Performance Monitoring by the Anterior Cingulate Cortex During Saccade Countermanding
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Performance Monitoring by the Anterior Cingulate Cortex During Saccade Countermanding

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Consensus is emerging that the medial frontal lobe of the brain is involved in monitoring performance, but precisely what is monitored remains unclear. A saccade-countermanding task affords an experimental dissociation of neural signals of error, reinforcement, and conflict. Single-unit activity was monitored in the anterior cingulate cortex of monkeys performing this task. Neurons that signaled errors were found, half of which responded to the omission of earned reinforcement. A further diversity of neurons signaled earned or unexpected reinforcement. No neurons signaled the form of conflict engendered by interruption of saccade preparation produced in this task. These results are consistent with the hypothesis that the anterior cingulate cortex monitors the consequences of actions.

The anterior cingulate cortex (ACC) plays a central role in the self-monitoring that is necessary for adaptive goal-directed behavior (*1*, *2*). Two general hypotheses have been formulated to explain ACC function. The first proposes that the ACC signals a comparison either between the intended and actual response (*3*) or between the intended and actual reinforcement (*4*). The second proposes that the ACC signals the amount of conflict engendered by the coactivation of incompatible response processes that results in frequent errors (*5*). These alternative hypotheses were tested by recording neurons in the ACC of macaque monkeys performing a saccade countermanding task (*6*–*8*). This task manipulates the monkeys' ability to withhold planned saccades, which depends on the stochastic balance of activation between gaze-shifting and gaze-holding neural processes in the frontal eye field (FEF) and superior colliculus (SC) (*9*–*11*).

Neural recordings from the supplementary eye field (SEF) of monkeys performing this task provided evidence for performance-monitoring signals (*12*). Error-related neurons were preferentially active after the saccades of noncanceled trials when no conflict was present. Reinforcement-related neurons were active before and after primary juice or secondary tone reinforcers. Conflict-related neurons were characterized by the variation of modulation after cancellation of the saccade that was inversely proportional to the probability of canceling the partially prepared movement. This variation corresponds to the magnitude of coactivation of movement and fixation neurons in the FEF and SC. These results are the basis of the claim that this countermanding task dissociates error, reinforcement, and conflict signals.

Two macaque monkeys performed the saccade-countermanding task. Their performance was qualitatively identical to that reported in previous studies of macaques. The average saccade latency for trials with no stop signal was 278 ms for monkey H and 359 ms for monkey N. The fraction of errors varied with stop signal delay as observed previously. Stop signal delay was adjusted between 150 and 400 ms to provide approximately equal numbers of correct canceled and incorrect noncanceled stop signal trials; the error rate averaged 41% for monkey H and 43% for monkey N. The average stop signal reaction time was 120 ms for monkey H and 80 ms for monkey N.

In two hemispheres of these monkeys, 454 neurons were recorded (72 in H and 382 in N). The data can be compared directly to those obtained in the SEF of the same monkeys (*12*). The majority of ACC neurons were modulated not at all or inconsistently during the task. We report the characteristics of two populations of task-related neurons.

Error-related neurons discharged after the saccade on noncanceled stop signal trials (12 in monkey H; 43 in monkey N) (Fig. 1, top). Like their counterparts in the SEF, these neurons had characteristics distinct from typical saccade-related movement neurons. They were not modulated during correct saccades on trials with no stop signal, and they were equally active after contraversive and ipsiversive errors. Also, these neurons were not modulated in relation to anticipation or delivery of reinforcement.

No significant activity was observed during canceled stop signal trials as compared to latency-matched no stop signal trials (Fig. 1, middle). Thus, the error-related neurons in the ACC were not active in the period when SEF neurons signaled conflict. Error-related activation may correspond to conflict arising from preparation of a corrective response while the errant response is being executed (*5*). We therefore examined the endpoint and latency of the saccade produced after the noncanceled error. The ocular motor system is designed to prevent concurrent preparation of successive saccades; however, it can occur (*13*) concomitant with conflicting activation of presaccadic neurons coding different saccade endpoints before but not after saccade execution (*14*). Therefore, an analysis was performed to determine whether a relationship exists between the latency of the saccade made after the error and the magnitude of the activity of error-related neurons. No difference was observed in the magnitude of the error-related modulation when monkeys made a saccade sooner or later after an error (fig. S2). In fact, monkeys rarely shifted gaze away from the errant target in less than 200 ms. For 55% of the sessions in which error-related neurons were recorded, no posterror saccades with intersaccade intervals less than 200 ms were observed. In the remaining sessions, only 5% of all trials (2% for H, 6% for N) exhibited posterror saccades with intersaccade intervals less than 200 ms. The fact that the overwhelming majority of errors were not followed by immediate corrective movements and the absence of any difference in error-related activity even when immediate saccades were made exclude the possibility that conflict occurred after errors through concurrent activation of saccade-related movement neurons producing opposing saccades.

The mean (±SEM) latency of error-related activity for the population of ACC neurons was 180 ± 13 ms, which was significantly later than that observed in the SEF of the same monkeys [$t(98)=4.33$, $P < 0.001$] (Fig. 2). Forty-eight neurons with error-related activity were recorded in the SEF of three monkeys, two of which contributed to this study (14 neurons from monkey A, 19 from H, 15 from N). The mean latency of the activity was 111 ± 13 ms. The duration of the error-related activity in the SEF was 295 ± 24 ms (25% = 180 ms, 75% = 332 ms). The mean duration of error-related modulation of ACC neurons was 346 ± 41 ms (25% = 131 ms, 75% = 455 ms), which was not significantly different from that in the SEF ($t(98) = 1.06$).

Error-related activity could originate from the lack of reinforcement. We therefore tested error-related neurons from one monkey by withholding reinforcement on successful trials. Sixteen of 29 neurons responded to the omission of reinforcement (Fig. 1, bottom). For this group of neurons, the latency of response to omission of reinforcement (434 ± 64 ms; 25% = 201 ms, 75% = 595 ms) was significantly later than the latency of response to the error (224 ± 32 ms; 25% = 125 ms, 75% = 271 ms) ($t(15) = 2.93$, $P < 0.01$).

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Reinforcement-related neurons were modulated in relation to the presentation of the juice reinforcement (17 from H, 45 from N). Unlike in the SEF, some responded specifically to juice delivered after successful trials (Fig. 3A) (1 from H, 13 from N), others to juice delivered unexpectedly during the intertrial interval (Fig. 3B) (6 from H, 27 from N), and some to both types of presentation (10 from H, 5 from N) (Fig. 3C). These will be referred to as primary, unexpected, and dual types. Reinforcement-related neurons were not active after errors or in relation to conflict on canceled trials. The timing of modulation for these neurons did not coincide with the saccades after the trial or to oral movements based on direct observation. A proportion of these neurons were tested for response to omission of reinforcement (10 primary, 23 unexpected, 4 dual). Some were more active in response to omission of reinforcement (30% primary, 13% unexpected). Others were more active in response to primary reinforcement (30% primary, 25% dual). The remaining neurons exhibited no difference between the two conditions.

Nearly all of the error-related neurons [50 out of 52 (50/52)] and reinforcement-related neurons (57/62) were recorded from the dorsal bank of the anterior cingulate sulcus, within area 24c as judged by depth relative to the overlying SEF and other landmarks (Fig. 4). No clustering was observed among the error and reinforcement neurons distributed in a strip extending from 3 mm caudal to 4 mm rostral to the SEF. This is coextensive with the area of the ACC that is reciprocally connected with the SEF (*15*, *16*).

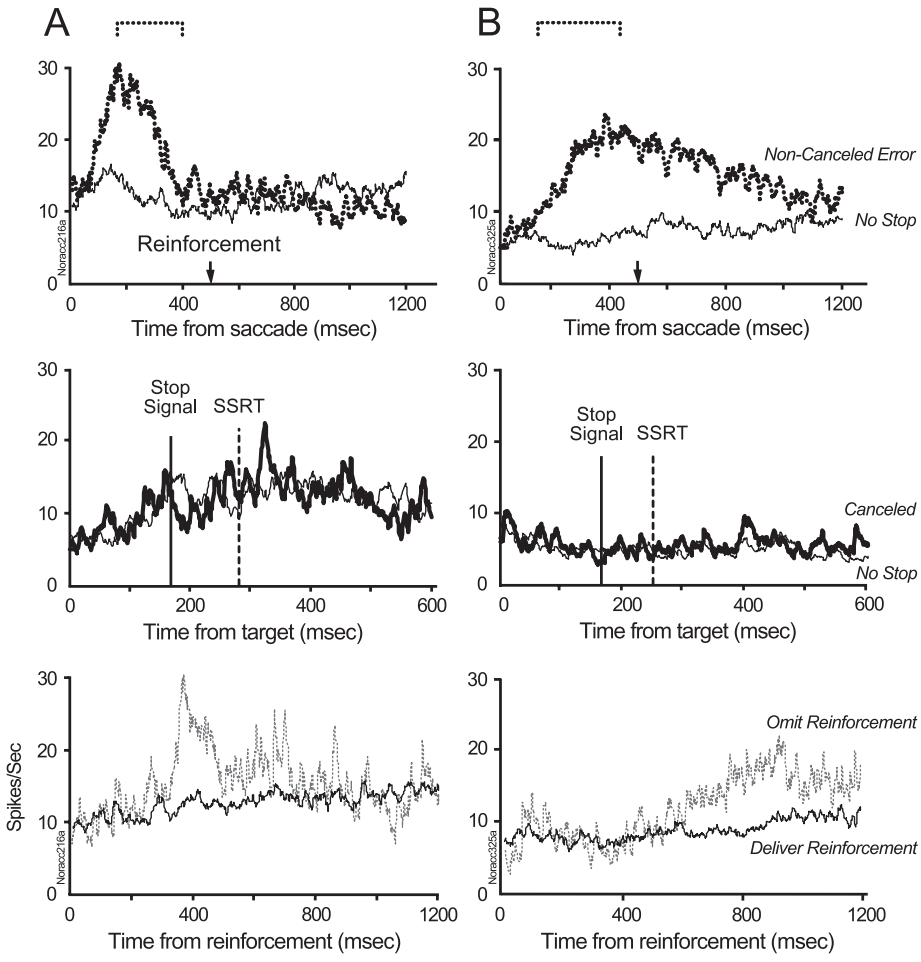

Fig. 1. Neurons exhibiting phasic (**A**) and tonic (**B**) error-related activity. (Top) Activity aligned on initiation of saccade for successful no stop signal trials [thin solid line: (A), 361 trials; (B), 329 trials] and erroneous noncanceled trials [thick dotted line: (A), 110 trials; (B), 135 trials]. The range of times of initiation of saccades after the error is marked by the bracket at the top of each panel. Arrows indicate the time of reinforcement on no stop signal trials. (Middle) Activity aligned on target presentation for canceled trials [thick solid line: (A), 34 trials; (B), 50 trials] and latency-matched no stop signal trials [thin solid line: (A), 90 trials; (B), 145 trials] for one stop signal delay. Stop signal presentation time is indicated by a solid vertical line. Stop signal reaction time (SSRT) is indicated by a dashed vertical line [(A), SSRT = 114 ms; (B), SSRT = 74 ms]. The absence of any difference indicates that these neurons do not signal conflict in this task. (Bottom) Activity aligned on time of reinforcement that is delivered [solid line: (A), 392 trials; (B), 390 trials] or withheld [dotted line: (A), 37 trials; (B), 42 trials]. These error-related neurons also signal omission of reinforcement.

The absence of neurons in the ACC signaling conflict during this task is incompatible with the conflict-monitoring hypothesis (*5*). The possibility of incomplete sampling can never be completely excluded, but the number of penetrations over a broad expanse of cortex made in two monkeys yielding a majority of unmodulated neurons shows that our sampling was not biased. Conflict could be expressed after errors if monkeys made rapid corrective saccades to the fixation point if activation of the movement neurons producing the corrective saccade coincided with activation of the movement neurons producing the noncanceled error saccade. However, scant noncanceled error trials were followed by saccades with sufficiently short latencies to permit concurrent activation. Therefore, posterror conflict was unlikely to occur in most trials.

A signal of conflict when saccade preparation is interrupted may be present in the SEF but not the ACC because the SEF, in contrast to the ACC, is densely connected with ocular motor structures such as the FEF and SC (*15*–*17*). On the other hand, conflict signals may be observed in the human ACC because of differences in species, task, or effector. Species and task differences clearly require further investigation, but differences due to the effector may be more subtle. Only one saccade can be made at a time, but bimanual movements, for example, are common. Therefore, conflict between competing bimanual responses may be more common than conflict between competing saccade responses.

The hypothesis that the ACC compares intended and actual movements using an efferent copy cannot accommodate the present results. First, error-related modulation occurred several hundred milliseconds after movements were concluded. Second, the ACC is not heavily innervated by structures of the ocular motor system, so it can be influenced only indirectly by execution of eye movements. In fact, the error signal observed in the SEF is significantly earlier than that observed in the ACC.

Previous studies have reported neurons in the ACC that are modulated according to expected and actual reinforcement (*18*–*20*).

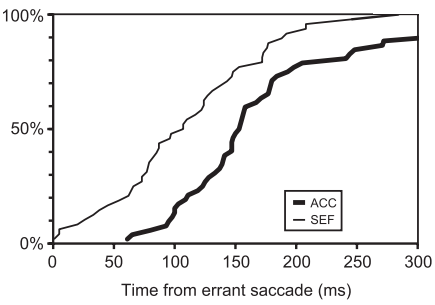

Fig. 2. Cumulative distributions of the latency after the erroneous saccade of error-related activity in the ACC (thick line) and SEF (thin line). The difference is statistically significant.

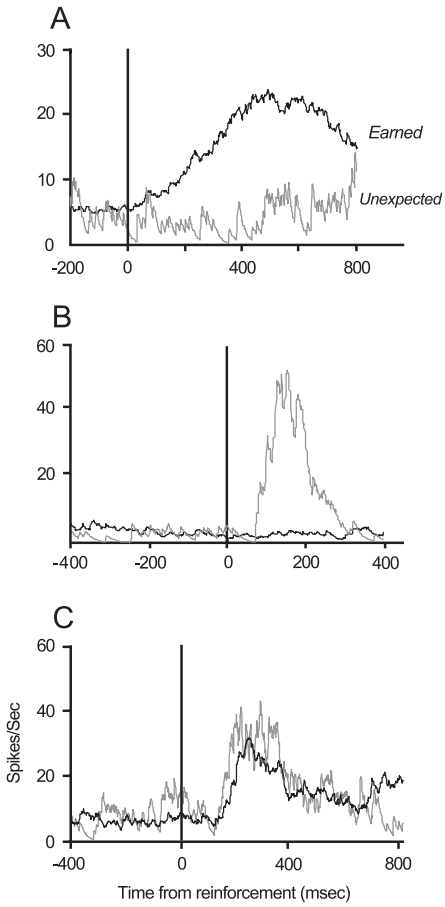

Fig. 3. Diversity of neurons with reinforcement-related activity. Plots are aligned on delivery of reinforcement that is earned in canceled stop signal or in no stop signal trials [black line: (A), 534 trials; (B), 137 trials; (C), 99 trials] or unexpected in the intertrial interval [gray line: (A), 20 trials; (B), 23 trials; (C), 15 trials]. Some neurons discharged after only earned reinforcement (**A**), only unexpected reinforcement (**B**), or either (**C**).

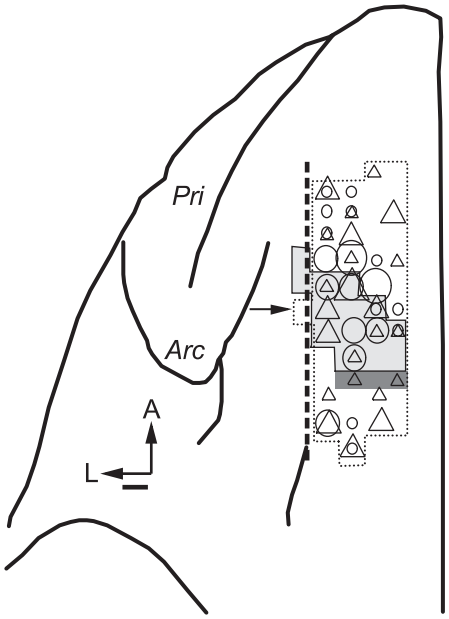

Fig. 4. Location of error and reinforcement neurons for monkey N. This illustrates a top view of the left hemisphere of the macaque frontal lobe. Neural activity was sampled within the region bounded by the dotted line. The incidence of error-related (circle) and reinforcement-related (triangle) neurons is indicated by the size of the symbols (small, 1; medium, 2 to 4; large, >4). Neurons were concentrated in the dorsal bank of the cingulate sulcus. Other landmarks include the extent of the SEF defined by low thresholds (<50 μA) for eliciting saccades with intracortical electrical stimulation (light gray fill) in the dorsal convexity of the cortex, the rostral extent of the forelimb representation in the supplementary motor area (dark gray fill), and the medial limit of the cingulate gyrus (thick vertical dotted line). The arcuate (*Arc*) and principal (*Pri*) sulci are labeled. The horizontal arrow marks 27 mm anterior to the interaural line. Scale bar, 1 mm.

This may occur through the action of afferent dopamine (*4*, *21*), because midbrain dopamine neurons are modulated by the delivery or withholding of reinforcement (*22*–*25*). The diversity of the reinforcement-related neurons and the fact that many error-related neurons also respond to the omission of earned reinforcement is most consistent with the hypothesis that the ACC signals a comparison of predicted with actual consequences.

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Supporting Online Material

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Figs. S1 and S2
References

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