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3. Motor cortical prediction of movement direction during an instructed delay period

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Summary. We studied the activity of 123 cells in the arm area of the motor cortex of three rhesus monkeys while the animals performed a 2-dimensional (2-D) step-tracking task with or without a delay interposed between a directional cue and a movement triggering signal. Movements of equal amplitude were made in eight directions on a planar working surface, from a central point to targets located equidistantly on a circle. The appearance of the target served as the cue, and its dimming, after a variable period of time (0.5–3.2 s), as the "go" stimulus to trigger the movement to the target; in a separate task, the target light appeared dim and the monkey moved its hand towards it without waiting. Population histograms were constructed for each direction after the spike trains of single trials were aligned to the onset of the cue. A significant increase (3–4×) in the population activity was observed 80–120 ms following the cue onset; since the minimum delay was 500 ms and the average reaction time approximately 300 ms, this increase in population activity occurred at least 680–720 ms before the onset of movement. A directional analysis (Georgopoulos et al. 1983, 1984) of the changes in population activity revealed that the population vector during the delay period pointed in the direction of movement that was to be made later.

Key words: Motor cortex – Arm movement – Movement direction – Delay task

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Introduction

Cells in the motor cortex have been traditionally regarded as "upper motor neurons" and study of their activity has been usually focused within the framework of execution of a motor act. Indeed, a wealth of information has been gathered concerning the relations of motor cortex to muscles, to the isometric force exerted by the animal, to peripheral somatic feedback (see Asanuma 1981; Evarts 1981; and Phillips and Porter 1977, for reviews of these topics), and to compound arm movements (Porter and Lewis 1975; Murphy et al. 1982, 1985; Georgopoulos et al. 1982, 1986, 1988; Schwartz et al. 1988; Kettner et al. 1988). Studies of motor cortical cell activity in the context of a simple reaction time paradigm showed that patterns of activity were similar when movements were triggered in response to visual, auditory or somesthetic stimuli (Lamarre et al. 1983). A more complex task was used in the study of Tanji and Evarts (1976) in which two stimuli were presented: first, either of two "instruction" visual stimuli indicated to the monkey the direction (push or pull) of the upcoming movement, and then a somesthetic perturbation was applied to the hand holding the manipulandum to trigger the movement. It was found that 103/122 (84.4%) of pyramidal tract neurons and 132/137 (96.4%) of non-pyramidal tract neurons studied changed activity within 0.5 s following the instruction stimulus and before the delivery of the triggering perturbation. No changes in the electromyographic (EMG) activity of muscles was observed during the waiting period. These results suggested that the patterns of activity of motor cortical cells can depend on the behavioral paradigm used. These authors also showed that changes in motor cortical cell activity can occur during the instruction period, that is in the absence of immediate motor output. Changes in motor cortical cell

activity during a waiting period preceding movement have also been observed in several subsequent studies (Kubota and Hamada 1979; Kubota and Funahashi 1982; Weinrich et al. 1984; Wise et al. 1986; Lecas et al. 1986).

In the present study we focused on the systematic study of changes in neuronal activity in tasks with or without delay with respect to the direction of movement in a 2-dimensional (2-D) space. This provided degrees of freedom unavailable in previous studies (quoted above) in which flexion-extension, or two-direction pointing movements were used; in such studies the changes in neuronal activity cannot be studied along a quantitative continuum because only two directions are used. In contrast, 2-D movements not only provide a directional continuum but, in addition, this continuum has proved to be meaningful for motor cortical cell activity, as evidenced by the orderly variation in this activity, with the direction of 2-D movements (Georgopoulos et al. 1982). In the present experiments we analyzed the instruction-related changes in activity of motor cortical cells with respect to the direction of 2-D arm movements. A visual stimulus was presented as the target of the movement but the monkeys were trained to withhold their movement until the light dimmed, after which the movement was executed. We wished to determine if changes in motor cortical cell activity during the delay period provided information concerning the direction of the upcoming movement in 2-D space. We found first, that changes in cell activity were indeed oserved during the delay period; this was a prerequisite for further analysis. Second, these changes in cell activity during the delay period were frequently but not always congruent with the changes observed in the non-delayed task. Third, decreases in activity were more frequent than increases. Fourth, there was a subset of cells that did not show changes during the delay period, although they did so in the non-delayed task; this means that the "anticipatory" changes affect only certain cells. But the basic result was that the neuronal population vector (Georgopoulos et al. 1983) computed during the waiting period predicted well the direction of the movement to be executed later. Preliminary results were reported (Crutcher et al.1985).

Methods

Animals and behavioral apparatus Three rhesus monkeys (3.5–4.5 kg body weight) were used. They were trained to move a low-friction, lightweight articulated manipulandum over a planar working surface and capture lighted targets within a circle attached to the manipulandum (Fig. 1). The two-dimensional apparatus has been described in detail previously (Georgopoulos et al. 1981).

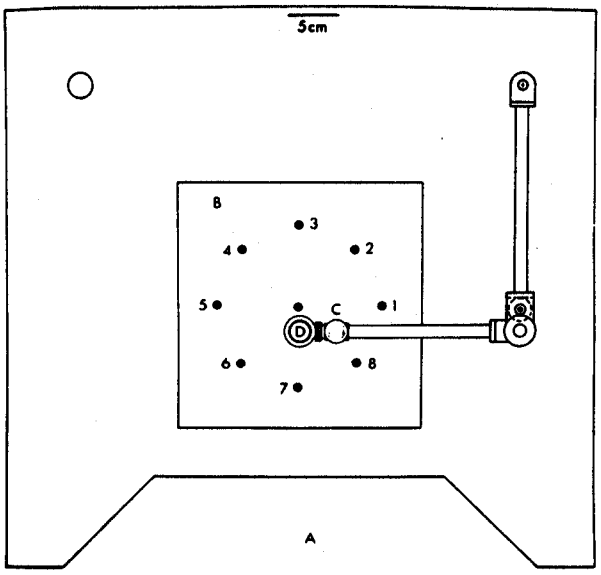

Fig. 1. Schematic drawing of the apparatus used. The monkey was sitting in a primate chair at A and grasped the articulated manipulandum at C to capture lighted targets (numbered dots) on surface B within the transparent plexiglass circle (D)

The plane was tilted 15° from the horizontal towards the animal. With gravity acting on the manipulandum, static forces on the *x* or *y* axis of the plane did not exceed 94 g. A circular pattern of light emitting diodes (LED) was used, with one LED at the center and eight at the circumference of a circle of 8 cm radius. The peripheral LEDs were arranged equidistantly on the circle so that the direction of movement from the center to peripheral LEDs ranged over the whole directional continuum of 360° every 45°. Figure 1 shows the experimental arrangement for operation by the right arm; when the left arm was used the manipulandum was repositioned on the left side of the working surface in a mirror-image configuration.

Behavioral tasks. Two tasks were used. In both tasks the center LED was turned on at the beginning of a trial, and the animal captured it with the manipulandum and held it captured for a variable period of time ("control period", 1.5–4 s) within a 10 mm diameter circular positional window centered on that LED. If the monkey moved the manipulandum out of that window, the trial was aborted. When the control period ended, the center LED was turned off as one of the peripheral LEDs was turned on. In the *nondelayed movement* task (Fig. 2, top) that LED was turned on *dim* ("go" signal), and the animals were trained to move promptly towards it without waiting, capture it within a 20 mm positional window centered on that LED, and hold it captured for at least 0.5 s in order to receive a liquid reward. In the *delayed movement* task (Fig. 2, bottom), the peripheral LED was turned on *bright* (cue signal): the animals were trained to wait and hold the manipulandum at the center position for as long as the peripheral LED remained bright. This time (the "delay" period) was variable from trial to trial and ranged from 0.5 to 3.2 s. At the end of the delay period the LED was dimmed; this served as the "go" signal for the animals to move towards that LED, capture it and hold it captured for at least 0.5 s in order to receive a liquid reward. In addition to monitoring the x-y position of the manipulandum (see below), the animal's behavior was continuously monitored using a

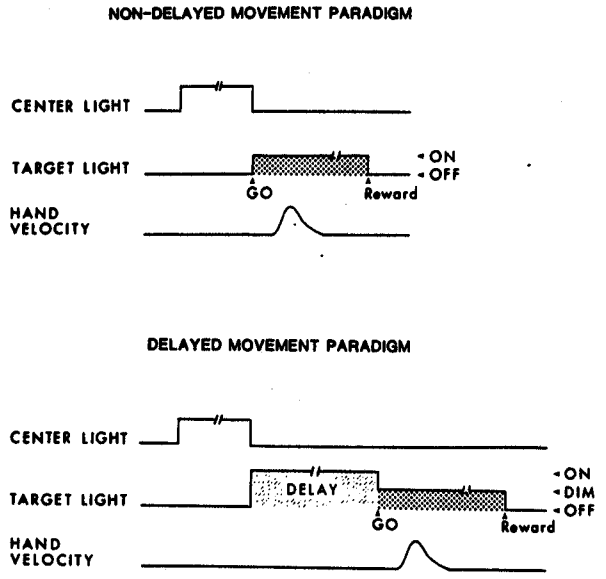

Fig. 2. Schematic description of single trials of the tasks used. (The capture at the center is not shown because very often the animals moved the manipulandum to the center during the intertrial interval preceding the lighting of the center light)

video camera to ensure that no movements or obvious changes in posture occurred while the animal held the manipulandum at the center window.

The animals were first trained in the non-delayed movement task for 30–40 days, and then in the delayed movement task for approximately two additional weeks. The activity of each cell was recorded during performance of both tasks; the order in which the two tasks were performed (first or second) was randomized from cell to cell. For each task, 64 trials, corresponding to 8 movements in 8 directions, were performed in a randomized block design (Cochran and Cox 1957).

Neural studies. After the training of the animals was completed, a recording chamber of 16 mm internal diameter was placed over the arm area of the motor cortex under general pentobarbital anesthesia and a T bar was positioned on the skull for the purpose of immobilizing the head during the experiment. The chamber and the T bar were held in place on the skull with dental acrylic. The electrical signs of activity of cells in the arm area of the motor cortex contralateral to the performing arm were recorded extracellularly (Mountcastle et al. 1969) using standard electrophysiological techniques (see Georgopoulos et al. 1982 for details). Once the action potential of a neuron was thus isolated, a detailed examination of the animal was carried out to determine whether the cell activity was related to the movements of the contralateral arm and, if so, the electrical signs of the cell activity were recorded while the monkey performed in the task. At the end of some penetrations, small lesions were made to facilitate the reconstruction of the penetration; typically, a 3 μA current was passed through the tip of the microelectrode for 3 s. At the end of the experiment, penetrations were made in which several lesions were placed for marking purposes. After 2 to 3 days, the animal was killed with an overdose of pentobarbital. The brain was fixed in buffered formalin, embedded in celloidin, and sectioned every 20 μm, and each section was stained with thionin. Microelectrode penetrations in which lesions were made were reconstructed from these sections. The point of entry into the brain of penetrations in which no lesions were made was determined relative to the identified penetrations using the grid map of the chamber.

Electromyographic studies. The EMG activity of the following muscles (Howell and Straus 1933) was sampled in the task using intramuscular, teflon coated, multistranded, stainless steel wires: acromiodeltoid, cleidodeltoid, spinal deltoid, pectoralis major, triceps and biceps. EMG recordings were made separately from neural recording sessions. The EMG signals were recorded differentially with an approximate gain of 3,000 and a bandpass below 100–500 Hz. They were then rectified and sampled every 10 ms.

Data collection. A PDP11/34 laboratory minicomputer was used to control the lights on the plane, to monitor and record behavior, and to collect data. Neural data were collected as interspike intervals with a resolution of 0.1 ms. The position (x, y) of the manipulandum was sampled every 10 ms with a resolution of 0.125 mm.

Data analysis. Standard analysis (Sokal and Rohlf 1969; Snedecor and Cochran 1980) and display (rasters, histogram, etc.) techniques were used to inspect, evaluate and analyze the data.

Analyses of single cell activity

Changes in cell activity. Peristimulus time histograms were constructed for each movement direction and each cell with a binwidth of 20 ms. For the non-delayed movement task, the rasters were aligned to the onset of the peripheral LED, whereas for the delayed movement task they were aligned to the onset of the cue signal. For a particular histogram, the mean and standard deviation of the frequency of discharge during the control period was calculated from the 25 bins (i.e. 500 ms) immediately preceding the event to which the rasters were aligned. A forward search from that event was then carried out. A significant change in cell activity was deemed to have occurred when three consecutive bins showed change in the same direction (i.e. increase of decrease in activity) and the discharge rate of at least two of the three bins was more than 3 standard deviations away from the mean control activity, as defined above. This criterion worked well for increases in activity but occasionally failed to detect decreases in activity when the lower interval was negative, a nonrealizable case in the histogram in which the lowest possible discharge rate is zero. Therefore, every latency value provided by this analysis was checked by all the three authors of this paper by inspection of the histogram and raster display, and a value was accepted by common agreement. This checking ensured that no aberrant values were accepted for either increases or decreases in cell activity. For the delayed movement task, first changes in cell activity were determined during the 500 ms following the cue onset because this was the minimum delay used in the task; longer search times would have contaminated the results with changes in activity occurring after the onset of the "go" signal.

Directional tuning. The frequency of cell discharge during the non-delayed movement task served to distinguish cells that were tuned with respect to the direction of the movement. For that purpose the average frequency of discharge from the onset of the peripheral LED until the manipulandum entered the positional window centered on that LED (see Methods) was analyzed in order to determine whether the cell activity was directionally tuned and, if so, calculate the preferred direction of the cell. The techniques for this analysis are described in detail in Georgopoulos et al. (1982) and will not be repeated here.

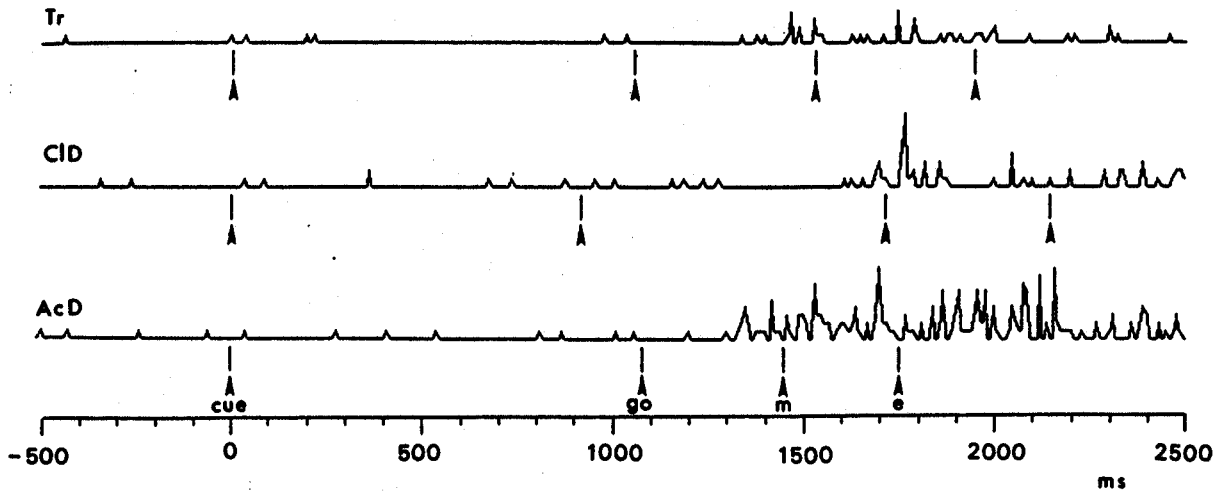

Fig. 3. EMG activity of three muscles recorded in three separate trials. Abscissa is time. Tr, triceps; ClD, cleidodeltoid; AcD, acromiodeltoid; m, onset of movement; e, entrance to the target window

Analysis of neuronal population activity

Population histogram. This provided information concerning changes in activity at the neuronal population level. A population histogram was constructed for each movement direction and each of the two tasks used by aligning the rasters from all cells to the event of interest (e.g. the onset of the cue or the "go" signal) and averaging across all trials.

Neuronal population vector. We calculated the population vector (Georgopoulos et al. 1984) every 20 ms from the cue onset forward in time to determine whether the changes in cell and population activity during the delay period could predict the direction of the movement triggered after the delay. Since the delay varied from 0.5 to 3.2 s, the population vector was calculated every 20 ms for 460 ms following the cue onset. This restriction of the time-analysis to the minimum delay ensured that no changes in cell activity were incorporated that were in response to the "go" signal that triggered the movement. The population vector was calculated using the directionally tuned cells and the techniques described in Georgopoulos et al. (1984). Briefly, the population was considered as an ensemble of cell vectors, each oriented along the cell's preferred direction. The length of a particular cell vector was proportional to the change in cell activity from the cell's mean activity during the last 500 ms of the control period (see above). The population vector was then obtained by summing these weighted cell vectors. For statistical purposes, the mean direction of the population vector during the minimum delay period (0.5 s) was also calculated. The directional congruence between the mean population vector and the direction of movement was evaluated using the circular correlation coefficient of Fisher and Lee (1983).

Results

Behavioral performance

The animals performed at a level of 95+% in both the non-delayed and the delayed movement task.

EMG studies

The biceps was not active in either task. The EMG activity of the other muscles studied changed in relation to the direction of movement following the "go" signal in both the non-delayed and the delayed movement tasks. However, no changes in EMG activity were observed during the delay period for the muscles studied. This is illustrated in Fig. 3 for three muscles during three single trials, and in Fig. 4 for the average EMG activity of acromiodeltoid muscle. This muscle was the most active of those studied (Fig. 3, bottom trace) and therefore most likely to show changes during the delay period if small contractions were made. The lack of EMG changes during the delay period was consistent with the fact that during that period the animal held the manipulandum within the 10 mm diameter positional window. Movements in particular directions elicited in response to the "go" signal were produced by the concomitant activation of more than one muscles, as observed before (Georgopoulos et al. 1984). Changes in EMG activity usually occurred 50–150 ms before movement onset, depending on the muscle and the direction of the movement.

Neural studies

A total of 123 cells were studied during 31 penetrations into the arm area of the motor cortex (Brodmann's area 4) contralateral to the performing arm in four hemispheres of three monkeys. The movement-related activity (see Methods) of 89/123 (72%) cells

was directionally tuned in a sinusoidal fashion, as described previously (Georgopoulos et al. 1982). Briefly, the frequency of cell discharge was highest with movements in a particular direction (i.e. the cell's preferred direction) and decreased progressively with movements made in directions farther and farther away from the preferred one.

Changes in neuronal activity during the delayed and non-delayed movement tasks

The changes in neuronal activity during the delay period were examined in detail for six movement directions, corresponding to LEDs 2–7 in Fig. 1 (right hand). LEDs 1 and 8 (for the right hand, or 5 and 6 for the left hand) were sometimes partially obstructed by the distal arm of the articulated manipulandum and/or the animal's forearm, and although the animals moved promptly to them in the non-delayed task, they had difficulty in detecting their dimming in the delayed movement task. Therefore, shorter delays were used for these two LEDs and the changes in activity during these periods were not incorporated in the results that follow.

Changes in cell activity during the delay period were observed frequently (see below). Figure 5 illustrates examples of increases (A–C) and decreases (D, E) in activity that occurred following the onset of the cue signal. The onset of the "go" signal (i.e. the end of the delay period) is indicated by a longer vertical bar and marked by a dot for the shortest (top) and longest (bottom) delay within a group of repeated trials. It can be seen that the changes in cell activity lasted throughout the delay period. In general, the changes in cell activity lasted at least 500 ms for 40% of increases and 74% of decreases in activity.

Finally, several cells did not change activity during the delay period in the delayed movement task although they did so during the non-delayed movement task; this indicates that the presence of strong changes in activity during the non-delayed task did not ensure changes in activity during the delay period. Figure 6 illustrates the activity of a cell which was strongly engaged in the non-delayed movement task but did not change activity at all during the delay period.

Table 1 summarizes the results concerning the changes in cell activity of the 89 directionally tuned cells during the non-delayed movement task and the delay period in the delayed movement task. Since changes in cell activity for six movement directions were analyzed for each cell (see above), the total N is $6 \times 89 = 534$ cases. It can be seen that changes in cell activity during the delay period were observed in

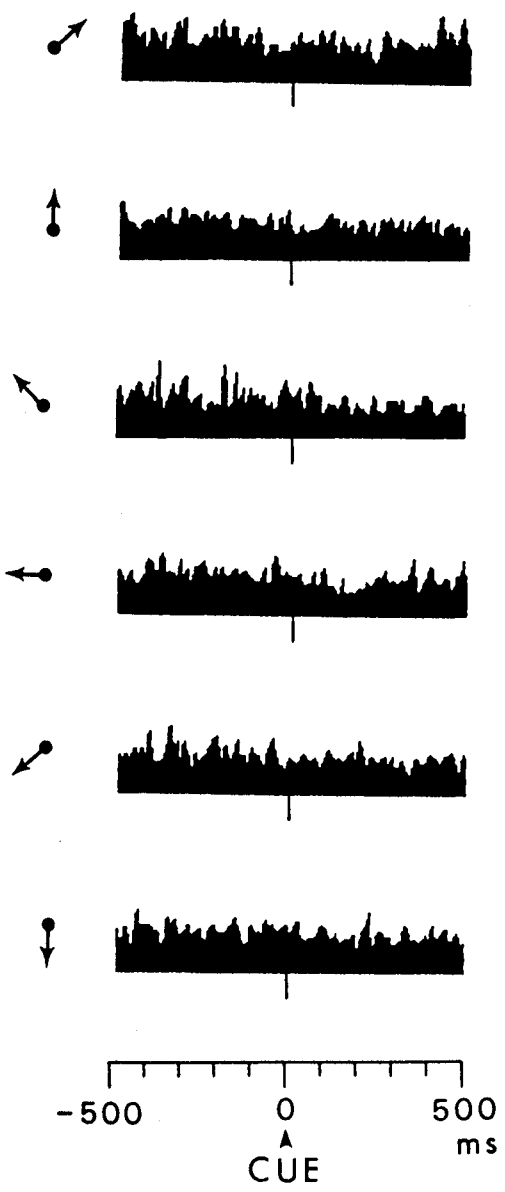

Fig. 4. Average EMGs (eight trials per direction) before and during 0.5 s following the cue onset. The direction of movement is indicated on the left. Recordings were from acromiodeltoid muscle (right hand)

50% of the cases, and most of those (201/267 = 75.3%) were in the same direction (increase or decrease) for both the non-delayed and the delay period of the delayed movement task. Finally, in 209/534 (39.1%) of cases changes in activity were observed in the non-delayed movement task but not during the delay period.

These findings suggest that the changes in cell activity followed similar trends both during the delay and the non-delayed movement task. This suggestion was evaluated by analyzing Table 1 using a R × C

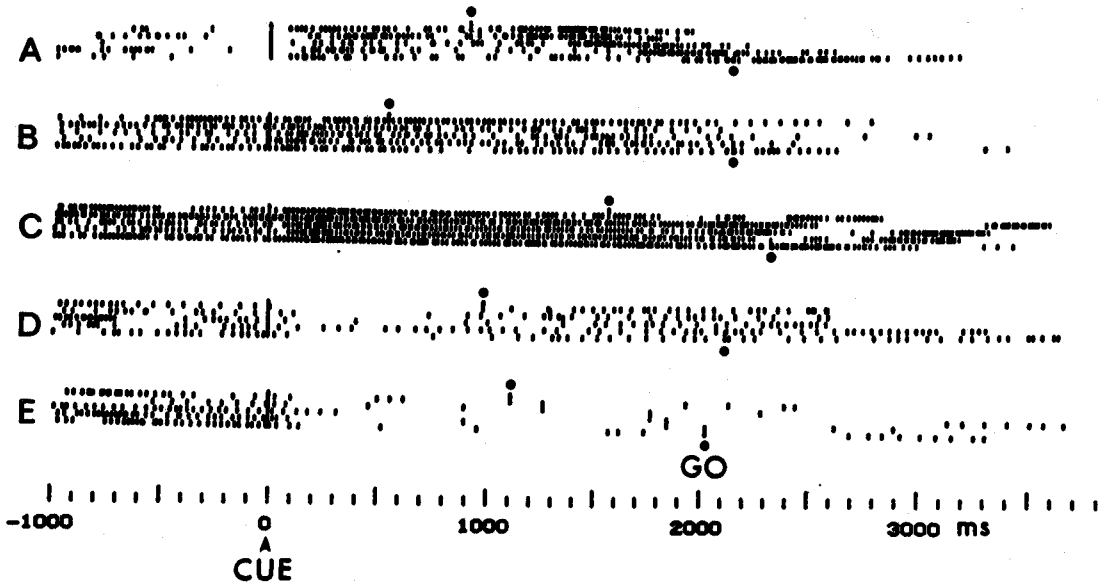

Fig. 5A–E. Examples of changes during the delay period from five different cells (A–E). For each cell, impulse activity is shown during five trials in the same direction. Rasters are aligned to the cue onset and arranged within each group, from top to bottom, according to the length of the delay period, from short to long. The onset of the "go" signal is indicated by a longer vertical bar following the cue onset and marked by a dot for the shortest and longest delay in the group

(3 × 3) test of independence (G-test, Sokal and Rohlf 1969). The null hypothesis is that the frequency of occurrence of increase, decrease, or no change in cell activity in one of the tasks is independent of the changes in the other task. This hypothesis was rejected ($G = 145.3$, 4 d.f., $P < 0.001$); therefore, the changes in cell activity in the two tasks were associated. It is possible that the result could be different if the "no change" in activity was excluded from the analysis. For that purpose we reanalyzed the data by constructing a 2 × 2 table containing only the frequencies of increase and decrase in activity (values 127, 36, 8, and 74 from Table 1). Again the null hypothesis was rejected ($G = 112.5$, 1 d.f., $P < 0.001$). These results indicate that the changes in cell activity are associated between the two tasks.

The results shown in Table 1 refer to the number of cases analyzed; a different question concerns the proportion of directionally tuned cells that would be engaged during the delay period for at least one movement direction, that is in at least one case. This proportion was 70/89 = 79% of cells in the present sample.

Latencies of changes in cell activity

Figure 7 shows the relative frequency distributions of the latencies of increases ($N = 146$) and decreases ($N = 121$) in activity (solid and dotted line, respectively) observed following the onset of the cue signal in the delayed movement task. Changes in cell activity were observed shortly after the cue onset; fifty percent of the changes in activity had occurred by 120 ms for increases and by 140 ms for decreases in activity. This preponderance in time of increases in activity was statistically significant (Kolmogorov-Smirnov test, $P < 0.001$).

Figure 8 shows the relative frequency distributions of the latencies of increases ($N = 333$) and decreases ($N = 121$) in activity (solid and dotted line, respectively) observed in the non-delayed movement task for the same cell population but following the onset of the "go" signal. The time course of increases and decreases did not differ significantly (Kolmogorov-Smirnov test).

Decreases in activity were observed with equal frequency in both tasks ($N = 121$ for both tasks), and their time course was very similar (dotted lines in Figs. 7 and 8; Kolmogorov-Smirnov test not significant). In contrast, increases in activity were observed more than twice as frequently in the non-delayed movement task than during the delay period ($N = 333$ versus $N = 146$), but they occurred earlier in time following the cue onset during the delay period in which case the rising phase of the distribution was steeper and late increases fewer, as compared to the non-delayed movement task (compare the two solid lines between Fig. 7 and Fig. 8).

Given that in many cases ($N = 245$) changes in activity were observed in both tasks, it is interesting

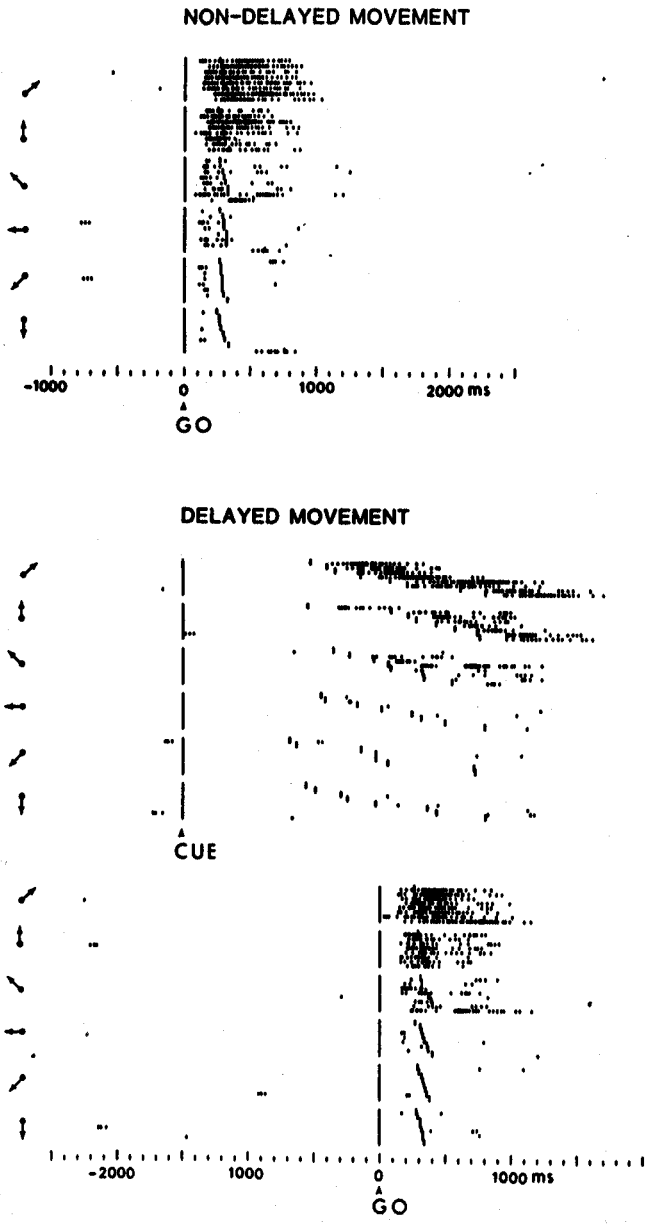

Fig. 6. Impulse activity of a cell that did not change its activity during the delay period but increased its activity following the "go" signal. Activity during eight repeated trials is shown for each movement direction indicated on the left. *Top*: impulse activity in the non-delayed movement task. Raters are aligned to the "go" stimulus; longer bars in each trial following the "go" signal denote the time at which the movement began. *Middle*: impulse activity of the same cell in the delayed movement task. Rasters are aligned to the onset of the cue signal; longer bars in each trial following the cue signal denote the onset of the "go" signal. *Bottom*: the same data as in *middle* are shown but rasters are aligned to the onset of the "go" signal

to know whether the latencies of these changes covaried in the two tasks; for example, are early increases in activity following the cue associated with early changes following the "go" signal in the non-

Table 1. Number of increase, decrease, or no change in cell activity following the cue onset in delayed movement task, and following the "go" signal in the non-delayed movement task. (N = 89 cells × 6 movement direction = 534)

		Changes during delay period of delayed movement task			
		Increase	Decrease	No change	Total
Changes during Non-delayed Movement task	Increase	127	36	170	333
	Decrease	8	74	39	121
	No change	11	11	58	80
	Total	146	121	267	534

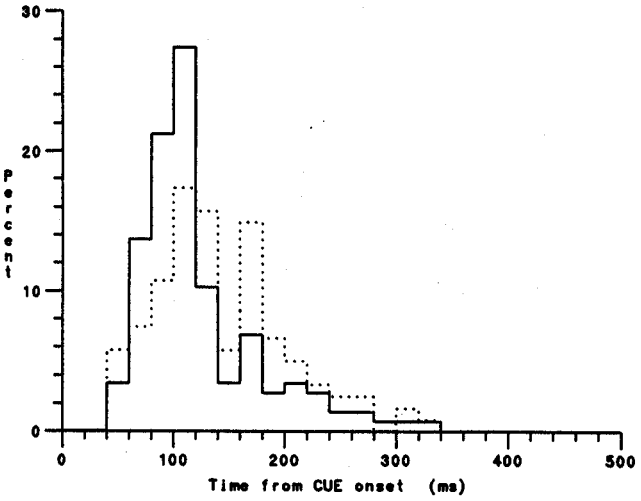

Fig. 7. Latencies of first changes in cell activity following cue onset; delayed movement task. *Solid line*, increases in activity (N = 146); *dotted line*, decreases in activity (N = 121)

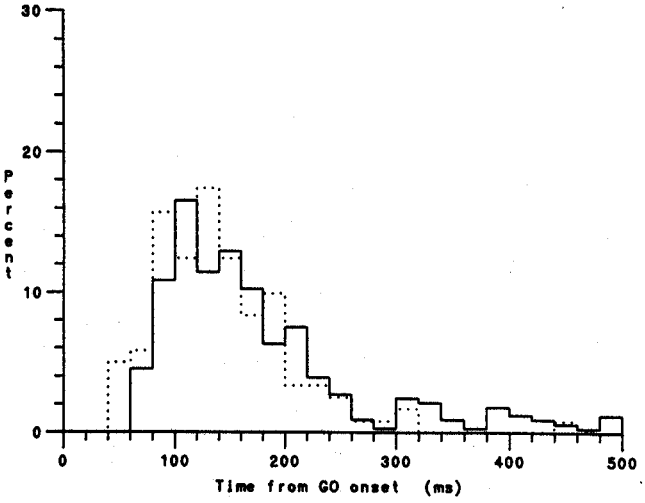

Fig. 8. Latencies of first changes in cell activity following "go" signal in non-delayed task. *Solid line*, increases in activity (N = 333); *dotted line*, decreases in activity (N = 121). Scale of the ordinate is the same as in Fig. 6

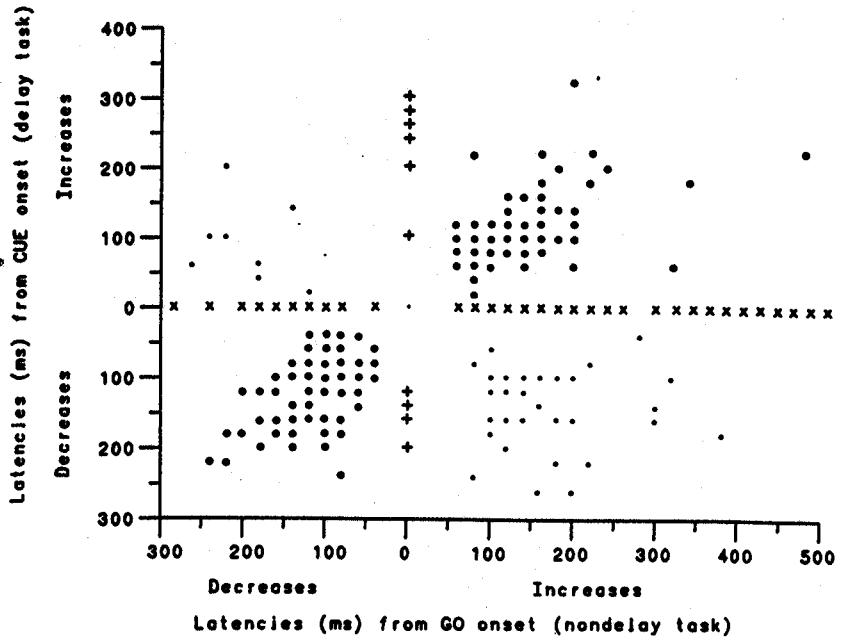

Fig. 9. Joint plot of latencies of first changes in cell activity following cue onset (delayed movement task; ordinate) or "go" onset (non-delayed movement task; abscissa). See text for explanation

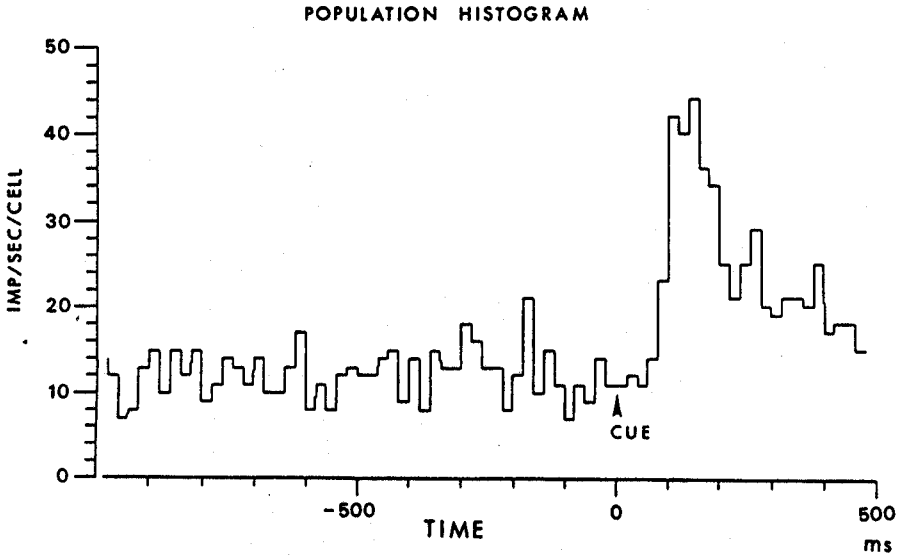

Fig. 10. Population histogram during the delay period for one movement direction (toward target no 2, see Fig. 1)

delayed movement task? Figure 9 shows the joint distribution of the latencies observed in the two tasks in the same population of cells. The total N in this plot is 89 cells × 6 directions = 534 (see Table 1); the number of actual points shown is smaller than that number because several points were overplotted but are shown as a single point. The numbers given below correspond to the actual observations and correspond to those given in Table 1. (Reference to the "delayed movement task" below concerns the delayed period only.)

The dot at [X = 0, Y = 0] indicates absence of changes in both tasks (N = 58). Points lying along the X-axis at Y = 0 (marked "x") indicate latencies of changes in cell activity observed *only* in the non-delayed movement task (N = 209); those lying on the Y-axis at X = 0 indicate latencies of changes in cell activity observed *only* in the delayed movement task (N = 22). The dots (large and small, total N = 245) indicate latencies of first changes in cell activity in both tasks. The large majority of these points (large dots, N = 201/245 = 82%) are concentrated within the upper right quadrant (increases in both tasks, N = 127) and the lower left quadrant (decreases in both tasks, N = 74); these are "congruent" changes in activity. These points are spread

around the digonal. The product-moment correlation coefficient (excluding the points at [0,0]) was 0,908 and the slope of the regression equation 0.877. This slope suggests that the latencies in the non-delayed task were slightly longer than those in the delayed movement task.

The small number of points ($N = 8$) in the upper left quadrant indicates that the combination of an increase in activity in the delayed movement task and a decrease in activity in the non-delayed movement task was infrequent. The opposite was observed more frequently; namely, a decrease in activity in the delayed movement task and an increase in the non-delayed movement task (points in the lower right quadrant, $N = 36$).

Changes in the activity of the neuronal population

The changes in cell activity during the delay period described and illustrated in the preceding sections were reflected in the total activity of the neuronal population. An example is shown in Fig. 10 in which the population histogram for movements to target 2 (Fig. 1) is shown. It can be seen that a steep increase (approximately 4x) in population activity was observed starting at approximately 100 ms following the cue onset. The overall changes in population activity shown in Fig. 10 combine both increases and decreases in the activity of individual cells. Separate plots of population histograms for increases or decreases only (data not illustrated), showed that both kinds of change in population activity began at approximately the same time (as expected from the latency distributions of Fig. 7) but that the magnitude of increase in population activity was higher than that of decrease.

Neuronal population vector

The results described in the preceding section indicate that there is a clear change in the activity of the population during the delay period: does this change carry information concerning the direction of the movement to be triggered later? We examined this question by calculating the population vector every 20 ms from the cue onset forward in time. This analysis yielded a directional measure of the population activity and enabled the comparison between the direction of the population vector and the direction of the upcoming movement. It was found that indeed the population vector during the delay period pointed in the direction of the movement that was triggered later. This is illustrated in Fig. 11 for three

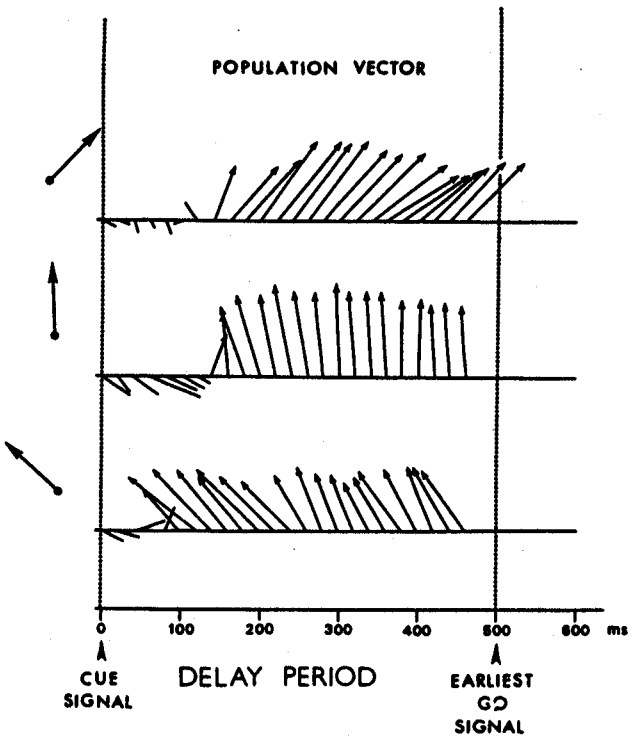

Fig. 11. Time evolution of the neuronal population vector during the delay period. Three movement directions are illustrated

movement directions. The circular correlation coefficient (Fisher and Lee 1983) between the mean direction of the population vector during the delay period and the direction of movement was statistically highly significant ($r = 0.906$, $P < 0.014$, randomized permutations method). Similarly, the population vector calculated during the reaction time in the non-delayed movement task also predicted well the direction of the upcoming movement.

Discussion

Methodological considerations

The results of the present study were obtained from animals trained to withhold their movement at the presentation of a cue and to emit it later in response to a "go" signal. In the beginning of training the animals learned to move towards a dim light, whereas later on they were trained *not* to move when a bright light came on but move to it when it dimmed later in time. Indeed, it took approximately two weeks for the animals to learn to withhold their movement. Behaviorally, the absence of movement was imposed by requiring the animal to hold the low-friction, lightweight manipulandum within a small

(10 mm diameter) circular positional window against a gravitational load for a variable period of time of up to 4 s during the control period, and for a subsequent time of 0.5 to 3.2 s during the delay period. Small movements or slow drift out of that window aborted the trial. In accordance with this behavior, the EMG activity did not change during the delay period. Tanji and Evarts (1976) also did not observe changes in EMG activity during the instruction period. It is, of course, possible that the EMG activity of muscles other than those recorded from in those studies could have changed. Nevertheless, the fact that our animals made no obvious movements during the delay period is the important consideration for the interpretation of these results.

Changes in single cell activity during the delay period

A change in cell activity was observed during the delay period in 79% of the directionally tuned cells, corresponding to 50% of the cases in the delayed movement task. This indicates a clear engagement of the motor cortex following the cue signal and during the delay period. These findings are in accord with those of other investigators (see below). For cells in which changes in activity occurred in the same direction (increase or decrease) in both the delayed and the non-delayed movement task, the latencies of these changes were comparable in the two tasks and were linearly related (large dots in Fig. 9). This suggests that the cells that were engaged in both tasks did so at similar latencies, although at slightly later times in the non-delayed as compared to the delayed movement task. However, there seemed to be a distinct subset of cells that were not engaged during the delay, despite the fact that they were engaged vigorously and at early times following the "go" signal in the non-delayed movement task (see Fig. 6).

There are several considerations regarding the interpretation of the present findings. First of all, it should be noted that in the task used the visual cue signal stayed on during the delay period; therefore, the changes in cell activity may not relate to memory mechanisms but to the intention to move, although engagement of memory aspects even in the presence of the lighted target of the movement cannot be ruled out. Thach (1978) described changes in motor cortical cell activity that were related to the intended direction of movement, when a sequence of flexion-extension movements at the wrist were produced from memory. Second, the direction of the intended or "instructed" movement was not dissociated from that of the triggered movement. In a study in which this dissociation was achieved, motor cortical cells showed changes in activity during the delay period that were related to the target shift and not to the direction of the ensuing movement (Alexander and Crutcher 1987). Third, the cue signal was not a behaviorally irrelevant visual stimulus but served as the target of, and indicated the direction of the movement triggered later. We believe that the changes in activity observed during the delay period in the present study relate to the upcoming movement rather than the mere presence of the visual stimulus. However, it is possible that the visual stimulation itself could have contributed to these changes in cell activity. For example, Kwan et al. (1981) described responses in motor cortical cells in the forelimb area following the presentation of visual cue; these responses seemed to relate to the presentation of the visual stimulus and not to the specific details of the visual cue or the direction of the ensuing movement.

Changes in cell activity during a delay period has been described by several workers in frontal areas anterior to the motor cortex (Kubota and Niki 1971; Fuster 1973; Tanji et al. 1980; Weinrich and Wise 1982; Kubota and Funahashi 1982; Weinrich et al. 1984; Godschalk et al. 1985; Wise et al. 1986). There is little doubt that prefrontal, supplementary motor and premotor areas are involved in preparatory motor processes, and that messages from these areas are likely to reach the motor cortex (see Humphrey 1979 for a review). Indeed, changes in activity of motor cortical cells during an imposed delay have also been observed (Weinrich and Wise 1982; Kubota and Funahashi 1982; Weinrich et al. 1984; Godschalk et al. 1985; Lecas et al. 1986; Wise et al. 1986). Wise et al. (1986) have argued convincingly that changes in cell activity in premotor and motor cortex are related to the upcoming movement than to the visuospatial cues themselves. Godschalk et al. (1985) have provided direct evidence for that idea by dissociating the direction of a reaching movement in space from the location or configuration of the visual stimulus that triggered the movement: under these conditions, the changes in the activity of postarcuate cells during a waiting period were related to the upcoming movement rather than the visuospatial cue itself. However, Vaadia et al. (1986) described cells in more anterior frontal regions which changed activity only when the monkey reached for an illuminated or a loud target but not when the same movement was made in the absence of such a target.

The changes in cell activity observed in the present study occurred during a waiting period. It is possible that they may relate to muscle events that were too weak to produce movement of the arm.

This possibiblity cannot be ruled out, even if the EMG studies did not show such changes in muscle activity. Certainly, the changes in cell activity observed during the delay period were fewer in number and weaker, overall, than those observed following the "go" signal. Thus, changes during the delay period were observed in only 50% of the cases, as compared to 85% of the cases observed in the same cells following the "go" signal in the non-delayed movement task. Moreover, several cells that increased their activity in the non-delayed movement task were actually inhibited (or disfacilitated) during the delay period. A similar observation was made by Wise et al. (1986) in the premotor cortex. It is possible that the output signal from the motor cortex during the delay period was not strong enough to drive subcortical structures to initiate the movement. An additional possibility is that the motor cortical output might be gated subcortically, so that it did not reach the motoneuronal pool level. Physiological, anatomical and behavioral studies in the cat (see Lundberg 1979 for a review; see also Alstermark et al. 1981, 1987; and Alstermark and Kummel 1986) have focused on the C3–C4 propriospinal system as a presegmental mediator of motor commands from supraspinal structures to motoneuronal pools innervating proximal muscles of the arm. A strong projection to that system comes from the motor cortex, and it is possible that motor cortical commands directed ultimately to proximal motoneuronal pools could be gated at the C3–C4 propriospinal system level. Inhibitory neurons acting on the propriospinal neurons have been described and their inputs from several supraspinal systems identified (Alstermark et al. 1984a, b). Activation of a system projecting onto those inhibitory interneurons could be a mechanism of gating motor cortical input to the propriospinal system.

Neuronal population vector during the delay period

The major question investigated in this study concerned the interpretation of the changes in neuronal activity observed during the delay period. The movements employed in the present experiments involved movement of the hand on a plane and motion about more than one joint. Do the changes in motor cortical activity observed during the delay period predict what the direction of the upcoming movement will be in 2-D space? We sought an answer to this question by calculating the neuronal population vector as it evolved in time, from the onset of the cue forward. Indeed, the population vector *during the delay period* predicted well the direction of the instructed movement (Fig. 11). This finding supports the usefulness of this measure in "reading out" the directional tendency of neuronal populations. It also shows that that "readout" is possible even when the signal is not very strong, as evidenced by the fact that in only 50% of the cases significant changes in cell activity were observed. Therefore, it is a sensitive as well as an accurate predictor of the direction of movement in space. Finally, the fact that a motor command can be visualized in the absence of immediate movement offers new opportunities for the study of the neural correlates of covert spatial-motor processes, such as directional transformations (see, for example, Georgopoulos and Massey 1987; Georgopoulos et al. 1988), or for the visualization of the neural representations of spatial trajectories with directional turns.

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