and intertrial interval (Table 1). In this task, each monkey was required to maintain gaze on a central fixation point that was presented for a variable duration (300-1500 ms). Following a 200 ms gap period, a single target (an LED, 0.3 cd/m<sup>2</sup>) appeared 10° to the left or right of the central fixation point (FP) for 800 ms. The side to which the target was presented was equally probable and randomly determined. The monkey received a liquid reward when it made a saccadic eye movement to the target's position within 500 ms of its presentation and held its gaze at that position for a minimum of 300 ms. The amount of time that elapsed between successive trials was manipulated by varying the duration of the central FP. Four different fixation durations were given in separate blocks of 200 trials. The order that the blocks were given was randomized across successive testing days.

The second series of experiments (Neuronal Recording Protocol) was conducted on 2 different animals and consisted of trials in which the monkey was required to look from the central FP to an eccentric target (T1), back to the central FP, and then to another eccentric target (T2). The monkey was initially required to fixate the central FP for 500 ms after which it was extinguished and T1 was presented simultaneously. The monkey was required to look at T1 within 500 ms of its appearance and then maintain fixation on T1 for 500 ms. T1 then disappeared and the central FP reappeared. The monkey had 500 ms to initiate a saccade to the FP. The second period of fixation had to be maintained for randomly interleaved periods of either 100 ms (short ITI) or 1000 ms (long ITI) before the FP disappeared. There was a 200 ms gap period in which no stimuli were presented followed by the appearance of T2. The location of T1 and T2 were determined by the response field of the neuron being recorded. T1 and T2 could appear either in the response field or at the mirror location, opposite the horizontal and vertical meridians. Thus, within each block of trials there were 8 trial types: 2 possible locations of T1, 2 possible locations of T2, and 2 ITI.

## RESULTS

To examine the time course of the repetition effect on saccadic reaction time (SRT), we measured SRT on compatible and incompatible trials as the intertrial

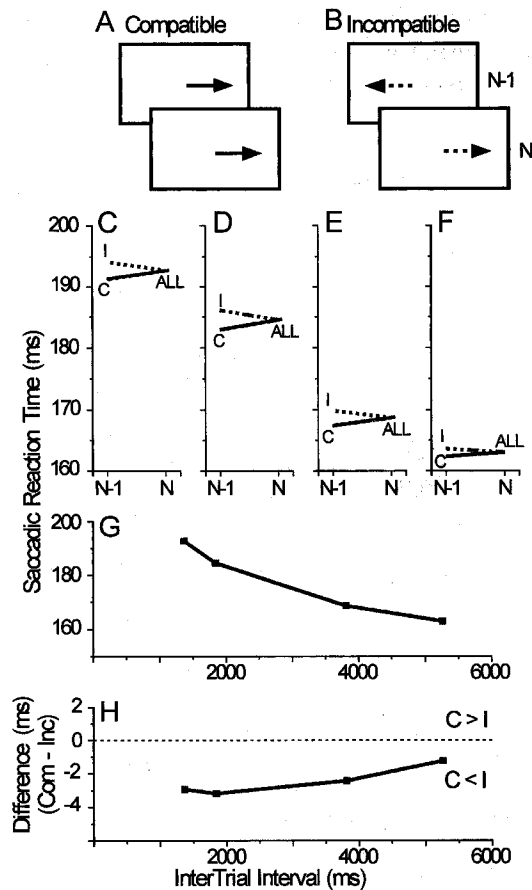


Fig. 1A, B. *Behavior.* - Schematic of a compatible and incompatible sequences of trials in which the previous (N-1) saccade is in either the same or opposite direction to the present (N) saccade, respectively. C-F. Distribution of mean SRT for both compatible (C) and incompatible (I) sequences as the intertrial interval (ITI) was varied. G. Distribution of the mean SRT for each of the 4 ITI. H. The mean difference in SRT between compatible and incompatible trials (compatible SRT - incompatible SRT). The negative value denotes that the reaction time for the compatible saccades was faster than for the incompatible saccades.

interval (ITI) was varied systematically (Fig. 1). The general finding of a repetition effect demonstrated here is consistent with previous results (4) and shows that the previous sequence of trials is one of the factors contributing to variations in SRT.

When the data were collapsed across all 4 monkeys there was an effect of both ITI and compatibility on SRT. The effect of compatibility was present for each of the 4 ITI tested (Fig. 1C-F); when trials were sorted based on compatibility of the previous trial (N-1) relative to the present trial (N), compatible trials had lower SRTs than incompatible trials (F test;  $p < 0.01$ ). There was also a significant difference in SRT across the 4 ITI tested (F test;  $p < 0.05$ ). As shown in Figure 1H, as the ITI increased, there was a trend toward a reduction in the SRT difference between the compatible and incompatible conditions. Consistent with previous reports<sup>12</sup>, as the period of fixation prior to target appearance increased (Table 1), SRT decreased (Fig. 1C-G).

We wished to determine whether the SC saccade-related activity was correlated to the behavioral time course underlying the repetition effect. Using a long (1000 ms) and a short (100 ms) fixation duration prior to T2 appearance, we recorded from the SC saccade-related neurons during the neuronal recording protocol version of the

Table 1. - Durations of the various epochs used in the four separate experiments in which the total trial duration was varied (see Fig. 1A-B for a schematic representation of the task). FP: fixation point; T: target; TTD: total trial duration.

Experiment	FP duration (ms)	Gap Duration (ms)	T duration (ms)	TTD (ms)
1a	300	200	800	1370
1b	700	200	800	1844
1c	1000	200	800	3815
1d	1500	200	800	5266

task. Figure 2 illustrates the activity recorded from a single neuron in the intermediate layers of the left SC that discharged for 10° rightward saccades. During compatible trials (Fig. 2C), a low frequency buildup and burst of activity preceded the rightward saccade made to T1 (into the response field of the cell). The saccade to T2, was also into the cell's response field and a low frequency buildup and burst of activity accompanied this saccade. Note that the buildup activity was initiated slightly before T2 appearance (vertical line in Figure 2C) and well before information of the visual stimulus being presented in the neuron's response field reached the SC. As

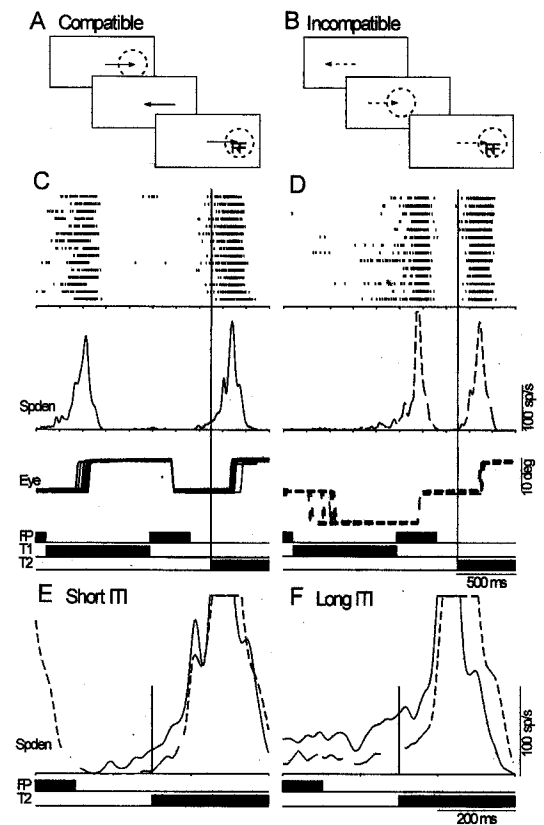


Fig. 2A, B. *Single cell example.* - Schematic of compatible trials (saccade to T1, into the response field of the neuron) and incompatible trials (saccade to T1 opposite to the response field of the neuron). C, D. Rasters, spike density waveform and eye position traces from a single neuron in compatible (C, solid line) and incompatible (D, dashed line) trials. The activity is aligned on T2 appearance, when the monkey made a saccade into the response field of the cell. Upward deflections on horizontal eye position traces represent rightward saccades. E, F. Single cell activity aligned on T2 appearance for short (E) and long (F) ITI trials. For compatible trials (solid trace) a buildup of activity precedes appearance of T2, for incompatible trials (dotted trace) no buildup activity is present during the gap.

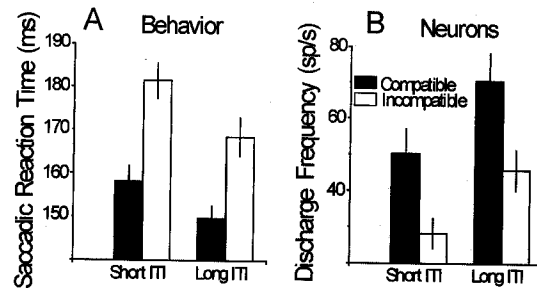


Fig. 3A, B. *Population activity.* - Mean SRT (A) and mean discharge frequency (B) for the compatible (dark gray) and incompatible (light gray) saccades in both the short and long ITI.

shown in Figure 2D, there was a different pattern of activity during incompatible trials. The return saccade to the FP was into the cell's response field and a burst of activity preceded these saccades. The final saccade to T2 was again into the response field of the cell, but the activity remained low and the buildup only occurred after T2 appearance (vertical line in Figure 2D). During the short ITI trials (Fig. 2E), preparatory activity for the compatible trials (solid line) preceded T2 appearance, but was reduced for the incompatible trials (dashed line) until after T2 appearance. As shown in Figure 2F, the neuron displayed higher activity during the longer ITI for both the compatible and incompatible trials, however, this activity was greater in the compatible condition. In addition, following FP disappearance there was a more robust buildup of activity on compatible trials.

We recorded pretarget buildup activity from 32 SC neurons while monkeys performed the task illustrated in Figure 2. As shown in Figure 3, across all of these recording sessions, the mean SRT was significantly reduced for compatible trials, at both the short and long ITI (t-test;  $p < 0.0001$ ). We measured the average discharge frequency from these 32 neurons in the interval spanning 0-50 ms after T2 appearance to represent the pretarget activity in the SC immediately prior to T2 information reaching the SC (2). The mean discharge frequency of the population of neurons was significantly greater for the compatible trials (t-test;  $p < 0.0001$ ). Both SRT and discharge frequency differed significantly between the short and long ITI for compatible and incompatible trials (t-test;  $p < 0.05$ ). These data are consistent with previous studies (2, 3, 4) showing a negative correlation between discharge frequency and SRT, and reveals a neural correlate for the time course of the repetition effect. The repetition advantage that is evident in SRTs is also evident in the early buildup activity of neurons in the SC, in that the pretarget activity of the buildup neurons was elevated if the previous saccade was made to the same location.

## DISCUSSION

The results from this study demonstrate that monkeys have a robust repetition effect on sequential trials, providing evidence for the hypothesis that previous experience is one of the components contributing to variations in SRT. Taken together,

this study reveals three important properties about the influence of the previous trial on saccadic eye movements. First, a robust repetition advantage exists for saccadic eye movements, in which the SRT is shorter if the target of a saccade is in the same position as the previous target. Second, this facilitation is correlated with an increase in the baseline activity of buildup neurons in the intermediate layers of the superior colliculus (SC) immediately preceding the presentation of the second target. Third, this repetition effect is of limited duration, as it disappears when the time that elapses between successive saccades is increased beyond 5000 ms.

The mechanism behind this repetition effect however, is unknown. There are at least 2 possible mechanisms by which this could occur. The SC receives input from areas that are involved in mechanisms of attention and cognitive functioning (10, 15) and may lead to a subjective expectancy of where the next target will be placed which influences movement preparation towards the expected target (2). This could lead to the reduced SRT, particularly after a long sequence of previous saccades in the same direction.

A second mechanism is that the previous sequence of saccades influences a topographical map of saccade generation like that present in the intermediate layers of the SC (5). In the neuronal recording experiments, the monkeys had to make a series of saccades during each trial. Compatible trials consisted of making a saccade to T1 and then back to center and then a second saccade out to T2 (compatible metric with respect to the saccade to T1, but incompatible with respect to the saccade back to the FP). Incompatible trials consisted of making a saccade to T1 and then back to center and then a second saccade to T2 (incompatible metric with respect to the saccade to T1, but compatible metric with respect to the saccade back to FP). It has been suggested that residual activity or inhibition on this map can persist for an extended period of time and can therefore influence SRT (5). Inhibition is believed to be necessary to clip the high frequency burst activity in the SC, therefore allowing the monkey to maintain stable fixation at the saccadic goal (11, 16). Residual inhibition at a given site in the SC can delay initiation of saccades with the same metric. An incompatible trial consists of a sequence of three saccades, the last two of which were of the same metric. The inhibition placed on neurons responsible for driving the saccade towards the FP will have to be overcome before a second saccade of the same metric can be made to T2. This residual inhibition could account for the general increase in SRT observed during the saccades to T2 on incompatible trials (5). On compatible trials, the metrics of each saccade changes from the immediately preceding saccade and residual inhibition would therefore not influence SRT.

The above mechanism could be implemented within the intermediate layers of the SC, which contain an oculocentric map for saccade generation (3). It has been shown that a subset of these neurons is responsible for preparation of the saccade and that pretarget activity of these neurons is inversely correlated with SRT (2, 3, 4). Thus, inhibition of these neurons would cause an increase in SRT, similar to what has been seen in this study, and also place an increase in the amount of time required to bring them up to threshold activity.

It is of interest to note that human subjects produce a very different pattern of

SRTs. Human subjects generate an alternation effect in which SRT is reduced on incompatible trials, relative to compatible trials (9). This incongruence may be explained by examining the different strategies used by humans and monkeys when they are anticipating the next location of the target. Humans tend to match the frequency of previous occurrences in their guesses (17) while the monkeys animals tend to choose the option that has occurred most frequently. Additionally, monkeys are trained to perform these eye movements thousands of times per week, which may result in over-training and an increased expectancy of repeated trials. This in turn may lead to a repetition effect, similar to the one observed here.

The results from this study, however, point towards an overall sequential effect, which can be specifically linked to the compatibility of previous trials with the current one. Importantly, this behavioral facilitation is associated with a neurophysiological correlate, specifically in the intermediate layers of the SC. Additionally, this effect is not stable and appears to diminish over time.

#### SUMMARY

Repeated training in a stimulus response task can lead to adaptive changes in the resulting behavior. Using a simple saccade task, we investigated the effect that the location of the target in the preceding trial had on the saccadic reaction time (SRT) of the current trial. To determine the time course of this effect, we varied the inter-trial interval (ITI). Finally, we examined the pretarget discharge of single neurons in the intermediate layers of the superior colliculus (SC) during the task. Our data reveal that monkeys have a robust repetition effect in which there was an overall decrease in SRT and increase in SC pretarget activity when the target of the previous saccade was in the same location as that of the current trial. Additionally, we have shown a robust time course of this repetition effect, revealing that it exists for only a limited amount of time.

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