A Motor Cortical Contribution to the Anticipatory Postural Adjustments That Precede Reaching in the Cat

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Yakovenko S, Drew T. A motor cortical contribution to the anticipatory postural adjustments that precede reaching in the cat. J Neurophysiol 102: 853–874, 2009. First published May 20, 2009; doi:10.1152/jn.00042.2009. We tested the hypothesis that pyramidal tract neurons (PTNs) in the motor cortex contribute to the anticipatory postural adjustments (APAs) that precede the onset of a reach in the standing cat. We recorded the discharge activity of 151 PTNs in area 4 of the pericruciate cortex during reaches of both the contralateral and the ipsilateral limbs in an instructed delay task. A total of 70/151 PTNs were identified as showing an initial short-latency period of discharge following the Go signal. Linear regression analysis showed that in many of these PTNs the short-latency discharge was time-locked to the Go signal and temporally dissociated from the subsequent voluntary movement of the limb. The onset of the change in activity of most of those Go-related neurons that we could test (62/70) was temporally related to the onset of the change in the center of vertical pressure. In 33/70 PTNs, Go-related activity was observed only during contralateral reach, in 13/70 only during ipsilateral reach, and in 24/70 during movements of each limb; most of these latter cells (20/24) showed nonreciprocal changes in activity. Although 35/151 (23%) cells showed significant changes during the instructed delay period for reaches made with at least one of the limbs, only one neuron showed a significant reciprocal change during reaches with either limb. We suggest that the discharge characteristics of these PTNs are compatible with our hypothesis that the motor cortex contributes to the production of the APAs preceding movement.

INTRODUCTION

Goal-directed limb movements that can potentially disrupt equilibrium are normally preceded by anticipatory postural adjustments (APAs) (Horak and Macpherson 1996; Massion 1992). In humans, such APAs are observed both during upper (Belenkii et al. 1967; Bouisset and Zattara 1981; Brown and Frank 1987; Cordo and Nasher 1982; Crenna and Frigo 1991; de Wolf et al. 1998; Dietz et al. 2000; Horak and Macpherson 1996) and lower limb movements (Beraud and Gahery 1995; Mouchinho et al. 1992; Rogers and Pai 1990). These postural adjustments serve to both stabilize the body and facilitate the subsequent movement. Anticipatory postural adjustments are also observed preceding voluntary movements in cats and dogs (Alstermark and Wessberg 1985; Birjukova et al. 1989; Di-Fabio 1983; Dufossé et al. 1984; Ioffé et al. 1982; Schepens and Drew 2003). In keeping with our previous work (Schepens and Drew 2003, 2004), we refer to the anticipatory postural adjustments that precede movement as pAPAs to distinguish them from those feedforward postural signals that accompany the movement (Massion 1992).

Recent work from this laboratory has emphasized the contribution of the pontomedullary reticular formation (PMRF) to the coordination of posture and movement (Schepens and Drew 2004, 2006; Schepens et al. 2008). However, it is unlikely that this structure is involved in the initial planning of either the movement or the APAs preceding the movement. Rather, we suggest that the PMRF is a site of integration of signals from both cortical and subcortical structures and that these signals ensure that the postural responses are appropriately scaled in time and magnitude to the planned movement (Drew et al. 2004). The signals observed in reticular neurons include those related to the production of the pAPAs, to the control of the movement itself, and to the associated postural adjustments that accompany the movement. If the PMRF is a site of integration then it should receive input signals from neural structures closer to the planning and execution stages of the movement that contain elements of the complex discharge patterns observed in reticular neurons.

Several cortical and subcortical structures have been implicated in the coordination of posture and movement. These regions include the motor areas of the cerebral cortex, the basal ganglia, and the cerebellum (Burleigh-Jacobs et al. 1997; Diener et al. 1989, 1990; Horak and Macpherson 1996; Massion 1992; Rogers et al. 1987; Viallet et al. 1987, 1992). All of these structures project to the PMRF in the cat (Canedo and Lamas 1993; Eccles et al. 1975; He and Wu 1985; Homma et al. 1995; Kably and Drew 1998; Keizer and Kuypers 1984; Matsuyama and Drew 1997; Rho et al. 1997; Rossi and Brodal 1956; Takakusaki et al. 2004) and all can potentially contribute to the complex signals observed in the PMRF. However, damage to the basal ganglia or the cerebellum affects primarily the timing and the magnitude of the pAPAs. In contrast, work by Viallet et al. (1992) showed that the motor cortex is necessary for the production of the APAs associated with the unloading reflex (Hugon et al. 1982). Their results suggest that coordination of movement and posture involves both sides of the motor cortex; one side produces the movement in one limb and the other side produces the associated postural response in the other limb. A similar suggestion was made on the basis of cortical lesions in the cat (Massion 1979).

There are several other lines of evidence that also suggest a contribution from the motor cortex to the production of APAs. A recent study by MacKinnon et al. (2007), for example, showed that transcranial magnetic stimulation modified the magnitude of the electromyographic (EMG) activity in the muscles involved in producing pAPAs. In the intact cat, Gah-
ery and Nieoullon (1978) showed that stimulation of the motor cortex evokes a simultaneous movement of the contralateral forelimb and evoked postural responses in the supporting limbs. However, in this case the postural responses accompany the movement rather than precede it. There are no specific single-unit studies that have examined the possible contribution of the motor cortex to the production of pAPAs, although Beloozerova et al. (2005) showed a contribution of this structure to the production of compensatory postural responses during oscillatory body sway.

Although the lesion and stimulation studies provide some evidence for a contribution of the motor cortex to the production of the pAPAs, they provide no information on the nature of the signal that may be transmitted to the PMRF or to the spinal cord. In the present study, we therefore examined the contribution of identified pyramidal tract neurons (PTNs) in the motor cortex to the production of these pAPAs in an instructed delay task. We previously reported (Schepens and Drew 2004, 2006; Schepens et al. 2008) that both EMGs and reticular neurons show short-latency responses, time-locked to the Go signal in this task. If motor cortex neurons contribute directly to the responses in the reticular neurons, or to the pAPAs themselves, we would predict they should likewise discharge at short latency with responses that are time-locked to the Go signal. Indeed, in support of this hypothesis, short-latency, stimulus-locked activity has been observed previously in the motor cortex of cats trained to perform reaching movements (Perfiliev 1998, 2005; Vicario et al. 1983) but, in both studies, this activity was interpreted as being involved in the sensorimotor transformations involved in motor planning rather than in the control of posture.

The question of whether neurons in the motor cortex contribute to pAPAs therefore remains open. In our task, in which there is both a clear need for pAPAs and a demonstration of their existence, we expect that changes in discharge activity of motor cortical neurons with short-latency and stimulus-locked activity should be temporally related to the pAPAs and should show a relationship between the discharge frequency of the cells and the magnitude of the postural responses. In addition, if these motor cortical neurons are involved in planning either movement or global measures of movement and posture, as suggested by Vicario et al. (1983) and byPerfiliev (2005), one would expect significant changes in discharge activity during the instructed delay period prior to the Go stimulus. Further, one would expect these changes in activity to be reciprocal for movements of the left and right limbs. Our results are more consistent with a contribution of the motor cortex to the control of the APAs than to the planning of the movement.

Preliminary results were previously published in abstract form (Yakovenko and Drew 2006).

METHODS

Training and task

These experiments were carried out in three male cats, RS24, MC28, and MC29, weighing respectively 6.6, 4.2, and 5.6 kg. Prior to surgical procedures the animals were trained for several months to stand quietly on four force platforms and to perform an instructed delay task in which they reached forward and pressed on a lever from an unrestrained standing posture (Schepens et al. 2008). Two auditory signals were used to instruct the cats during the task (Fig. 1A). The beginning of a trial was indicated by a 0.5-s tone, followed 1.5 s later by an instruction tone (cue signal, duration 0.5–1.5 s). The pitch of this instruction tone instructed the cat whether it should reach with the left or right limb (solid and dashed lines). The end of the tone, the Go signal, was accompanied by the simultaneous opening of a shutter overlying the lever (see Fig. 1B) and allowed the cat to initiate reaching with the instructed limb. The cats were trained to accomplish the task with >80% success rate with each limb. When the lever was pressed within 2 s following the Go signal, a feeding tray extended and the cat returned the limb to the starting position.

Surgery

All surgical procedures were performed under general anesthesia under aseptic conditions. Following pretreatment with ketamine (11 mg/kg), acepromazine (0.05 mg/kg), and glycopyrrolate (0.01 mg/kg), the animals were intubated and anesthesia was induced and maintained during surgery with 2–3% of isoflurane with oxygen. The cats were placed in a stereotaxic apparatus (David Kopf) using ear bars coated with lidocaine ointment (5% xylocaine); the surface of the eyes was coated with petroleum jelly (Vaseline) to prevent drying of the cornea. As described previously (Drew et al. 1986), pairs of Teflon-insulated, braided stainless steel wires (AS633: Cooner Wire, Chatsworth, CA) were sewn into the muscle bellies of 20–24 selected flexor and extensor muscles of the fore- and hindlimbs to record EMG activity. An array of six microwires (50-μm Tri-ML insulated stainless steel wires), staggered vertically by 0.5 mm, was implanted into the right pyramidal tract (L1.2 and P7) through a small craniotomy in

![FIG. 1. The instructed delay task used in this study. A: An initial tone alerted the cat to the beginning of a trial. After a period of 1.5 s, the cat received an instruction (cue signal) to initiate reaching with the instructed limb when the second tone ended and the shutter opened. The pitch of the second tone (solid vs. dashed trace) identified the reaching limb in a trial. B: At the Go signal a shutter opened, giving the cat access to the lever. When the cat depressed the lever, it received a food reward (see METHODS).](http://jn.physiology.org/issue)
the occipital bone caudal to the tentorium (Drew 1993; Palmer 1978). Both the EMG and the pyramidal tract connectors were fixed to the cranium with acrylic cement. Finally, a rectangular baseplate (internal measurements: 10 × 8 mm) was implanted over the right motor cortex to provide access to both pre- and postcruciate area 4. An analgesic (buprenorphine, 5 μg/kg) was administered two to three times daily for 2–3 days following the surgery. Antibiotics were administered over the period of experiments. These surgical and experimental procedures followed the guidelines of the Council of the American Physiological Society and the Canadian Council for the Protection of Animals and were approved by the Institutional Animal Care Committee.

Data collection

Following recovery from surgery, recording sessions were carried out for 2–4 h/day, 3–5 days/wk, and, in cats MC28 and MC29, for 3–6 mo. Recordings from single cells were made using glass-insulated, tungsten microelectrodes (0.5–1.5 MΩ) fixed in a custom-built micromanipulator attached to the baseplate of the recording chamber during each daily session. The electrode was lowered into the cortex until PTNs were identified based on constant latency to stimulation of the pyramidal tract and collisions at the appropriate delay with spontaneous action potentials (Lipski 1981). Once a single neuron was isolated, we recorded neuronal and EMG activity for a period of 3–5 min as the cat walked on a treadmill (data not reported). The cat was then transferred to the reaching apparatus. The antidromic response latency and the response waveform were verified intermittently throughout the experiment to ensure that recordings were from the same neuron.

Each data set consisted of blocks of 5 reaches with the left (contralateral) limb, followed by 10 with the right (ipsilateral) limb and then another 5 with the left limb. Additional data sets were collected when the trajectory of the reaching limb was modified by the presence of a robotic obstacle that was placed between the force platforms and the lever. All available trials, with and without the obstacle, were used in our analyses. The cat stood on four strain-gauge force platforms, one for each limb (Model MC3A-6-100; AMTI, Watertown, MA), supplying three force signals (vertical, V; anteroposterior, AP; and mediolateral, ML). Force and EMG signals were acquired at 1 kHz; neuronal waveforms were sampled at 100 kHz to allow accurate off-line discrimination.

After recording each cell, and providing that the unit was still well isolated, we identified the location of its sensory receptive field and whether it responded to brushing of the hairs or light touch (cutaneous). If a cell did not respond to light touch, we determined whether it could be activated by deep pressure or manipulation of the joint. Cells with cutaneous receptive fields were not further tested for deep or proprioceptive inputs because of the difficulty of differentiating the two types of input in the intact cat. At the end of each session we applied intracortical microstimulation (11 pulses each of 0.2 ms and at 330 Hz) at the site of the last recorded PTN. Stimulus strength was normally set at 25 μA but was increased to a maximum of 35 μA if no response was observed at the lower strength. Selected penetrations distributed over the motor cortical area were marked with electrolytic lesions (53–54°C cathodal DC current for 10 s) at the depth at which PTNs were recorded to serve as reference points in the reconstruction of the location of recorded cells. A maximum of five such lesions were made in any one cat.

In a few separate experimental sessions in cat MC29, we measured the distribution of the vertical force under the paw by using a pressure mapping system (Tekscan). The measures of the center of vertical pressure (CVP) and the temporal comparison of the pressure maps were calculated using custom software developed in Matlab (The MathWorks).

Data analysis

As an initial step in data analysis, all trials in which the reach began prior to the Go signal were removed from the database. In trials that were used to determine baseline biomechanical measures of EMG timing (referred to later as selected trials), we further included only trials in which the weight did not vary by >15% from the stable position (50% weight on each side and 60% weight on the forelimbs; see Schepens and Drew 2003). Only data sets containing a minimum of five reaches were included in the analysis. All neuronal activity was discriminated off-line by imposing time and amplitude constraints on the recorded waveforms using a custom interactive analysis package. In some cases, two units were sufficiently isolated for simultaneous discrimination. The instantaneous frequency of the discharge was calculated using the method of Udo et al. (1982). EMG signals were low-pass filtered (100 Hz) and rectified. Force platform signals were low-pass filtered (30 Hz) and offsets were removed using calibration recordings.

For the calculation of the conduction velocities of the PTNs we used a distance between the motor cortex and the medullary pyramid of 44 mm as in our previous publications (Armstrong and Drew 1984a; Kably and Drew 1998). No correction was made for utilization time so that the values presented in RESULTS undoubtedly underestimate the conduction velocities, especially for those neurons activated at the shortest latencies. However, the values obtained allow a direct comparison with the conduction velocities calculated for different classes of corticofugal neurons in a previous publication (Kably and Drew 1998).

A major goal of this study was to determine whether the neuronal discharge was related to the postural responses preceding the movement onset. As we have previously demonstrated and discussed (Schepens and Drew 2003, 2004), changes in EMG or neuronal activity that are related to these anticipatory postural responses occur at short latency and are time-locked to the Go stimulus (Go-related). However, because there is no simple statistical test to identify such Go-related cells we used a working definition based on two complementary analysis methods.

The first of these methods was based on a linear regression analysis as described in Schepens et al. (2008; see also Schepens and Drew 2003). In brief, we measured the time of onset of the variable, either cell or EMG onset, from each individual trial by using an interactive program. Latency was determined as the time at which the variable exceeded ±2SD of the control activity, as calculated from the averaged traces, for a period of ≥75 ms. We first determined whether a cell was movement related by performing linear regressions between the onset of the cell discharge and with the time of onset (latency) of the EMG activity in the cleidobrachialis (CIB) muscle (referred to as CIB onset). In general terms, any movement-related variable should show a significant relationship (P < 0.05) between the latency of that variable and the latency of the CIB. For example, Fig. 2C shows that the onset of EMG activity in the extensor digitorum communis (EDC) is significantly related to the onset of the CIB and is thus movement related. In contrast, the same linear regression performed for the onset of cell activity (open circles in Fig. 2D) showed no significant relationship with CIB onset. We thus eliminated from consideration any cells that were significantly related to movement onset.

For cells that were not significantly related to the CIB onset, we used our working definition to determine whether they were time-locked to the Go stimulus. In general, we consider that a cell that is time-locked to the Go stimulus will have a constant latency that is independent of the variability in movement onset. This relationship can be observed by plotting the lead time of the cell (CIB latency minus the cell latency) as a function of the CIB latency. A linear relationship between these two variables, as in Fig. 2D (filled circles), strongly suggests that the variable is related to the Go stimulus (effectively has a constant latency). This is the same method as that used by other authors who have examined Go-related responses in the
definition of a Go-related cell was based on a further consideration of the motor cortex (Lamarre et al. 1983; Perfiliev 2005; Vicario et al. 1983). To provide an objective measure of this relationship, our final working definition of a Go-related cell was based on a further consideration of the variance of the cell discharge (see the APPENDIX).

The linear regression analysis provides a robust and precise manner of determining whether a given cell is better related to the Go stimulus or to the movement. However, it has the disadvantage that it can be accurately used only on those cells that show an abrupt change in discharge frequency following the Go signal. We therefore devised a complementary method that was based on the averaged control discharge activity. The method assumes that a cell that is Go-related should discharge at short and short-latency change from the control level. The linear regression analysis between the time of the onset of the EMG activity in the extensor digitorum communis (EDC onset) and the time of the onset of the EMG activity in the cleidobracials (ClB onset). D: a similar plot for the time of the onset of the cell discharge (cell onset) and of the CVP EMG activity (CVP onset) and the associated plot of lead time (○). E: the threshold crossing analysis (TCA). The average profile was divided into 3 periods: 1) control, which is the 500-ms period preceding the Go-cue; 2) response period (RP), which spans the initial 50% between the Go-cue and the movement onset; and 3) the movement period (MP), the period between movement onset and lever press. Thick gray lines indicate parts of the unit activity that were significantly higher than the mean of the control period (dotted line) — = the confidence interval (dashed lines), as described in METHODS and the APPENDIX. Fv, vertical force; f, left; m, slope of the regression; N, number of trials; P, probability; r, right; R², coefficient of determination; TriL, triceps brachii, lateral head.

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the Go stimulus and that have similar latencies, we first subtracted the latency of the CIB activity from both that of the unit and of the CVP in each trial. This effectively synchronized the measures to the onset of the movement, as opposed to the onset of the stimulus. The level for significance was set at $P < 0.05$.

To examine the magnitude relationships we performed separate linear regressions using either force or EMG activity. For the correlations with the forces, we used the three planes of force recorded from under the /FL plus the two components of the CVP. For the correlations with EMG activity, we used the recordings from the left and right lateral heads of the triceps (TrIL) the left and right CIB and the left (contralateral to the recording site) palmaris longus (PaL). All regressions were made using the average discharge frequency calculated from the interval between 0 and 50% of the response period (see earlier text) for each trial plotted as a function of the integrated force, CVP, or EMG values during the same time period. Because our initial regressions showed a high percentage of correlated traces, we also checked for false positives by shuffling the data trials (correlating neural data from one trial with the biomechanical measures from another trial) and by repeating the correlations. Shuffling the data in this manner ensures that there can be no correlation between the two variables and provides an indication of the proportion of false positives that might be expected from these correlations. This analysis showed that about 25% of the regressions made with shuffled trials were significant at the $P < 0.05$ level. We thus repeated the analysis, considering a relationship to be functionally significant only when a correlation between the cell and two of the five traces (force and CVP) was significant. In this case, the shuffled traces showed only 5% of false positives, suggesting that the method provided a reasonable working definition of determining whether changes in discharge frequency in a given cell were related to changes in the magnitude of the pAPA.

Histology

At the end of the experiments, cats were killed with an overdose of sodium pentobarbital. The cerebral cortex and brain stem were removed, cryoprotected, sectioned (40 µm), and stained with cresyl violet. The location of the electrolytic lesions made during the experiments together with the relative depth of layer V, as determined from the recording sessions, was then used to guide the reconstruction of the recording tracks in the pericruciate cortex. To compare the location of cells with different properties, each histological tracing was flattened and aligned to the fundus of the cruciate sulcus. The anteroposterior location of a cell was then determined along the resulting line (resolution 200 µm). The mediolateral location was determined by the distance of the section from the midline. No correction was made for shrinkage. The method is described in detail in Rho et al. (1997) and Andujar and Drew (2007). To superimpose data from different cats, each two-dimensional representation was normalized to the tip of the cruciate sulcus. Although sulci vary from one cat to another, this superimposition maintained the essential localization of the cells with respect to both the rostrocaudal and the mediolateral planes.

RESULTS

Behavior

Goal-directed reaching movements in this task were preceded by anticipatory postural adjustments. The characteristics of the postural activity in the current task and a similar reaching task have been described in detail in previous reports from our laboratory (Schepens and Drew 2003; Schepens et al. 2008). In brief, the pAPA (indicated by the vertical gray bar in Fig. 2, A and B) is characterized by a transient loading of the reaching forelimb (rFLV in Fig. 2B), unloading of the supporting forelimb /FLV, and a shift of the center of vertical pressure to the reaching side and posteriorly. These changes in posture are produced by a transient increase in activity in extensor muscles of the reaching limb, such as the lateral head of the triceps (rTrIL) and by concomitant decreased activity in extensors of the supporting forelimb (not illustrated). In this study, as in Schepens et al. (2008), the pAPA is defined as occupying the period between the onset of EMG activity in the TrIL of the reaching limb until the onset of activity in the EMG of the prime flexor muscle, the CIB. At the onset of the reaching movement, there was a concomitant increase in the activity of the extensor muscles of the supporting forelimb (not illustrated), leading to a maintained increase in $F_L$ in this limb (FLV). The changes observed in the TrIL were equally observed in muscles acting more distally, such as the PaL (Schepens and Drew 2003). Changes in hindlimb vertical forces were also observed during the reaching task, with the hindlimb ipsilateral to the reaching limb being loaded and that contralateral unloaded (Schepens and Drew 2003; see also Fig. 3).

Given that many cells in the motor cortex have receptive fields on the distal limb, including the ventral surface of the pad (see the following text), we also examined how the changes in force under the four limbs were distributed across the paws and digits during the reach. For this analysis we used a Tekscan pressure mapping system to measure forces under one foot at a time. Figure 3 illustrates the changes in ground reaction forces and the corresponding force distribution under each paw during a left reach. The force distribution under the paw is illustrated at three different points during the reach: 1) the period just preceding the onset of the pAPA; 2) the moment of maximal change in $F_V$; and 3) the period just before lift of the reaching limb (Fig. 3A, left). The two panels to the right show the differences in force between events 2 and 3 and between events 1 and 2. As can be seen, the changes in postural loading during the pAPA lead to clear modification of the forces under the paws and digits. In the /FL, the forces under the paw were initially increased (2–1) and then decreased (3–2), whereas in the rFL the force distribution was reciprocal, with clear increases in loading both in the pad of the paw and in the digits during the reach. Similar, but less intense, changes were also observed in the hindlimbs in the latter period, corresponding to the classical diagonal pattern observed in cats during postural adjustments (Dufossé et al. 1984; Schepens and Drew 2003).

In addition to the forces exerted on the pads of the paw, there were also sometimes modifications of the distal wrist and digit dorsiflexor, the EDC, during the pAPA in one of the cats, MC28. An example of the changes is shown in Fig. 3, D and E. These illustrations clearly show activity in the EDC, preceding the activity of the CIB, during both the left and the right reaches. During the left reach, this period of activity is followed by a large movement-related period of activity. It should be emphasized, however, that this activity was observed only in cat MC28 and, even in this cat, it was facultative in that it was not observed in every trial.

We analyzed the timing of different components of the reach from 150 trials in cat MC28 and 316 trials in cat MC29 that were chosen on the basis of the criteria provided in METHODS (selected trials). This analysis showed that the initial period of activity in the CIB during the left reach occurred at an average of 243 ms (SD = 71 ms) in cat MC28 and at 430 ms (SD = 230 ms) in cat MC29.
Similar values were obtained during the right reach (mean 278 ms for MC28 and 419 ms for MC29). The longer mean values for MC29 were explained by the presence of a number of responses that were quite slow in this cat. The mean onset of the pAPA, as measured from the initial deflection in the anteroposterior component of the CVP, ranged from 82 to 112 ms in these same two cats. These values are similar to those observed previously in cats trained in a similar (Schepens and Drew 2003) and an identical task (Schepens et al. 2008).

Neuronal activity

DATABASE AND LOCATION OF RECORDINGS. This report is based on the discharge patterns of 151 PTNs that we recorded from area 4 of the pericruciate cortex of three cats during at least five reaching movements with each forelimb. Neurons were recorded in 10 penetrations in cat RS24 (11 PTNs), 22 penetrations in cat MC28 (45 PTNs), and 42 penetrations in cat MC29 (95 PTNs). The latency of activation of 150/151 PTNs ranged from 0.8 to 4.8 ms. Using a value of 44 mm for conduction distance (see METHODS), this provides a range of conduction velocities from 9.2 to 55 m s$^{-1}$ (Fig. 4). The majority of the PTNs (96/150, 64%) had conduction velocities $\leq 22$ m s$^{-1}$ and were therefore classified as fast PTNs according to the criterion of Takahashi (1965). Subtracting a constant utilization time of 0.2 ms would increase the maximum conduction velocity to 73 m s$^{-1}$ but would increase the proportion of fast PTNs only slightly to 98/150 (65%).

The location of the 151 PTNs that we recorded within the pericruciate cortex is illustrated in Fig. 5 for all three cats. The
majority of the cells (129/151) either had a receptive field on the contralateral forelimb or were recorded in close proximity to neurons with such receptive fields. Most of the other cells (16/151) either had receptive fields on the contralateral hindlimb or, likewise, were recorded in close proximity to neurons with hindlimb receptive fields.

GENERAL CHARACTERISTICS. Cells with Go-related responses were observed in cells with distal receptive fields on the forelimb, with receptive fields around the shoulder, and with receptive fields on the hindlimbs. Examples of Go-related cells with each of these receptive fields are illustrated in Figs. 6 and 7.

Figure 6 shows three examples of PTNs with receptive fields on the distal forelimb that showed Go-related discharge, as defined by both the regression analysis and the threshold crossing analysis (see the Appendix), during reaches of each forelimb. The neurons illustrated in Fig. 6, A and B both showed Go-related increases of activity during the left (contralateral) and right (ipsilateral) reaches. In the example of Fig. 6A, there was also a pronounced period of increased movement-related activity during the left reach and a slight decrease in activity during the right reach. The neuron illustrated in Fig. 6B showed a decrease in activity during the movement for both the left and right reaches. At the end of the right reach there was a subsequent increase in activity. Figure 6C shows an example of a reciprocal pattern of Go-related activity in which cell activity was decreased before the onset of the left reach and increased before the onset of the right reach. In this example, the cell remained quiescent throughout the left reach but showed increased movement-related activity during the right reach. The linear regressions showing the relationship between lead time and CIB activity for the contralateral reach for these three cells, together with examples of the threshold crossing analysis is shown in the Appendix (Fig. A1).

Similar Go-related discharges were observed in cells with receptive fields that were restricted to (Fig. 7A), or included (Fig. 7B), the shoulder and had no input from the ventral pads. In the example illustrated in Fig. 7A the cell showed qualitatively symmetrical responses for both left and right reaches, exhibiting both a Go-related response and a later movement-related discharge. The cell in Fig. 7B likewise showed a symmetrical response to the left and right reaches during the pAPA, although in this case, the Go-related effect was a decrease in activity. During the left reach, there was a subsequent increase in activity later in the movement. Go-related discharge was not restricted to cells with forelimb receptive fields but was also observed in cells with hindlimb receptive fields. An example of such a cell is shown in Fig. 7C. During the left reach, the discharge rate of this PTN decreased during the pAPA but showed a subsequent increase in activity later in the reach. In contrast, during the right reach there was a short-latency increase in cell discharge that was maintained throughout the reach. In all three illustrated examples, the onset of the change in cell activity was identified as Go-related on the basis of both the regression analysis and the threshold crossing analysis.

Altogether, the combined use of the linear regression and the threshold crossing analysis identified a total of 70 PTNs as Go-related (Table 1, top right). These PTNs included some showing Go-related activity only in response to movement of a single limb and others that discharged to movement of each limb. The latter, bilateral, cells (24/70) included PTNs with both reciprocal and nonreciprocal changes in activity (see Table 1). Allowing for those cells that discharged to each limb our total database included 94 cases (a Go-related change to one limb or to the other). In all except five of these cases, the Go-related discharges were followed by movement-related activity as in the examples in Figs. 6 and 7. Go-related changes were observed in 64/129 (50%) of cells with receptive fields on the forelimb and in 6/16 (30%) of the PTNs with receptive fields on the hindlimbs.

The range of the peak discharge frequencies of the 94 Go-related responses is summarized in Fig. 8, A and B (open bars). The peak frequency (as measured from the averaged postevent histograms) of those 35 Go-related cells with significant increases in discharge frequency was 73.2 ± 44.0 Hz during the contralateral reach (Fig. 8A). This was not significantly different from the 29 cells showing significantly increased activity during the ipsilateral reach (Fig. 8B: 68.7 ± 41.4 Hz). The mean latency of the change in discharge frequency of that population of cells that were identified as Go-related on the basis of the linear regression analysis was 75 ± 30.6 ms. For the cells that were identified as Go-related on the basis of the threshold crossing analysis, the mean latency was 72.2 ± 50.0 ms.

We further identified four subgroups from this population, which together comprised 60/70 (86%) of the Go-related cells and 76/94 (81%) of the total cases. These four subgroups, identified in Table 1, included 1) cells having bilateral, nonreciprocal increases in activity (+/+; 16/70 PTNs; 2) those showing Go-related unilateral increases of activity in the contralateral limb (+/0; 17/70); 3) cells with a unilateral decrease of activity in the contralateral limb (−/0; 16/70); and 4) those showing a unilateral increase of activity in the ipsilateral limb (0/+; 11/70). Comparison of both the frequencies of discharge and the latency of these four groups of cells with ANOVA showed no significant differences in either variable (not illustrated). Cells with Go-related responses were localized widely within the total area from which neurons were recorded (Fig. 8C) and there was no evidence of any segregation in these four subgroups of neurons. Examination of the conduction velocities of 69 Go-related PTNs showed that 52/69 (75%) had a conduction velocity ≥22 m s⁻¹ (see Fig. 4, filled bars).

RELATIONSHIP TO RECEPTIVE FIELD. It is reasonable to expect that the major changes in postural activity prior to a movement...
Indeed, the receptive field of fully 51/64 Go-related PTNs in the forelimb representation of the motor cortex included the distal forelimb.

To determine whether there was a relationship between the receptive field and the Go-related response pattern of the cell we examined the properties of cells in the forelimb representation of the motor cortex from the perspectives of both the discharge pattern and the receptive field. In the first place we asked to what extent cells showing similar Go-related activity have similar receptive fields. In the second place, we asked...
whether cells with a similar receptive field showed similar Go-related discharge patterns. For this analysis, we considered only cells with a receptive field 1) including or restricted to the ventral paw pads; 2) including or restricted to the shoulder; or 3) including the distal forelimb, normally as a stocking-like receptive field. To simplify this comparison we restricted the analysis to the four categories that included 10 cells (see Table 1). The results of this analysis are detailed in Table 2.

In brief, all four classifications of Go-related discharge activity examined included cells with each of the three types of receptive field that we considered. Similarly, cells with each different type of receptive field were included in each classification. This can equally be appreciated from Fig. 6, A and C, which shows two cells with identical receptive fields restricted to the ventral pad that had different patterns of activation. The cell in Fig. 6A had a receptive field restricted to the ventral pads of the paw and showed an increase in discharge activity during both the left and right reaches. In contrast, the cell illustrated in Fig. 6C had an identical receptive field but discharged in a reciprocal manner, with discharge being depressed during reaches made with the contralateral limb.

Considering together the four classes of cells detailed in Table 2, 19/28 cells showing a Go-related increase in activity during contralateral reach had a receptive field that included the paw. However, 7/13 cells showing a Go-related decrease during contralateral reach equally had receptive fields including the paw. Sixteen (16/23) cells with a receptive field on the ventral paw also showed an increase in activity during the ipsilateral reach (10 bilateral nonreciprocal cells and 6 cells with only an ipsilateral increase). A similar lack of correlation was found with the other two classes of forelimb receptive field that we examined (Table 2). An examination of the peak frequency (Fig. 8, A and B, hatched bars) and the latency (not illustrated) of those cells with receptive fields including the ventral paw showed no significant differences from the overall population of Go-related cells.

![Figure 6](http://jn.physiology.org/)

**FIG. 6.** Examples of 3 PTNs with distal receptive fields showing Go-related activity during left and right reaches. A–C: for each PTN we show the PEH and raster display of the discharge triggered on the Go signal and illustrate the receptive field of the cell (middle) and the effects evoked by microstimulation at the site of the recording (right). The shaded area on the paws indicates a cutaneous receptive field; the arrow on the paw of the cell in Fig. 6B indicates it was activated by pressure to the ventral pad. Arrows on the microstimulation traces indicate the direction of the movement evoked by the stimulation. D: selected EMG and force traces are shown from the cell illustrated in Fig. 6A. The shaded gray bars indicate the approximate period of the pAPA. T, threshold.
Cells with a receptive field including the shoulder were found in all four of the classifications of cell discharge considered in this analysis, although only one cell with a bilateral nonreciprocal pattern of activity included input from the shoulder. Moreover, we also found few differences between cells with receptive fields including the ventral pad and those with receptive fields including the shoulder but excluding the pads. For example, as illustrated for the examples in Figs. 6 and 7, cells with both types of receptive fields generally showed separated bursts of activity related, respectively, to the stimulus (Go-related) and to the movement. Moreover, an ANOVA showed no significant differences in either peak frequency of the Go-related discharge or of the latency of the response for both classes of cell.

RELATIONSHIP TO RESPONSES EVOKED BY MICROSTIMULATION. Microstimulation at 25 μA evoked motor responses at 43/49 sites in the forelimb representation from which Go-related responses were recorded. Thresholds for the 43 sites in which movement was evoked ranged from 3 to 25 μA with 22/43 effective sites evoking movements at strengths of ≤10 μA. The microstimulation most frequently evoked shoulder retraction (26/49 sites), elbow flexion (25/49 sites), and wrist dorsiflexion (12/49) sites. Elbow extension was observed in only 3/49 sites. Note that the different categories of movement add up to more than 49 because most sites evoked movement at more than one joint. At many sites, the microstimulation evoked responses at more than one joint, even at threshold intensities. This pattern of stimulation has been frequently observed within the motor cortex (see e.g., Armstrong and Drew 1984b, 1985). Receptive fields of the cells recorded at most of these locations were located on the forearm and paw (see e.g., Fig. 6). However, in addition to these commonly observed responses, microstimulation at some sites (8/49) evoked shoulder movements, other than retraction, including abduction, adduction, and elevation of the shoulder. Most of these latter sites were located rostro-medially (see also Armstrong and Drew 1984b) and the cells recorded in these sites had receptive fields around the shoulder (e.g., Fig. 7B). No movements were evoked in 6/49 sites even when the stimulus strength was increased to 35 μA; these
s sites were also located medially in areas in which cells with receptive fields on the shoulder were recorded (Fig. 7A).

SPIKE-TRIGGERED AVERAGING. We used spike-triggered averaging to try to determine a causal relationship between PTN and EMG activity (Fetz and Cheney 1980). Action potentials from the entire recording period defined in Fig. 1A were used to average EMG activity for a period of 50 ms prior to and 100 ms following the action potential. Averages were made separately for reaches with the left and the right limbs for all cells classified as forelimb related. No significant postspike facilitation or depression was observed for any of the recorded cells with any of the contralateral forelimb EMGs that we recorded (14 in cat MC28, 15 in cat MC29, and 8 in cat RS24).

TEMPORAL CORRELATIONS WITH CHANGES IN CVP. As in our previous studies on the discharge characteristics of neurons in the PMRF (Schepens and Drew 2004, 2006), we suggest that motor cortical neurons that show short-latency, Go-related activity contribute to the production of the APAs that precede the movement. To test this hypothesis further, we examined the relationships between cell latency and the time of the initial changes in activity in the anteroposterior and mediolateral components of the CVP. These latter measures were used because they are the sum result of the activation of a number of muscles and the resulting changes in ground reaction forces in all three planes. In addition, these changes were normally very clear (see Fig. 9A) and easier to measure than the changes in force.

One example (same cell as Fig. 6A) is illustrated in Fig. 9. In this cell, there was a short-latency increase in cell discharge that preceded CiB onset for both the left and the right reaches. During the pAPA preceding CiB onset the initial change in the mediolateral component of the CVP...
TABLE 2. Forelimb receptive fields of different cell classifications

<table>
<thead>
<tr>
<th>Receptive Field</th>
<th>Bilateral Nonreciprocal</th>
<th>Unilateral</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>+/+</td>
<td>-/+</td>
</tr>
<tr>
<td>Includes pad</td>
<td>10/13</td>
<td>9/15</td>
</tr>
<tr>
<td>Restricted pad</td>
<td>3/13</td>
<td>3/15</td>
</tr>
<tr>
<td>Includes shoulder</td>
<td>1/13</td>
<td>4/15</td>
</tr>
<tr>
<td>Restricted shoulder</td>
<td>1/13</td>
<td>3/15</td>
</tr>
<tr>
<td>Includes forearm</td>
<td>7/13</td>
<td>9/15</td>
</tr>
</tbody>
</table>

Receptive fields of Go-related cells discharging with different patterns of activity. Most receptive fields were cutaneous except for PTNs activated from around the shoulder (see RESULTS). Forearm receptive fields generally included the anterior and posterior margins of the forearm (often referred to as stocking-like receptive fields).

was to the left during the left reach and to the right during the right reach. The anteroposterior component of the CVP was initially displaced backwards in both situations. This cell showed a strong linear relationship between the onset of the cell discharge and the onset of both the anteroposterior and the mediolateral components of the CVP for both the contralateral and the ipsilateral reaches (Fig. 9B).

A similar significant temporal relationship to the anteroposterior component of the CVP during both contralateral and ipsilateral reaches (Fig. 9C) was observed for the cell recorded in the hindlimb representation and is illustrated in Fig. 7C. This cell also showed a significant linear relationship to the onset of the change in vertical force in the supporting hindlimb (Fig. 9C).

Overall, regressions between the onset of cell discharge and the anteroposterior component of the CVP could be performed for 70/94 of the stimulus related cases. Of these, 62/70 (89%) showed a significant relationship between these two measures. As a comparison we performed the same analysis on 33 movement-related cases with short latencies, overlapping those of the Go-related cells. In these cells only 7/33 (21%) of cases showed a significant relationship between cell onset and the anteroposterior component of the CVP. In 4/7 of these cases the slope of the movement-related regression was less than that of the regression made with lead time, suggesting that despite a significant correlation with the CIB onset, these cells were probably better related to the Go-stimulus than to the movement.

On average the onset of the cell discharge preceded the onset of the change in the anteroposterior component of the CVP (as measured from averaged postevent histograms) by 93 ± 51 ms during the reach with the left, contralateral limb (Fig. 9D, left) and by 95 ± 52 ms for reaches with the right, ipsilateral limb (Fig. 9D, right). Restricting the measures to the 70 cases in which a significant relationship with the anteroposterior component of the CVP was obtained (hatched bars in Fig. 9D) showed no significant differences with the measures obtained from the entire population of 94 cases.

RELATIONSHIP BETWEEN CELL DISCHARGE FREQUENCY AND THE MAGNITUDE OF THE ANTICIPATORY POSTURAL ADJUSTMENT. Linear regressions between cell discharge activity and different EMG and force recordings (see METHODS) during the approximate time of the anticipatory postural adjustment (0–50% of the response period; see Fig. 2E) were made using data from all 94 cases identified as Go-related and from 137 cases identified as movement-related (and without preceding Go-related activity). It included 58 PTNs that showed movement-related activity during reach of either limb, 16 PTNs showing movement-related activity only during contralateral reach, and 5 PTNs only during ipsilateral reach.

For cells with Go-related activity, significant relationships between average cell discharge and at least two of the five force (including CVP) or five EMG traces were found in 32/94 (34%) of the cases. For 29 cases in which a receptive field could be determined, 7/29 had a receptive field around the shoulder, whereas the other 22/29 had a receptive field on the distal forelimb and/or the pad. For the movement-related cells, a smaller proportion 28/137 (20%) showed positive relationships with force or EMG activity. Inspection of the pattern of discharge frequency in these 28 movement-related cells showed that many of them (22/28) showed qualitatively similar short-latency increases or decreases in discharge activity to those of the Go-related cells. However, this change in activity was not found to be significant by either of our analysis methods. In addition, although most of these 17 cells showed a significant linear regression with CIB onset and were thus classified as movement-related by definition, the slope of the regression of lead time versus CIB onset was frequently greater than that for cell latency versus CIB onset. Such cells may be examples of false negatives (see DISCUSSION).

ACTIVITY DURING THE INSTRUCTED DELAY PERIOD. It might be expected that if PTNs were involved in motor planning, as suggested by Perfiliev (2005), changes in neuronal discharge rate would occur during the instructed delay period when the cat is provided information as to which limb to move. Indeed, analysis of the activity during the instruction period showed that 35/151 (23%) PTNs showed a change in activity that exceeded the interval of the confidence of the control period for reaches with at least one limb. However, taking into account reaches with either limb, changes during the instructed delay were observed in only 42/302 cases (13%). In addition, only 7 PTNs showed significant changes in instructed delay activity prior to reaches with both limbs and in 6/7 cells the sign of the change in discharge (increase or decrease) was the same regardless of the limb that was moved (see e.g., Fig. 10, A and B).

A proportion (15/42) of the cases with significant increases in instructed delay activity also exhibited short-latency Go-related activity. In 11/15 of these cases, the change in activity was in the same direction. Moreover, comparing only the sign of the change in activity during the instructed delay period with the sign of the initial short-latency change following the Go signal showed that 33/42 showed the same sign of change (Fig. 10). In other words, the change in activity during the instructed delay better predicted the sign of the change in cell discharge activity following the Go signal than the limb to be moved. This suggests that the changes in instructed delay activity might better reflect changes in posture or limb loading than a motor plan.

Some support for this view comes from inspection of the vertical force in the left forelimb in the period preceding the Go signal. In 19 cases with forelimb receptive fields and showing significant changes in discharge activity during the instructed delay period during a left reach, a decrease in both vertical force in the left forelimb and in cell discharge...
was observed in 14/19 cases. Two examples of this relationship can be seen in Fig. 10, A and C. Eleven (11/14) of these cases had a receptive field that included the ventral surface of the pad. However, as for the changes in discharge activity following the Go stimulus, changes in activity were not consistently related to receptive field. For example, in Fig. 10B, the cell also shows a decrease in activity during the instructed delay period prior to the right reach despite an increase in force under the left paw. In a similar manner, the cell illustrated in Fig. 10D shows an increase in discharge frequency during the instructed delay period despite a decrease in force in the IFL prior to the Go stimulus. Together, these results suggest that the same mechanisms that determine how the cell will discharge during the pAPA also contribute to the changes in cell discharge activity during the instructed delay period. This is more consistent with a mechanism that is modifying cell activity related to the postural requirements preceding the movement than one that is planning which of the two limbs is to be moved.

**Discussion**

The data in this study show that a substantial proportion of cells in the cat motor cortex shows short-latency responses that are time-locked to the Go-stimulus. In this respect the results confirm previous results by Ghez (Martin and Ghez 1985; Vicario et al. 1983) and Perfiliev (1998, 2005). However, whereas these authors interpreted this discharge activity as being primarily related to sensorimotor transformations and motor planning, we suggest that these data constitute a better indicator of a contribution to the production of the anticipatory postural responses that precede the onset of the reach.

**Methodological considerations**

One of the assumptions underlying the analysis in this study is that neuronal responses related to pAPAs should be present at short latency following the Go stimulus and should be time-locked to that Go stimulus (see following text); thus an
initial consideration is the extent to which we have been able
to accurately identify this target population of cells.

In our previous studies examining postural responses in neu-
rons in the PMRF (Schepens and Drew 2004, 2006; Schepens
et al. 2008), we used linear regression analyses, based on mea-
sures of response latency in individual trials, to identify cells
whose activity is time-locked to the Go stimulus. A similar
method has been used in several other studies of motor cortical
activity (Lamarre et al. 1983;Perfiliev 1998, 2005; Vicario et al.
1983). In Schepens et al. (2008), we further imposed limits on the
variance of the cell discharge to provide a very restrictive classi-
fication of Go-related neurons. Most figures used herein to illus-
strate Go-related changes in neuronal response fulfilled these strin-
gent criteria. However, as we have stated, this method can be used
only in PTNs in which there is an abrupt change in neuronal
activity in individual trials. More gradual changes in activity or
small differences in discharge activity in the control period with
respect to the response period produce more variable and possibly
inaccurate results. We therefore devised the threshold crossing
analysis, which we applied to all cells that could not be identified
by the linear regression analysis.

One possible disadvantage of the threshold crossing analysis is
that it is based purely on latency and might give a false positive in
cells in which the reaction time for the movement is quite short.
Indeed, it is possible that our constraint that the onset should begin
within 200 ms of the Go signal might be too generous and result
in false positives, that is, cells falsely identified as Go-related.
However, our comparison of the cell classifications provided by
the two methods (see the Appendix) showed a high level of overlap
in the results. In all, 84% of the cells identified as Go-related on
the basis of linear regression analysis were also similarly classified
on the basis of the threshold crossing analysis. Moreover, both the
temporal analysis of the cell discharge and the analysis of mag-
nitude (see following text) support the view that cells identified
using the threshold crossing analysis were indeed better related to
the Go signal than to the onset of the movement. In the absence of
any absolute method of identifying a Go-related cell, we believe
that the combination of analytical approaches used in this study
provides a very good objective method of identifying such cells.

General characteristics

Our analysis identified 70/151 (46%) PTNs as Go-related
during reach of at least one limb (Table 1). These values may
be compared with those from the study of Perfiliev (2005) in
which 12% of cells were identified as having a pure sensory

(Go-related) response, although a much larger percentage (69%) had a combined sensory and motor response. In the study of Vicario et al. (1983), 16% of the total population of neurons was identified as being Go-related. The differences in proportions probably reflect differences in analytical techniques and acceptance criteria, topographical sampling biases, and the fact that we included only PTNs in our study. With respect to the onset of cell discharge, the average latency of the stimulus-locked responses was 75 ms in our task compared with 51 ms in the study of Vicario et al. (1983) and 66 ms in the study of Perfiliev (2005).

In contrast to the relatively high proportion of Go-related cells recorded in the cat in this study and that of Perfiliev (2005), a study in the primate that specifically examined the extent to which discharge activity was time-locked to the stimulus-triggering movement (Lamarre et al. 1983; see also Evarts 1966) reported that only 3% of cells showed a response time-locked to a visual stimulus, although 11% showed Go-related activity to an auditory stimulus. Lamarre et al. (1983) concluded that most motor cortical cells in the monkey are thus not involved in sensorimotor transformation prior to a voluntary movement. The difference in the proportion of Go-related cells in the cat and the monkey was interpreted by Vicario et al. (1983) and by Perfiliev (2005) as a result of species differences. The argument made is that the relatively poorly developed premotor areas in the cat with respect to the monkey result in more of the sensorimotor transformations being processed in the motor cortex. In contrast, on the basis of the arguments made in the following section we would suggest that these differences are more related to the constraints of the task than to differences in species.

Last, as in the study of Perfiliev (2005), we identified Go-related cells that discharged both during movement of either limb or to movement of one limb or the other. In our study, 47% of Go-related neurons discharged only during contralateral reach, a further 22% discharged only during ipsilateral reach, and 31% during movements of either arm. This is similar to the study of Perfiliev (2005). It should be noted that several studies in primates (Cisek et al. 2003; Donchin et al. 1998, 2002; Kermadi et al. 1998; Tani et al. 1988) also reported increases in motor cortical activity to reach of either the ipsilateral arm or to movement of both but in none of these studies was there any attempt to determine whether discharge activity was better related to the Go stimulus or to the following movement.

Functional relationship of the Go-related discharge

We suggest that the stimulus-locked activity observed in our studies contributes to the production of the postural responses that precede the reach and that are essential for ensuring equilibrium. Several arguments support our position.

First, the latency of this Go-related activity is comparable to that of the APA-related changes in force and EMG activity that we have detailed in previous studies using this and a similar reaching task (Schepens and Drew 2003; Schepens et al. 2008). In those studies we showed that the initial changes in postural EMG activity occurred at mean latencies of 60–70 ms following the Go stimulus, that they were time-locked to the Go signal, and that they were temporally dissociated from the subsequent movement. Similar changes in force and EMG activity were observed in the present study (see Figs. 2, 3, and 6). Such a temporal dissociation from the voluntary movement is more compatible with a contribution to postural control than to planning the movement that occurred only several hundreds of milliseconds later. We have previously reported short-latency discharges with identical characteristics in cells recorded from the PMRF (Schepens and Drew 2004, 2006; Schepens et al. 2008), a structure that is closely identified as having a function in the control of posture (Drew et al. 2004; Mori 1987, 1989; Peterson 1979) and that is not generally associated with motor planning.

Second, our temporal analysis (Fig. 9) showed that the Go-related change in activity of these PTNs was correlated to the onset of the change in the AP component of the CVP in 89% of the cells that we tested. We also found positive relationships between the average discharge frequency of 34% of the PTNs during the pAPA and the changes in magnitude of the vertical forces under the limbs and the CVP during the same time period. This further supports our view that these cells contribute to the production of the pAPA. However, it should also be noted that similar positive relations were seen in 20% of the movement-related cells. As detailed in RESULTS, most of the movement-related cells either showed tonic activity during the pAPA or showed short-latency changes that were not detected by our analyses. This leads to two suggestions: 1) that the number of posture-related cells was underestimated by our analysis methods; and 2) that even cells without a dynamic change during the pAPA may contribute to these postural changes, perhaps as a more general signal modulating the underlying tonic muscle tonus.

Third, we found that cells with receptive fields on the hindlimbs or recorded in close proximity to such cells also showed Go-related activity. It is very unlikely that such activity would be related to planning movements of the forelimbs. Rather, it is more likely that this discharge activity contributes to the postural changes observed in the hindlimbs and that the Go-related activity recorded in both the forelimb and hindlimb representations has a common function in regulating postural activity preceding the onset of the movement.

Fourth, the task we used was an instructed delay task. As such, the cat was instructed which limb to use in the task and had ample time (0.5–1.5 s) to formulate a motor plan to ensure that the reaching movement was made with the correct limb. That the cat used this time appropriately plan the movement is suggested by the fact that movements were very rarely made with the wrong limb, even when changing from one block to another. Consequently, if the motor cortex were involved in sensorimotor transformations, at least during this delay period, one would expect consistent changes in discharge activity during the delay period, as is commonly observed in the premotor and posterior parietal cortices in the primate (Crammond and Kalaska 2000; Johnson et al. 1996; Kalaska 1996; Riehle and Requin 1989; Weinrich and Wise 1982). However, only a relatively small proportion of our cells (23%) showed any significant change in activity during the instructed delay period and only 1/151 PTNs showed significant changes of opposite sign during the left and right reaches. It is generally accepted that a lack of activity during the instruction period followed by changes in discharge activity following the Go stimulus suggests that the discharge activity is more likely to be related to the requirements of the movement than to a
sensorimotor transformation (Kalaska 1996), although the latter cannot be completely ruled out. Moreover, it should also be emphasized that 23% of these Go-related cells also showed significant changes in activity during the instructed delay period that could be related to sensorimotor transformations. However, in only few cells was there significant activity during movements of both limbs, as might be expected if the signal was determining which limb should be used to make the movement. Instead, we suggest that at least in some cases, as illustrated in Fig. 10, these changes in activity during the ID period are related to changes in body posture or loading of the limbs preceding the Go stimulus.

These changes in discharge activity during the instructed delay period may be compared with those observed in primate studies in which more sophisticated experiments have been used to specifically examine the contribution of cells in different cortical areas to decision-making processes, including which limb to use to make a movement. For example, Cisek et al. (2003) found that 23% of cells in the motor cortex discharged during the instructed delay period preceding movement of the ipsilateral limb (but not the contralateral limb), but only 7% discharged during the instructed delay period prior to movements of either limb. This percentage was substantially less than that observed for a population of cells in premotor cortex recorded in the same task (61% tuned to movements of either arm during the instructed delay period). Cisek et al. (2003) specifically considered the possibility that the activity in the instructed delay period prior to the ipsilateral limb movement may reflect covert planning of movement of the contralateral limb as suggested by Perfiliev (2005) but rejected this hypothesis. The argument of Cisek et al. (2003) was based on the finding that, although cells in the premotor cortex may, indeed, reflect contralateral limb movement when the limb to be moved is not specified, this activity was suppressed as soon as information on the requested movement was supplied (Cisek and Kalaska 2002, 2005; Kalaska and Crammond 1995). In other words, many cells that discharged strongly when the information was ambiguous ceased to discharge as soon as the monkey received information that it was the ipsilateral limb that was to be moved. A similar argument may be made for our task in which unambiguous information about the limb to move was present throughout the instructed delay period.

Clearly our conclusions as to the function of this short-latency discharge are different from those of Perfiliev (2005). On the basis of the discharge activity observed during the instructed delay period in our task, we think it unlikely that Go-related activity preceding movement of both the contralateral and ipsilateral arm reflect covert planning. Moreover, it should be emphasized that the suggestion by Perfiliev that the short-latency discharge in motor cortex in his experiments was related to motor planning was based in large part on the rejection of the hypothesis that the discharge was related to posture. The primary reason for rejecting such a relationship was his conclusion that reaching from a sitting posture does not require APAs, at least in the forelimbs. However, the evidence for this is not conclusive. There were no recordings of ground reaction force under the limbs and postural changes were monitored by recordings of only a single muscle, the triceps brachii. It should be noted that even in our task, in the standing cat, changes in the triceps are not always clear (Schepens et al. 2008). In addition, it should be noted that the mean reaction time for movement of the forelimb in Perfiliev’s study varied between 370 and 520 ms in different cats. This is similar to the reaction time changes observed in our studies, including this one, and much longer than the reaction times that are observed in seated primates (Evarts 1966; Lamarre 1983) or those reported by Ghez in his studies (Vicario et al. 1983). The most obvious reason for the long latencies in the experiments of Perfiliev (2005), as in ours, is the need for the cat to produce an appropriate postural response prior to the movement. Although we cannot completely reject some contribution to planning, the Go-related activity observed in both his and our studies is certainly consistent with the idea that it contributes to the control of the anticipatory postural adjustments preceding reaching movements in both standing and sitting cats.

**Function of the posture-related activity**

The evidence presented in the previous paragraphs argues strongly for a contribution of the Go-related activity that we recorded in the motor cortex to the production of the pAPAs preceding the movement. The question than arises as to the nature of that contribution.

Consideration of the receptive fields of the population of the PTNs with Go-related responses together with the effects of the microstimulation suggest that there are two broad groups of cell. One of these groups includes those cells with receptive fields on the forearm and the paw. Microstimulation in regions in which these cells were recorded most frequently produced some combination of shoulder retraction, elbow flexion, and wrist dorsiflexion. The second population included those cells with receptive fields restricted to the shoulder and recorded in sites in which microstimulation produced isolated movements at the shoulder or were without effect. In this respect, we make a distinction between retraction of the shoulder that is normally produced in the same sites that produce elbow flexion and movements such as elevation or abduction, which were generally produced in isolation. Although one must be careful in interpreting the effects of trains of microstimulation because neurons at a distance from the stimulation site might be activated synaptically, stimulation sites producing responses in more distal muscles rarely produced abduction or elevation of the shoulder and, vice versa, stimulation sites producing shoulder movements (other than retraction) rarely activated more distal sites. Moreover, most cells recorded in sites in which microstimulation produced shoulder movements also had receptive fields including, or restricted to, the shoulder and these sites were clustered in the rostromedial regions of the motor cortex. Taken together, we believe that these results support a view of two populations of neurons with different functional contributions to the behavior.

The presence of Go-related cells with receptive fields on the more proximal limb and recorded in locations in which microstimulation produced responses in proximal muscles is to be expected on the basis of our studies of the strategies involved in this reaching task in the cat (Schepens and Drew 2003). These studies showed that most shoulder muscles showed Go-related activity compatible with a contribution to the pAPAs. One might therefore suggest that cells such as those illustrated in Fig. 7 contribute to the production of the APA-related activity in these proximal muscles. The changes in activity during movement of the ipsilateral limb are also not
unexpected because several of these more proximal muscles show changes in activity during movements of both the left and right limbs (Schepens and Drew 2006).

The contribution of those cells with more distal receptive fields is less obvious. The movements produced by stimulation at these sites are those primarily involved in the movement of the limb and not those that might be expected to be involved in the production of the pAPA. In some cases the discharge of the cell might simply be the result of passive activation of a receptive field on the ventral pad of the paw. The cell illustrated in Fig. 6A, for example, would be activated by the increased pressure on the pad that is observed during the left reach (Fig. 3A). However, this cell was also activated during the reach of the limb (when the paw was lifted from the ground) and equally showed Go-related activity during the right reach when the pressure under the left pad would be reduced (Fig. 3). In addition, it should be noted that some cells with receptive fields on the ventral paw showed decreased activity during contralateral reaches (when pressure on the receptive field was increased). Similarly, there was no clear relationship between the change in cell discharge during the instructed delay period and the corresponding change in the force in the IFL (Fig. 10). As such, it is quite possible that the changes in activity in many cells should be considered as driven centrally, rather than being a simple obligatory reflection of the passive activation of a receptive field. A similar dissociation between receptive field location and cell discharge characteristics, in particular when the receptive field includes the ventral paw, has been reported for many cells during voluntary gait modifications (Drew 1993; Drew et al. 1996) and during postural adjustment (Beloozerova et al. 2005).

Nonetheless, as mentioned earlier, microstimulation in loci in which cells with distal receptive fields were recorded rarely produced contraction of muscles related to the production of the pAPA, leaving open the issue of how they might contribute to postural control. One possibility is that such cells are involved in stabilization of the distal limb during the pAPA. Such a contribution should also be considered as a postural function, but one that is distinct from the changes in CVP and the associated changes in center of mass that are essential in preparation for the movement. Some evidence for this is provided by the data illustrated in Fig. 3, showing activation of the EDC prior to the movement during both contralateral and ipsilateral reach. Although such activation of the EDC was not seen consistently, it should be noted that activation in single muscles may not provide an accurate indication of the behavioral responses observed during complex movement. For example, we have previously reported that changes in CVP preceding a movement and detected by the force platforms are not always obvious in the activity of the recorded EMGs (Schepens and Drew 2004).

A cortical contribution to the control of posture

Our suggestion that the motor cortex contributes to postural control is not without precedent and support. As mentioned in the introduction, MacKinnon et al. (2007) demonstrated that transcranial magnetic stimulation over the motor cortex in human subjects in the period just prior to the production of a pAPA leads to a facilitation of the muscles involved in the production of the pAPA. Similarly, Viallet et al. (1992) showed in hemiparetic patients that the APA that is normally observed in the postural arm during the unloading reflex was absent in the arm contralateral to the damaged motor cortex. In addition, Beloozerova et al. (2005) showed that motor cortical cells are rhythmically activated in association with the compensatory postural responses that are produced in response to oscillatory sway of the body. Jacobs and Horak (2007) reviewed the literature showing cortical regulation of compensatory postural responses. Last, motor cortical neurons also discharge during a postural hold task in which the major constraint is to maintain a stable position of the arm (Crammond and Kalaska 1996; Kurtzer et al. 2005). Kurtzer et al. (2005) also suggested that there may be some independence in the control of the postural hold and the subsequent movement (although see Crammond and Kalaska 1996). This would be compatible with our results that show that a few PTNs discharge only in response to the pAPA (not illustrated).

Pathways responsible for postural modification

In this study, we placed stimulating electrodes only in the pyramidal tract. We can thus not address the question of whether the motor cortical cells that we recorded contribute directly to the production of the postural responses via the corticospinal tract or whether there is also an indirect contribution, via the large corticoreticular projection to the PMRF (Jankowska and Edgley 2006; Matsuyama and Drew 1997; Rho et al. 1997). However, previous results from this laboratory suggest that the contribution would likely be via both

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**FIG. 11.** Summary diagram illustrating the possible origins and projections of the signals responsible for the coordination of posture and movement. The figure is adapted from a previous figure designed to illustrate the theoretical signals responsible for the coordination of posture and movement (Schepens and Drew 2004) and is originally derived from a model by Massion (1992). aAPA, anticipatory postural adjustments that accompany movement.
pathways. For example, we have previously shown that many PTNs with fast conduction velocities, similar to those of the majority of PTNs showing Go-related discharges (see Fig. 4), project to both the spinal cord and to the PMRF (Kably and Drew 1998). Moreover, this projection is larger from neurons in the proximal forelimb representation than in the representation of the more distal forelimbs, although the latter is also present (Kably and Drew 1998; Rho et al. 1997). Indeed, although the direct projection to the spinal cord may contribute to the pAPA, especially for the stabilization of the distal forelimb, it is probable that the major contribution of these Go-related cells is to activate those populations of neurons in the PMRF that are required to produce the appropriate postural adjustments (see also Luccarini et al. 1990). Given that there is extensive divergence and convergence (Jinnai 1984; Kably and Drew 1998; Matsuyama and Drew 1997; Rho et al. 1997) in the projections from the motor cortex to the PMRF, the signal from the motor cortex would be amplified in the PMRF to produce a more extensive signal during the pAPA. This amplification is probably important in several ways. For example, because of the diffuse and divergent nature of the reticulospinal pathway (Drew and Rossignol 1990a,b) it would ensure a coordinated response in all four limbs. The same diffuse nature of the PMRF output would equally ensure a coordinated response within any given limb. In particular, it would ensure the appropriate activation of muscles, such as the elbow extensors, that are only weakly activated by cortical microstimulation. For example, the long and lateral heads of the triceps brachii, which are elbow extensors, are strongly modulated during the pAPA but were activated by microstimulation in only 3/49 sites in which Go-related PTNs were recorded in these experiments.

Comparisons with Go-related activity in the PMRF

Changes in motor cortical discharge activity during the pAPA showed several similarities to those observed in reticular neurons recorded from the PMRF (Schepens and Drew 2004, 2006; Schepens et al. 2008). In common with the neuronal activity recorded from the PMRF, a substantial proportion of cells showed initial changes in activity related to the Go stimulus. As in the current study, we found cells that showed bilateral activity, including both reciprocal and nonreciprocal changes, as well as those that showed changes only during left or right reach (Schepens and Drew 2006; Schepens et al. 2008). The average latency of these Go-related changes in the PMRF was 70–85 ms. This is similar to the average latencies described in this study from the motor cortex. As such, these results are compatible with a view that the motor cortex may be one source of input to the PMRF, providing the information necessary to produce the appropriate pAPA (Fig. 11).

Concluding remarks

A general question arises as to the position of the motor cortex in the hierarchy responsible for the planning and coordination of movement and posture. The relative lack of any increase in activity during the instructed delay period in the motor cortex and the short latency of the responses in the motor cortex following the Go signal argue that it is not involved in the global planning of these processes. One would expect that neurons participating in determining which limb is required to make a movement and in determining how the appropriate postural responses should be organized should increase their activity during the delay period as information is processed. As discussed earlier, such increases in activity during the delay

Left (contralateral) Reach

![FIG. A1. Comparison of the 2 methods used to determine Go-related activity. A–C: the linear regressions and threshold crossing analysis obtained during left (contralateral) reach for the 3 cells illustrated in Fig. 6. Regressions are shown for cell latency (○) and lead time (●) vs. CIB onset. i, intercept of the regression; L, mean latency (ms) of the cell discharge calculated from individual trials; Var, the variance of the cell discharge (ms).](Image)
period have been seen extensively in the premotor cortices in primates trained to make movements of one or the other limbs or to make decisions between two choices but less frequently in the motor cortex. Similarly, the short latency of the responses in the motor cortex following the Go stimulus would suggest the release of a program compiled elsewhere. It is possible that the premotor cortex in the cat might perform a similar function. Alternatively, it is possible that such a signal might be observed in other cell populations in the made cortex (e.g., in layer III) given that recordings in this study were made only from PTNs in layer V. In addition, one has to question whether the motor cortex is the sole or even the major source of a signal providing information about the timing and required composition of the pAPA, given that the major input to the PMRF is from the premotor cortex rather than the motor cortex (Matsuyama and Drew 1997; Rho et al. 1997). Conceivably, the premotor cortex might provide a signal confirming the requirement for a pAPA (Fig. 11), whereas the more muscle-related activity from the motor cortex may be important in specifying the exact synergies that need to be produced from the PMRF.

**APPENDIX**

**Linear regressions**

As a working definition of a Go-related cell, we used the same method as in Schepens et al. (2008). In brief, we first removed from our data set all cells that showed a significant correlation ($P < 0.05$) between the latency of cell discharge and the latency of the CIB. These cells were automatically classified as movement-related regardless of the slope (regression coefficient) of the relationship. Next, for all of the remaining cells we selected those cells that had an $R^2$ of $<0.2$ when the onset of the cell discharge was plotted against CIB onset and an $R^2$ of $>0.81$ when lead time was plotted against CIB onset. For this population of cells we calculated the mean of the variance of the latency of each cell and used that to determine the interval of confidence. We then reexamined the entire population of non-movement-related neurons and considered all cells that had a variance $<\mu$ interval of confidence of the mean value as time-locked to the onset of the Go signal (Go-related).

**Threshold crossing analysis**

For this analysis we filtered the averaged perievent histogram at 30 Hz and then we used the control period of the unit activity, 500 ms prior to the Go-cue, to set a 99% confidence level for identification of significant changes in activity during the response period (RP), which spanned the initial 50% of the period between the Go-cue and CIB onset (Fig. 2E). We normalized the period between the Go signal and movement in each trial by fitting data points with a cubic spline and resampling the signal to 100 data points during the response period. To be defined as Go-related the average profile of activity in response period had extended above or below the mean $\pm$ confidence level for $>10\%$ of response period. Moreover this change had to occur during the first 50% of the response period and the latency of the change had to be $<200$ ms after the Go-cue. The time constraint of 200 ms was used to reduce the possibility of false-positive selections of the responses related to the reaching movement. The example unit in Fig. 2 significantly increased its discharge during the response period at a latency of 36 ms (Fig. 2E). The method was repeated separately on reaches with left and right forelimbs. We refer to this as a threshold crossing analysis.

**Combined analysis**

We used both methods of analysis to obtain a realistic indication of the prevalence of Go-related activity in the population of PTNs recorded in this study. The linear regression analysis is a robust method but can be used only on PTNs that show an abrupt change in discharge activity limiting its application. The threshold crossing analysis can be used on the entire population of PTNs but the identification of Go-related cells is based primarily on a consideration of analysis and needs to be validated (see following text).

To obtain the final database we applied three rules. In the first step, all PTNs identified as movement-related on the basis of the linear regression analysis were removed from the database. In the second step, all PTNs that fulfilled the criteria applied during the linear regression analysis were automatically defined as Go-related. This identified 32 PTNs as Go-related. Ten (10/32) discharged during movement of either limb, providing a total of 42 cases (Table 1). In the third step all additional cells identified as Go-related on the basis of the threshold crossing analysis were added to the database. The final, combined database included 70 PTNs (Table 1, top, “TCA + Regression”). Twenty four (24/70) of these were Go-related to movement of either limb, providing a total of 94 cases. The combined
proportion of cells showing bilateral or unilateral responses is similar to that obtained by using only the regression analysis.

Comparison of the results from the linear regression analysis and from the threshold crossing analysis

Figure A1 shows the results of one comparison of the two methods that was made on the three cells illustrated in Fig. 6. None of the three cells showed a significant relationship with movement (regressions with open circles) during either left (A–C) or right (not illustrated) reach. In contrast, all three of them showed a strong linear relationship between lead time and the onset of CIB and all three of them were characterized by a low variance of the cell latency. As such, they were all classified as Go-related during both left and right reaches on the basis of the linear regressions. Equally, all three of the cells during left and right reaches were identified as Go-related on the basis of the threshold crossing analysis.

We compared the results from the two methods using all of the Go-related responses from the 151 PTNs recorded during reach of both forelimbs plus some additional Go-related responses from PTNs recorded only during reach of the left, contralateral limb. This provided a total of 46 cases identified as Go-related on the basis of the linear regression analysis. Altogether, we found that 38/46 (83%) of the cases identified by the regression analysis were also classified as Go-related by the threshold crossing analysis. Four (4/8) of the false negatives were caused by a short-latency inhibition that was not detected by the threshold crossing analysis and the other 4 because of short reaction times that did not allow dissociation of the two periods. From the opposite perspective, of 67 cases identified as Go-related on the basis of the threshold crossing analysis method, and for which it was possible to perform a regression analysis, only 56/67 (84%) were identified as movement-related by the latter analysis.

That the combined method of identifying Go-related cells is appropriate is supported by the data illustrated in Fig. A2, which plots the coefficient of determination ($R^2$) obtained from the regressions of lead time versus CIB onset as a function of the $R^2$ determined from the regression of cell latency versus CIB onset. Cells identified as Go-related on the basis of either the regression analysis (blue filled circles) or the threshold crossing analysis (red filled circles) are clearly separate from those that were identified as movement-related on the basis of the regression analysis (green filled circles). Similarly, as shown in Fig. A2B, the latency of the cell discharge of the two subsets of Go-related cells (blue and red boxes) is distinct from that of the movement-related cells (green box). Note that the distribution of the latencies of the cells identified on the basis of the regression analysis (blue box) and that of those identified by the threshold crossing analysis (red box) overlap almost entirely (Fig. A2B).

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