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Motor Cortical Activity in a Context-Recall Task

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A monkey was trained to respond on the basis of the serial position of a test stimulus in a sequence. First, three stimuli were presented successively on a circle. Then one of them (except the last) changed color (test stimulus) and served as the go signal: The monkey was required to produce a motor response in the direction of the stimulus that followed the test stimulus. When the test stimulus was the second in the sequence, there was a change in motor cortical activity from a pattern reflecting the direction of this stimulus to the pattern associated with the direction of the motor response. This change was abrupt, occurred 100 to 150 milliseconds after the go signal, and was evident both in the activity of single cells and in the time-varying neuronal population vector. These findings identify the neural correlates of a switching process that is different from a mental rotation described previously.

The elucidation of the neural mechanisms underlying cognitive processing is a basic goal of behavioral neuroscience (*1*). The recording of the activity of single cells in the brains of behaving animals has provided a powerful tool by which these mechanisms can be studied. In a previous study (*2*, *3*), we identified the neural correlates of a mental rotation process as the orderly rotation of the neuronal population vector (*4*) from a stimulus to a movement direction, through successive directions within a specified angle. This rotation exemplified the spatial rule operating in the mental rotation task, which required the production of a movement at an angle from a stimulus direction. In the present study, we sought instead to determine the neural correlates of a cognitive process, the rule of which was based not on a spatial constraint but on the serial position of stimuli in a sequence: Given an arbitrary sequence of stimuli on a circle, one of which was identified as the test stimulus, the motor response had to be

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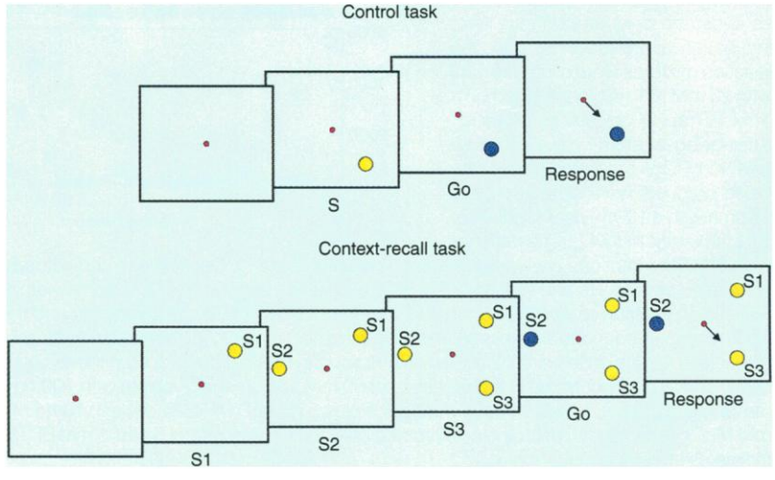

Fig. 1. Schematic diagram of two trials of the tasks used. In the control task (**top**), the yellow stimulus S changed to blue after 400 ms, which gave the go signal. The correct motor response was in the direction of this stimulus. In the context-recall task (**bottom**), three yellow stimuli (S1, S2, and S3) were presented sequentially at 400-ms intervals and stayed on the screen; these stimuli defined the sequence for this trial. In this trial, S2 changed to blue, which now dictated a motor response toward S3.

toward the stimulus that followed the test stimulus in the sequence. This task is a visuomotor version (5, 6) of the context-recall memory scanning task (7). Previous psychophysical studies (6) have suggested that the processing mechanisms differ between the mental rotation and context-recall tasks. In order to determine the neural mechanisms in the latter task, we recorded the activity of single cells in the motor cortex of a monkey trained to perform a context-recall and a control, instructed delay task (8). Moreover, we reanalyzed the neural data from the mental rotation study (3) to compare them with those obtained in the present study.

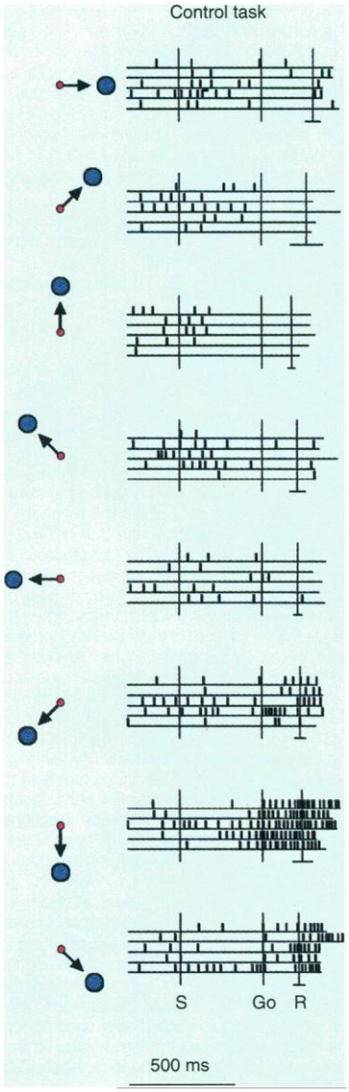

Fig. 2. Rasters of impulse activity of a motor cortical cell are shown for eight directions in the control task. The rasters shown start 250 ms before the appearance of the stimulus (S or S1) and end when the cursor exceeded a threshold (9). The times of occurrence of the stimuli (S), of the go signal (Go) and the average time of the onset of the motor response (R) are shown as long vertical lines. (The standard deviation of the response time is indicated by a horizontal bar over R.) The Go-R time is the response time.

In the control task (Fig. 1, top panel), a yellow stimulus was presented in one of eight positions on a circle and stayed on for 400 ms, after which it turned blue. This provided the go signal for the monkey to exert a force pulse such that the force feedback cursor (8) exceeded a certain threshold (9). In the context-recall task (Fig. 1, bottom panel), three yellow stimuli (list stimuli) were presented successively (every 400 ms) at different positions on the circle and stayed on the screen. After an additional 400 ms, one of these stimuli (except the last) turned blue. This identified the test stimulus, and provided the go signal: Now the monkey had to move the cursor in the direction of the stimulus that followed the test stimulus in the sequence (*10*).

The activity of 544 single cells in the motor cortex was recorded while the monkey performed these two tasks (*11*). The impulse activity of a cell for the eight directions in the control task is shown in Fig. 2. This cell was mostly activated with a downward direction and therefore provided a good marker for that direction. This marker was in turn used as an indicator of the directional information processed during the response time (9) in the context-recall task. Cell activity during two conditions of this task are illustrated in the left and right panels of Fig. 3. In both conditions, the motor responses were in the same downward direction and the test stimuli (blue) were in the same location (up and to the left). However, these stimuli differed in their serial position in the sequence, which provided the meaningful information for correct performance of the task; namely, in the left panel the test stimulus was the first stimulus (S1) in the sequence, whereas in the right panel the test stimulus was the second stimulus (S2) in the sequence. This difference in the serial position of the test stimuli, and the associated motor responses, was reflected in the different patterns of cell activity during the response time. In the left panel of Fig. 3, the cell was activated almost at the onset of the go signal (*12*), and its activation indicated the downward direction, toward S2. This suggests that the monkey anticipated and prepared for such a response, which was the appropriate one in this case. In contrast, in the right panel, this activation did not occur until later in the response time, which indicates that the monkey did not anticipate this direction initially but switched to it 100 to 150 ms after the go signal. Fig. 4 illustrates data from another cell. These effects were routinely observed in other cells.

This switching process was visualized at the ensemble level with the use of the neuronal population vector, computed as a time-varying signal (*2*, *3*, *13*). When the response anticipated did not have to change, the population vector pointed in the appropriate direction throughout the response time. In contrast, when the response had to be changed, the population vector changed direction abruptly, from the direction of the test stimulus to the direction of the motor response (*14*).

The use in this study of the patterns of single-cell activity as markers for behavior is similar to the strategy followed by other investigators (*15*). This approach, together with the population vector, indicated that task constraints were reflected in the neural events and provided evidence for the kind of process involved in the selection of the appropriate motor response. For example, a significant task constraint was that the second stimulus, unlike the first or the third, played a role in every trial by being either the test stimulus or the response direction. Therefore, it is not surprising that it was routinely anticipated at the onset of the response time (*16*). On the other hand, these patterns of neural activity reflecting the direction of the second stimulus changed abruptly to those appropriate for the motor response. This change was evident at both the single-cell and the neuronal population levels (*17*).

The abrupt change in the direction of the neuronal population vector observed in

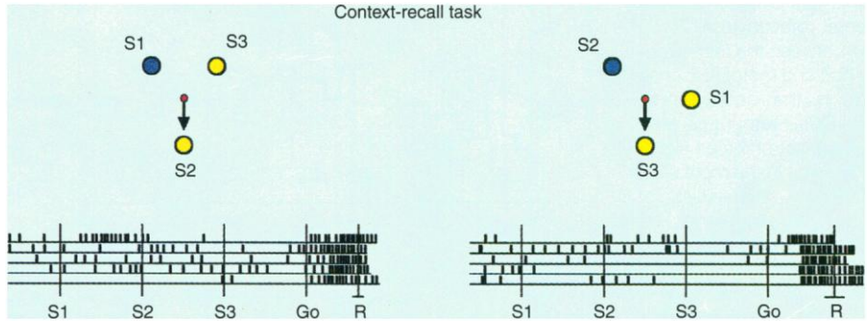

Fig. 3. Rasters of impulse activity of the cell illustrated in Fig. 2 for two cases of the context-recall task. Conventions and time scale are as in Fig. 2.

the present study is quite different from the slow rotation observed in a previous study of mental rotation (*2*, *3*, *18*). Additional evidence for the different nature of the two neural processes was provided by the following analysis. The idea is that in a rotation process, the set of cells with preferred directions in the intermediate direction between the stimulus and response directions should change activity during the response time. In contrast, a switching operation such as postulated for the context-recall task should not involve the activation of cells in directions intermediate between the test stimulus (S2) and motor response (S3). Indeed, this was observed (Fig. 5). It seems then that the time taken to derive the motor direction in the mental rotation task reflects a transformation, whereas the time taken in the context-recall task reflects a selection process. Finally, it should be noted that these studies provide an insight into the neural mechanisms of these processes in a particular brain area, namely the motor cortex, but it is obvious that other brain areas are likely to be involved. Additional experiments are needed to delineate the identification of such areas and elucidate their relative contributions to the performance of the task.

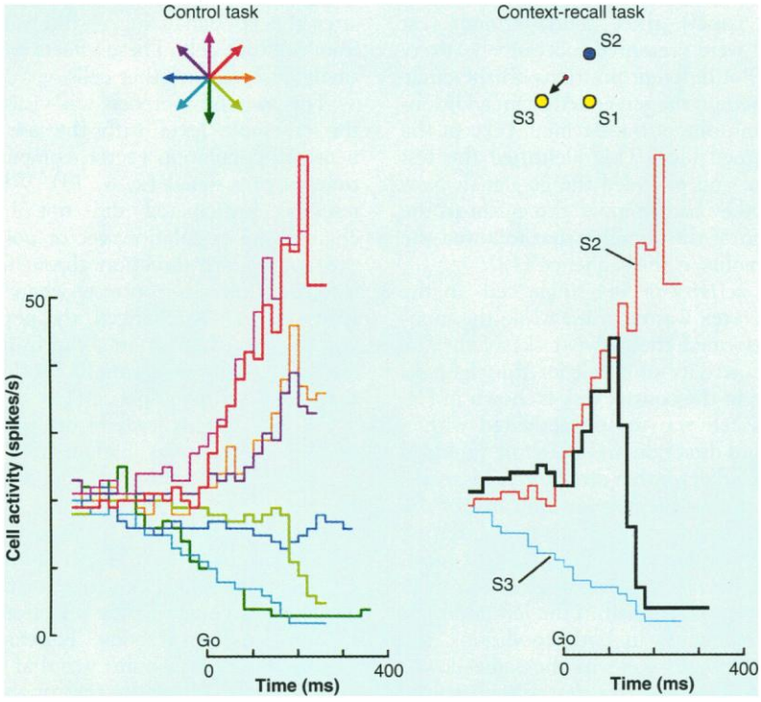

Fig. 4. Peristimulus histograms of activity of a motor cortical cell are shown for eight directions in the control task (**left**) and for one case of the context-recall task (**right**). In the left panel, histograms of cell activity are color coded for motor responses in different directions in the control task. In the right panel, two of these histograms are reproduced as thinner lines together with the histogram (black) of cell activity in the condition of the context-recall task illustrated at the top. After the go signal, cell activity (black) initially increased in the same way as in the control case (thin red line) for the direction toward the test stimulus (S2) and then changed abruptly and decreased to the level corresponding to the control activity for the direction of the motor response (toward S3).

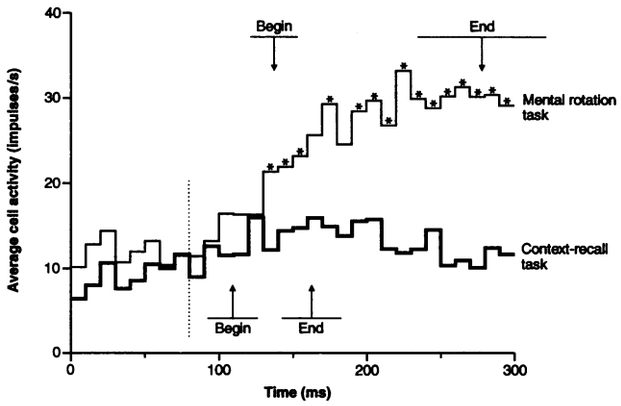

Fig. 5. Peristimulus time histograms (bin width, 10 ms) of the activity of cells with preferred direction at the intermediate direction (±10°) between the stimulus and movement directions in the mental rotation task (*2*, *3*), and between the test stimulus (S2) and motor response (S3) in the context-recall task (*20*). Histograms start at the onset of the go signal (time zero). In the mental rotation task, the activity of such cells (thin line) increased by more than threefold and was statistically significant (indicated by asterisks), whereas in the context-recall task cell activity remained almost constant (thick line) and was not statistically significantly different, as compared with cell activity during the first 80 ms (dotted line; baseline period) (*21*). The arrows indicate the average time (±SD) at which the population vector began to change direction (begin) and when it attained the direction of the motor response (end) (*22*).

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8. The monkey was trained to exert a force pulse on a two-dimensional semi-isometric handle in eight different directions (at 45° intervals). The manipulandum was a vertical rigid metal rod with a disc attached to the top, which was placed in front of the animal in the midsagittal plane and which the animal grasped with the hand pronated. A net force feedback cursor was displayed on a monitor in front of the monkey. This cursor was deflected constantly downward to simulate a bias force of 54 g of force and reflected, at any given moment, the net force: that is, the vector sum of this simulated force and the force exerted by the animal on the manipulandum. At the beginning of the trial, a white stimulus appeared in the center of the screen, and the monkey had to place the force feedback cursor on the center stimulus by exerting 54 g of force in the upward direction and then keep it there within a circular window with a radius of 54 g of force. After 1 s (center hold period), one (control task) or three (context-recall task) yellow stimuli were presented in different directions on a circle with a radius of 270 g of force. During the presentation of the stimuli, the force feedback cursor had to stay within the central window. The order of the tasks for each recording session was the same, with the instructed delay task being performed first.
9. The response was considered correct if the threshold of 270 g of force was exceeded and the direction of the force pulse stayed within ±22.5° from the ideal direction, from the center to the stimulus. The monkey received a liquid reward after each correct trial. The response time was the time elapsed from the onset of the go signal until the force feedback cursor crossed the central window.
10. There are $\left[\frac{8!}{(8-3)!}\right] = 336$ combinations of three different stimuli selected out of eight. All of these combinations were used during training of the animal in the context-recall task. Because the test stimulus could be the first or the second stimulus (serial position) in a combination, a total of 672 conditions were implemented (336 combinations times two test stimulus serial positions). During neurophysiological recording sessions, only 32 of these conditions were used to allow for five repetitions of the same condition within the time constraints of the experiment. These conditions comprised 16 combinations for each of

the two serial positions of the test stimulus, selected such that (i) there were equal numbers of motor responses for each of the eight directions available; (ii) the angle between the test stimulus and the direction of the motor response in a trial was 90°, 135°, or 180°; (iii) the number of the list stimuli presented was the same for each direction; and (iv) the test stimulus was presented in each direction an equal number of times.

11. The rate of successful trials was 91% in the control and 85% in the context-recall task. The electrical signs of cell activity were recorded extracellularly with seven independently movable microelectrodes [V. B. Mountcastle, H. J. Reitboeck, G. F. Poggio, M. A. Steinmetz, *J. Neurosci. Methods* **36**, 77 (1991)]. The collection of neural and behavioral data and the control of the experiment were done with the use of a personal computer. The placement of the recording chamber was done aseptically under general pentobarbitol anesthesia (28 mg per kilogram of body weight). All electrode penetrations were within the primary motor cortex and were confined in the anterior bank and crown of the central sulcus, medial to the level of the genu of the arcuate sulcus and lateral to the precentral dimple.
12. This was due most probably to the fact that the time elapsed from the onset of the first stimulus to the onset of the go signal was constant (at 1200 ms) and therefore allowed the monkey to predict the onset of the go signal.
13. The directional tuning of each cell was computed from the frequency of discharge during the response time in the control task. The preferred direction of the cell corresponded to the direction of the mean resultant [K. V. Mardia, *Statistics of Directional Data* (Academic Press, New York, 1972)]. The statistical significance of the directional tuning was determined by a nonparametric bootstrapping procedure (1000 resamplings) (*3*). The cell was considered tuned when its mean resultant exceeded the 95th percentile of the bootstrap distribution. Two hundred twenty-five cells were directionally tuned. For the calculation of the population vector, peristimulus time histograms of counts of fractional interspike intervals (*2, 3*) were computed (bin width, 10 ms) for each cell and each condition (*8*) as a measure of the time-varying intensity of cell discharge. A square root transformation was applied to the binned data to stabilize the variance (*19*). For a given time bin, each cell made a vectorial contribution in its preferred direction and of magnitude equal to the change in cell activity from that observed during 0.5 s preceding the first peripheral stimulus ("control rate"). The population vector P for the j^{th} condition and k^{th} time bin is

$$P_{jk} = \sum_{i}^{225} w_{ijk} C_i$$

where C_i is the preferred direction of the i^{th} cell and w_{ijk} is a weighting function

$$w_{ijk} = d_{ijk} - a_{ij}$$

where d_{ijk} is the square-root transformed discharge rate of the i^{th} cell for the j^{th} condition and k^{th} time bin, and a_{ij} is the similarly transformed control rate of the i^{th} cell for the j^{th} condition.

14. The change in the direction of the population vector began 111 ± 3.8 ms (mean ± SEM, n = 16 conditions in which S2 was the test stimulus) after the go signal and was completed within a short time (56.9 ± 4.4 ms, mean ± SEM, n = 16). This time is an overestimate of the time of the switching operation because it incorporates the trial-to-trial variability in the time of the switch.
15. L. Chelazzi, E. K. Miller, J. Duncan, R. Desimone, *Nature* **363**, 345 (1993). See also (*1*).
16. The result of this strategy was reflected in the behavioral response. The response time was faster when the test stimulus was the first stimulus in the sequence (mean ± SEM = 250 ± 0.61 ms, n = 9112 trials) than when the test stimulus was the second in the sequence (mean ± SEM = 281 ± 0.62, n = 9113 trials); this difference was statistically significant (t test, $P < 0.001$).
17. In contrast, changes in electromyographic (EMG) activity occurred only shortly before and during the production of the force, which they reflected; they did not reflect the changes in cell activity indicating the switching of directions, such as those illustrated in Figs. 3 and 4. The EMG activity of the following muscles of the upper arm and forearm was recorded with intramuscular, multistranded stainless steel wires [A. B. Schwartz, R. E. Kettner, A. P. Georgopoulos, *J. Neurosci.* **8**, 2913 (1988)]: infraspinatus, supraspinatus, trapezius (lower, middle, and upper parts), triceps (medial and lateral heads), anterior deltoid, posterior deltoid, biceps, forearm extensor, paraspinal, and pectoralis.
18. For example, the average time of change of the direction of the population vector for the 90° mental rotation was (mean ± SD) 141.2 ± 43.2 ms [data from table 5 in (*3*)], as compared with 53.3 ± 11.5 ms and 53.7 ± 21.3 ms for the 90° and 135° angles, respectively, between S2 and S3 in the context-recall task. These results show that the time of change was almost three times longer in the mental rotation task and was the same for the 90° and 135° angles in the context-recall task. This lack of increase with the angle is evidence against a rotation process occurring at a constant rate of angular rotation. It is also interesting that the average duration of change of the direction of the population vector for the 180° angle in the present study was 64.0 ± 13.4 ms and that it was not statistically different (t test) from the values above corresponding to 90° and 135°.
19. G. W. Snedecor and W. G. Cochran, *Statistical Methods* (Iowa State Univ. Press, Ames, IA, ed. 8, 1989).
20. Histograms are means of counts (converted to impulses/s) from 96 and 134 cases for the mental rotation (*3*) and context-recall tasks, respectively. (Each case is an average of four to eight repetitions.) For the mental rotation task, the "intermediate" direction bisected the 90° angle between stimulus and response directions, whereas for the context-recall task it bisected the acute angle (90° or 135°) between the S2 and S3 directions. (The data from the 180° angle were not used in this analysis in order to avoid uncertainty in defining the intermediate direction uniquely.)
21. For each task, a total of 30 10-ms bins (= 300 ms) were analyzed; the first 8 bins (baseline period) were used to construct the control distribution against which each one of the distributions of the remaining 22 bins was tested with the Kolmogorov-Smirnov test [one-sample test; J. H. Zar, *Biostatistical Analysis* (Prentice Hall, Englewood Cliffs, NJ, ed. 2, 1984)]. As 22 simultaneous comparisons were made for each task, the nominal probability level of $\alpha = 0.05$ was adjusted according to the Bonferroni inequality (*19*) to $\alpha' = 0.05/22 \approx 0.002$, so that $P < 0.002$ was considered statistically significant. The frequency distributions of counts of impulses in the control distribution consisted of 1072 values (8 bins × 134 cases) for the mental rotation task, and 768 values (8 bins × 96 cases) for the context-recall task. The frequency distributions of each one of the remaining 22 bins consisted of 134 and 96 values for the mental rotation and context-recall tasks, respectively (*20*).
22. The data for the mental rotation task are from table 5 in (*3*): begin, 137.5 ± 15.8 ms (mean ± SD); end, 278.5 ± 43.6 ms. The data for the context-recall task refer to the angle (90° or 135°) between the S2 and S3 directions: begin, 109.1 ± 17.0 ms; end, 162.7 ± 20.0 ms.
23. Supported by U.S. Public Health Service grant NS17413 and the Department of Veterans Affairs. We thank an anonymous reviewer for suggesting the analysis illustrated in Fig. 5.

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