

Mapping From Motor Cortex to Biceps and Triceps Altered By Elbow Angle

Michael S. A. Graziano, Kaushal T. Patel, and Charlotte S. R. Taylor

Department of Psychology, Princeton University, Princeton, New Jersey 08544

Submitted 19 December 2003; accepted in final form 24 February 2004

Graziano, Michael S. A., Kaushal T. Patel, and Charlotte S. R. Taylor. Mapping from motor cortex to biceps and triceps altered by elbow angle. *J Neurophysiol* 92: 395–407, 2004. First published February 25, 2004; 10.1152/jn.01241.2003. This experiment used cortical microstimulation to probe the mapping from primary motor cortex to the biceps and triceps muscles of the arm in monkeys. The mapping appeared to change depending on the angle at which the elbow was fixed. For sites in the dorsal part of the arm and hand representation, the effects of stimulation were consistent with initiating a movement of the elbow to an extended angle. Stimulation evoked more triceps activity than biceps activity, and this difference was largest when the elbow was fixed in a flexed angle. For sites in the ventral part of the arm and hand representation, stimulation had the opposite effect, consistent with initiating a movement of the elbow to a flexed angle. For these sites, stimulation evoked more biceps activity than triceps activity, and the difference was largest when the elbow was fixed in an extended angle. For sites located in intermediate positions, stimulation evoked an intermediate effect consistent with initiating a movement of the elbow to a middle, partially flexed angle. For these sites, when the elbow was fixed at a flexed angle, the evoked activity was largest in the triceps, and when the elbow was fixed at an extended angle, the evoked activity was largest in the biceps. These effects were obtained with 400-ms-long trains of biphasic pulses presented at 200 Hz and 30 μ A. They were also obtained by averaging the effects of individual, 30- μ A pulses presented at 15 Hz. How this stimulation-evoked topography relates to the normal function of motor cortex is not yet clear. One hypothesis is that these results reflect a cortical map of desired joint angle.

INTRODUCTION

In a recent set of studies of the motor cortex in monkeys, we electrically stimulated cortical sites using 500-ms trains of electrical pulses (Cooke and Graziano 2004; Graziano et al. 2002a,b, 2004). These stimulation trains were longer than those typically used in studies of motor cortex, but they approximated the time scale of the reaching and grasping movements that monkeys normally make. The stimulation trains evoked complex, coordinated movements that appeared to match common gestures in the monkey's natural repertoire. For example, stimulation of one site caused the arm to reach out to the space \sim 30 cm in front of the monkey while the hand shaped in an apparent precision-grip posture. The hand slowed as it approached this final position, much like the typical movement of the hand during a voluntary reach. Stimulation of another site caused the hand to move to the mouth and close in a grip posture and caused the mouth to open. Stimulation of yet another type of site caused an apparent defensive gesture including a squint and grimace, a turning aside of the head, and a thrusting of the hand into lateral space as if to block a nearby threatening object. Stimulation of other sites evoked other

complex movements. These movements were reliable and could even be evoked under anesthesia.

Two general observations emerged from this stimulation study. First, stimulation of each site caused the relevant joints to move in a goal-directed fashion into a specific final posture regardless of the initial posture. Second, the stimulation-evoked movements of the arm and hand were organized across the cortex in a rough topographic map. Stimulation of ventral sites within the arm representation resulted in hand locations in upper space; stimulation of dorsal sites resulted in hand locations in lower space, stimulation of anterior-dorsal sites resulted in hand locations in lateral space, and stimulation of posterior-ventral sites resulted in hand locations that crossed the midline.

The purpose of the present experiment was to further probe these stimulation-evoked postures. We focused on the effect of stimulation on the biceps and triceps muscles, the main flexor and extensor muscles that rotate the elbow joint. In our previous study, for some sites, stimulation evoked a final limb posture in which the elbow was partly flexed. If the elbow was initially fully extended, stimulation would cause it to flex until it reached the final posture. If the elbow was initially fully flexed, stimulation would cause it to extend until it reached the same final posture. The present experiment explored the muscle activity patterns that might underlie the initiation of these elbow movements to a final angle. We fixed the monkey's elbow into four different possible angles, stimulated sites in primary motor cortex, and measured the effect on the biceps and triceps with electromyographic (EMG) electrodes inserted into the muscle. We hypothesized that the effect of cortical stimulation would vary depending on joint angle in a manner consistent with pulling the joint toward a goal angle.

In specific, we predicted that the patterns of muscle activity evoked by stimulation should change systematically along the cortical surface, reflecting the apparent map of arm postures obtained in our previous study. Dorsal sites in the arm representation should be associated with goal elbow angles that are fully or mostly extended. Therefore stimulation of these sites while the elbow is held stationary should evoke more triceps than biceps activity. Greater triceps activity should be evoked when the elbow is fixed in a flexed angle, far from the hypothesized goal, and less triceps activity should be evoked when the elbow is fixed in an extended angle, near the hypothesized goal. Ventral sites should be associated with goal angles that are fully or mostly flexed, and therefore stimulation of these sites should evoke mostly biceps activity. Greater biceps activity should be evoked when the elbow is fixed in an extended angle, and less biceps activity should be evoked when the

Address reprint requests and other correspondence to: M. Graziano (E-mail: graziano@princeton.edu).

The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked "advertisement" in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

elbow is fixed in a flexed angle. Sites at intermediate locations should be associated with intermediate goal angles. In this case, stimulation of the same site in cortex with the same parameters should evoke greater activity in one or another muscle depending on arm position. Greater triceps activity should be evoked when the elbow is fixed in a flexed angle, and greater biceps activity should be evoked when the elbow is fixed in an extended angle. In effect, the mapping from the studied site in cortex to the muscles should switch from the extensor to the flexor muscle depending on elbow angle.

A secondary purpose of the experiment was to investigate the effect of different kinds of electrical stimulation. In our previous study of motor cortex, we stimulated cortical sites in awake monkeys using trains of biphasic pulses at 200 Hz. The train duration ranged from 100 to 1,000 ms (typically 500 ms), and the currents ranged from 25 to 150 μA . These parameters were adopted from the oculomotor literature where they have been used to evoke movements of the eyes and head (e.g., Bruce et al. 1985; Freedman et al. 1996; Gottlieb et al. 1993; Tehovnik and Lee 1993). Some concerns have been raised about the use of these stimulation parameters in motor cortex where experimenters traditionally use currents $<50 \mu\text{A}$ and trains $<50 \text{ ms}$ (Strick 2002). To address these concerns, in the present study we stimulated each cortical site in two ways. First, 200-Hz stimulation: each stimulation train was 400 ms long. The stimulus pulses were presented at 30 μA . The results of 8–20 trains were averaged together to obtain the mean effect of a stimulus train on the muscle activity. Second, 15-Hz stimulation: each pulse had a current of 30 μA . The results of 2,250–4,500 individual pulses were averaged together to measure the mean short-latency effect on the muscles of a pulse of current applied to motor cortex. This technique of 15-Hz stimulation has been used previously to probe the mapping between motor cortex and muscles (Cheney et al. 1985; Park et al. 2001).

Data were collected in awake monkeys and monkeys sedated with ketamine to allow their limbs to be easily placed in specific postures. The results were similar in both conditions. The signal-to-noise appeared to be optimal when the monkey was lightly sedated or awake but quietly resting.

METHODS

All husbandry, surgical, and behavioral procedures were approved by the Princeton University Institutional Animal Care and Use Committee and the attendant veterinarian and were in accordance with National Institutes of Health and U.S. Department of Agriculture guidelines. We studied two adult male *Macaca fascicularis* (4.5–6.0 kg).

Surgery

For each monkey, an initial surgical operation was performed under isoflurane anesthesia and strict aseptic conditions, during which an acrylic skull cap was fixed to the skull with bone screws. A steel bolt for holding the head and a 2.5-cm diameter steel chamber for neuronal recording and electrical stimulation were also imbedded in the acrylic. The recording chamber was positioned for a vertical approach to the precentral gyrus in the right hemisphere. The well was centered 20 mm anterior and 15 mm lateral to stereotaxic zero. Each animal recovered from the surgery within a week, but was given two additional weeks to allow the skull to grow tightly around the skull screws. In a subsequent procedure, also under deep anesthesia and aseptic conditions, the recording chamber was opened and a hole $\sim 10 \text{ mm}$ in

diameter was drilled through the layer of acrylic and the bone, exposing the dura.

Experimental sessions

During the daily sessions, the monkey sat in a Lexan primate chair with the head restrained by the head bolt. A hydraulic microdrive (Narishige) was mounted to the top of the recording chamber. A steel guide cannulus (18-gauge syringe needle) was lowered through the hole in the skull and into the dura. Then the varnish-coated tungsten microelectrode (Frederick Haer, impedance 0.5–5 M Ω) was advanced from the guide cannulus into the brain. Typically an electrode would begin at 4–5 M Ω . After repeated use on multiple penetrations, as the insulation began to wear off near the tip, the impedance would begin to drop. When we were no longer able to isolate clear single neurons on the electrode, it was discarded and a new one was used. Neuronal activity was monitored on an oscilloscope and over a loud speaker. Once the electrode was in cortex, as indicated by the presence of neuronal activity, we tested somatosensory responsiveness with light touch and rotation of joints. We then electrically stimulated the cortical site. When the testing at a site was complete, we lowered the electrode 0.5 mm to a new site and tested again. On most electrode penetrations, three depths were tested.

During the experimental session, the monkey was given an injection of ketamine (10 mg/kg im). Within 10 min of injection the animal was fully sedated, that is, no longer emitting spontaneous behavior and no longer reactive to touch. It was then possible to insert the EMG wires in the muscles. On most days, supplemental doses of ketamine were administered to maintain the monkey in a lightly tranquilized state throughout the experiment. On five testing days, the monkey was allowed to awaken from the initial ketamine dosage during the following 4- to 5-h experimental session, such that the effects of stimulation could be tested in the awake condition. The results were similar in both conditions and thus were combined in the analysis. The finding of similar stimulation-evoked movements in the awake and the sedated conditions was expected on the basis of previous results (Cooke and Graziano 2004; Graziano et al. 2002a).

Stimulation

Stimulation was applied by an S88 stimulator and two SIU6 stimulus isolation units (Grass, West Warwick, RI). Stimulation consisted of biphasic pulses. Each pulse had a negative followed by a positive phase, each phase 0.2 ms in duration. Current was measured by means of the voltage drop across a 1K-ohm resistor in series with the return lead of the stimulus isolation units. Two types of stimulation were applied:

200-HZ STIMULATION. Each train was 400 ms in duration. Within a train, pulses were presented at 200 Hz. For each site, we first varied the current until an evoked movement was observed. The threshold, the current at which the movement was evoked 50% of the time, was determined by two observers. The average threshold was 13.3 μA , with a range of 7–21 and a SD of 3.9. This threshold testing was used to confirm that the electrode was in primary motor cortex. After testing the threshold, we then collected quantitative data, with the current usually set to 30 μA . (In 2 cases, the current was set to 25 μA .) During the test, the elbow was fixed by an adjustable arm holder in one of the four angles shown in Fig. 1. All other joints including the shoulder, wrist, and fingers were held constant, with the thumb oriented upward and the fifth digit oriented downward. Only the elbow joint varied. Once the elbow joint was fixed in one of the four positions, a 400-ms stimulation train was presented. Then during the 14.6-s interval between stimulation trains, the elbow was moved to a different angle and fixed into position, and the next stimulation train was initiated. In this fashion, each of the four elbow angles was tested with 8–20 interleaved trials, for a total of 36–80 trials.

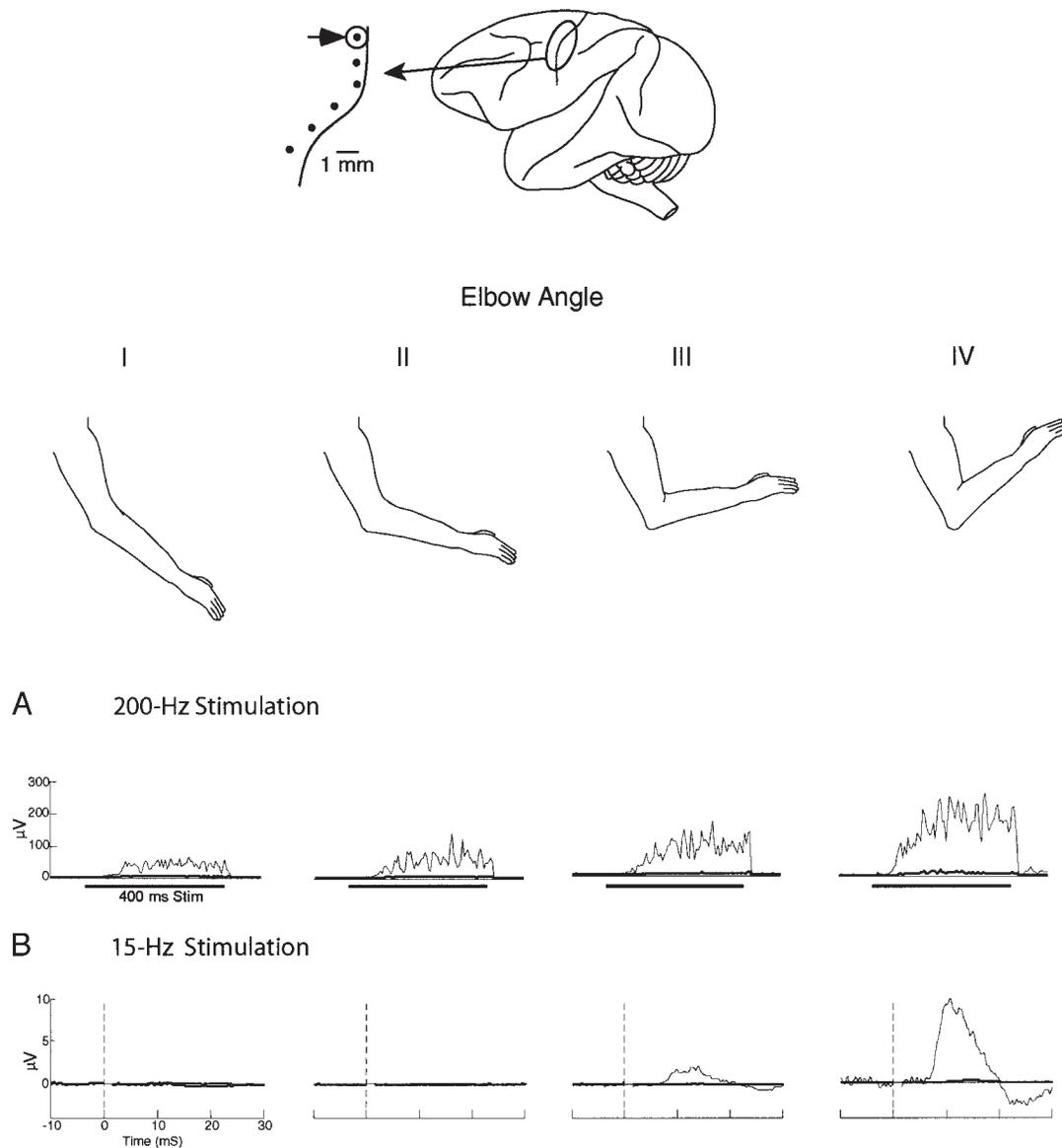


FIG. 1. Brain (*top*) shows the locations of 6 example sites in primary motor cortex. The brain drawing is schematized; the enlarged drawing of the central sulcus is based on data from *monkey 1*. The site indicated by the circle and the arrow is illustrated in the histograms. The monkey was tranquilized with ketamine during testing. *A*: electromyographic (EMG) activity of the biceps (thick line in each histogram) and triceps (thin line in each histogram) evoked by 200-Hz stimulation at $30 \mu\text{A}$ when the elbow was fixed at 4 different angles. Thick black line under each histogram indicates time of stimulation train. Each histogram is a mean of 15 trials. Evoked activity in both muscles was significantly affected by elbow angle (triceps, $F = 74.6$, $P < 0.001$; biceps, $F = 24.5$, $P < 0.001$). *B*: EMG activity evoked by 15-Hz stimulation. Vertical line on each histogram indicates time of biphasic pulse delivered to brain. Time from 0.2 ms before to 1.5 ms after the pulse is removed from the EMG data to avoid electrical artifact. Each histogram is a mean of 2,000–4,500 pulses. Evoked activity in both muscles was significantly affected by elbow angle (triceps, $F = 101.1$, $P < 0.001$; biceps, $F = 125.3$, $P < 0.001$).

15-HZ STIMULATION. During testing, the elbow was fixed in one of the four angles shown in Fig. 1 and $30\text{-}\mu\text{A}$ biphasic pulses were presented at a rate of 15 Hz for 10 s. Thus 150 pulses were presented in a block. Then during a 5-s inter-block interval, the elbow was moved to a different angle and fixed into position and the next block of testing was initiated. In this fashion, each of the four elbow angles was tested with 15–30 interleaved blocks, for a total of 2,250–4,500 stimulation pulses per elbow angle.

Some sites were tested first with 200-Hz stimulation and then with 15-Hz stimulation; other sites were tested in the reverse order. In this way, the results from 15-Hz stimulation could not be attributed to an alteration or rewiring of the brain caused by prior stimulation at 200 Hz.

It is important to note the differences between the 15- and the 200-Hz stimulation. In the case of the 15-Hz stimulation, each pulse evokes a small EMG increase with a latency between ~ 4 and 12 ms (Cheney et al. 1985). This increase then returns to baseline. In the case of 200-Hz stimulation, each pulse is presumed to evoke a short latency response just as in the 15-Hz stimulation. However, because the pulses are delivered 5 ms apart from each other, the effects of one pulse overlap with the effects of the next pulse. Thus a train of pulses at 200 Hz results in an overall, gradually building change in EMG during the train. In the case of the 15-Hz stimulation, enough pulses were averaged together to see the small, transient change in EMG that occurs subsequent to each pulse. This is the central goal of the

technique. In the case of the 200-Hz stimulation, 8–20 trials were averaged, enough to see the overall, large changes in EMG that accumulate during the train but not enough to see the initial small changes that are the result of the first few pulses of the train. Thus the observed latency in the case of 200-Hz stimulation was longer. In essence, the two techniques examine different aspects of the electrically evoked muscle activity.

EMG recordings

Fine insulated stainless steel wires were threaded into a 22-gauge syringe needle and inserted into the long biceps and lateral triceps of the arm contralateral to the stimulating electrode. The wires had an exposed tip of 1–2 mm. Three wires spaced ~5 mm apart were inserted in each muscle to provide input to a differential amplifier and its ground (single neuron amplifier model 1800, A-M Systems, Sequim, WA). The amplifier filters were set with a low cutoff at 300 Hz and a high cutoff at 1,000 Hz. Although some studies use a lower level for the low cutoff (e.g., Cheney et al. 1985), we found that a 300-Hz cutoff was helpful to remove low-frequency noise. The EMG signal was digitized at a rate of 10,000 Hz (Datawave Technologies, DT-300). The time of each pulse of stimulation to the brain was also stored at 10,000 Hz using the same data-acquisition unit. Stimulation pulses applied to the brain sometimes caused an electrical artifact in the EMG signal. To avoid this stimulation artifact, the time period from 0.2 ms before each stimulation pulse to 1.5 ms after the pulse was removed from the EMG data. The EMG signal was then rectified.

Analysis of 200-Hz stimulation

Figure 1A shows the results of stimulating a site in motor cortex with 200-Hz stimulation trains. Each of the two muscles was tested with four elbow angles. To test whether elbow angle significantly affected the EMG evoked in a muscle, we performed the following steps. For each trial, we calculated the amount of activity evoked by stimulation, defined as the mean activity during the 400-ms stimulation train minus the mean activity during a baseline period from 100 ms before to 0.2 ms before the onset of the stimulation train. We then used a one-way, between-subjects ANOVA to test if this evoked muscle activity was significantly different for different elbow angles.

To obtain the mean pattern of activity across sites, we performed the following steps. For each site, the evoked activity in the eight conditions (2 muscles \times 4 elbow positions) was divided by the maximum of the eight conditions and multiplied by 100 to express the results for that site as a percent of maximum. In this fashion, the relative pattern of activity across the eight conditions was obtained, independent of the overall magnitude of the activity evoked at that site. The resultant patterns from different sites were then averaged together. These averages are shown in Figs. 7–9. These graphs represent an average of the relative levels of activity among the eight conditions; they do not represent the absolute levels of activity.

Analysis of 15-Hz stimulation

For the 15-Hz stimulation, we analyzed the time period from 10 ms before to 30 ms after the presentation of each biphasic current pulse to the brain. We averaged the results across pulses to obtain eight average EMG traces, corresponding to two muscles \times four elbow angles. For example, in Fig. 1B, the four thick traces show the mean biceps EMG for the four elbow angles; and the four thin traces show the mean triceps EMG for the four elbow angles. In each trace, *time 0* corresponds to the time at which the current pulse was presented. For each of these average traces, we calculated a mean baseline activity based on the time from 10 ms before to 0.2 ms before the stimulation pulse. The data are plotted in microvolts relative to this baseline level. To obtain a measure of the amount of muscle activity evoked by the stimulation pulse, we used the mean change from

baseline during a response period. For the biceps, the response period was between 7 and 15 ms after the onset of the stimulation pulse because this matched the typical response of the biceps. For the triceps, the response period was between 7 and 10 ms after the onset of the stimulation pulse because this matched the typical excitatory response of the triceps, which was most often a brief spike in activity. We then used a one-way, between-subjects ANOVA to test if the muscle activity during the response period was significantly different for different elbow angles. Group averages across sites (shown in Figs. 7–9) were performed in the same manner as for the 200-Hz data.

Location of stimulation sites

In both monkeys, the approximate location of the central sulcus was first measured by shining a bright light on the dura during the initial craniotomy surgery. During recording and stimulating sessions, the location of the sulcus was confirmed by making electrode penetrations to either side of it. Penetrations just posterior to the sulcus resulted in the finding of neurons with small tactile receptive fields on the hand or fingers and in the finding of no movements evoked by electrical stimulation. Penetrations just anterior to the sulcus resulted in the finding of neurons with either larger tactile receptive fields or no tactile responses and in the finding of stimulation-evoked movements that had a low threshold (in all cases $<25 \mu\text{A}$). In this fashion, during the experiment, the sulcus could be located to within 0.5-mm accuracy. Data from motor cortex were collected by making electrode penetrations along a line near the central sulcus, <1 mm anterior to it. Stimulation sites along the depth of the penetration were therefore in the anterior bank of the central sulcus. We did not have sufficient information to assign sites to individual layers in cortex. Although we tested stimulation of sites more anterior to the sulcus during initial mapping, these sites were tested qualitatively and not used in the quantitative study; in this way, we ensured that all sites included in the analysis were in classical primary motor cortex. Stimulation of sites in the most ventral part of the studied area of cortex evoked movements of the face and mouth; stimulation of the dorsal-most sites evoked movements of the back and legs; and stimulation of intermediate sites evoked movements of the arm and hand. Data on biceps and triceps activity were collected from this arm and hand representation. Locations of penetrations were pseudo-randomly placed from one experimental session to the next, such that any systematic changes across the cortical surface could not be attributed to an effect of the order in which they were studied.

One monkey was killed with an overdose of sodium pentobarbital and perfused through the heart with 4% paraformaldehyde. The brain was exposed and the location of the central and arcuate sulci photographed. The location of the stimulation sites was reconstructed based on damage visible in the cortex and on the stereotaxic coordinates of the electrode penetrations. The stimulation sites were confirmed to be in primary motor cortex, in the anterior bank of the sulcus and on the cortical surface within 1 mm of the sulcus. The second monkey is still in use in experiments.

RESULTS

We tested 35 sites in primary motor cortex by applying 200-Hz stimulation trains of 400-ms duration while the elbow was fixed at four different angles. For 26 sites (74%), the evoked biceps activity was significantly different for different elbow angles (ANOVA, $P < 0.05$). For 24 sites (69%), the evoked triceps activity was significantly different for different elbow angles ($P < 0.05$).

We tested the same 35 sites with 15-Hz stimulation. For 35 sites (100%), the evoked biceps activity was significantly different for different elbow angles (ANOVA, $P < 0.05$). For 34 sites (97%), the evoked triceps activity was significantly different for different elbow angles ($P < 0.05$).

In the following text, we discuss six example sites in detail to illustrate these findings. We then describe the mean result.

Example 1

Figure 1 shows the results from one example site. The location of the site on the cortical surface is shown on the brain diagram (top). This site was located in the dorsal-most portion of the arm and hand representation. We tested the effect of stimulating the site while the elbow was fixed in the four different positions shown in Fig. 1. The shoulder, wrist, and fingers were stabilized; only the elbow angle was varied. The histograms in Fig. 1A show the EMG activity evoked by 200-Hz, 400-ms stimulation trains. During the stimulation train, the activity in the triceps (thin line) was largest when the elbow was in position IV, the most flexed posture tested. It was smallest when the elbow was in position I, the most extended posture tested. This dependence of evoked muscle activity on elbow angle was significant ($F = 74.6$, $P < 0.001$). The evoked activity in the biceps was much smaller than that in the triceps but had a similar dependence on elbow angle. It was slightly but significantly larger in position IV than in position I ($F = 24.5$, $P < 0.001$).

Figure 1B shows the results of 15-Hz stimulation. *Time 0* represents the time at which a 30- μ A, biphasic pulse of current was delivered to the brain. In this example 2,000–4,500 pulses were averaged together for each elbow angle to arrive at the mean effect of a pulse of current applied to cortex. Stimulation evoked a transient increase in triceps activity that began with a latency of ~ 7 ms. This triceps response was greatest when the elbow was in position IV and small or absent when the elbow was in position I. This effect of elbow angle on the evoked triceps activity was significant ($F = 101.1$, $P < 0.001$). In comparison to the triceps, stimulation evoked almost no change in biceps activity. When the elbow was in position IV, stimulation evoked a small rise in biceps activity; when the elbow was in position I, stimulation evoked a small dip in biceps activity. Both the increase and the decrease, though small in comparison to the triceps response, were statistically significant (for increase at position IV, $t = 10.17$, $P < 0.001$; for decrease at position I, $t = -24.78$, $P < 0.001$; for overall differences among positions, $F = 125.3$, $P < 0.001$).

Note that for this site, the effect of 15-Hz stimulation (Fig. 1B) was similar to the effect of 200-Hz stimulation (Fig. 1A) in the following ways: for both types of stimulation, the evoked triceps activity was greater than the evoked biceps activity; and for both types of stimulation, this discrepancy between triceps and biceps activity was largest when the elbow was fixed at position IV in a flexed posture. The effects of the two types of stimulation, however, were not identical. For example, for 200-Hz stimulation, substantial triceps activity was evoked at all elbow angles, whereas for 15-Hz stimulation, little or no triceps activity was evoked when the elbow was in the extended positions I and II. Also, 15-Hz stimulation evoked an excitatory phase followed by an inhibitory phase in the triceps, whereas 200-Hz stimulation evoked only an excitatory response.

Example 2

Figure 2 shows the results of testing another cortical site, located ventral to the previous example site. Figure 2A shows the

results for 200-Hz stimulation (see figure caption for details of statistics). When the elbow was in positions II–IV, we measured more stimulation-evoked activity in the triceps than in the biceps. When the elbow was in position I, stimulation evoked a similar level of activity in the two muscles, although slightly larger in the biceps. Figure 2B shows a similar pattern of results obtained with 15-Hz stimulation. As in the previous example, the 15-Hz stimulation was different from the 200-Hz stimulation in that it evoked an excitatory phase followed by an inhibitory phase, whereas the 200-Hz stimulation evoked only an excitatory response.

Example 3

Figure 3 shows the results for another example site. When the elbow was in positions I and II, stimulation evoked more activity in the biceps than in the triceps. When the elbow was in position IV, the direction of the effect reversed, and stimulation evoked more activity in the triceps than in the biceps. When the elbow was in position III, stimulation evoked a similar level of activity in the two muscles, although slightly larger in the biceps. This pattern of results was similar for both 200- and 15-Hz stimulation. As in the previous examples, the 15-Hz stimulation was different from the 200-Hz stimulation in that it evoked an excitatory phase followed by an inhibitory phase, whereas the 200-Hz stimulation evoked only an excitatory response.

Example 4

The example in Fig. 4 shows a pattern of results similar to the pattern in Fig. 3. When the elbow was in positions I and II, stimulation evoked more activity in the biceps than in the triceps. When the elbow was in position IV, stimulation evoked more activity in the triceps than in the biceps. When the elbow was in position III, stimulation evoked a similar level of activity in the two muscles, though slightly larger in the biceps. The pattern was similar for 200- and 15-Hz stimulation.

Example 5

In this example, stimulation evoked greater activity in the biceps than in the triceps for all elbow angles. The level of activity evoked in the biceps was greater for extended elbow angles than for flexed elbow angles. This pattern was similar though not identical for both 200- and 15-Hz stimulation. For 200-Hz stimulation, the biceps activation was greatest in position I, whereas for 15-Hz stimulation, the biceps activation peaked at position II. For 200-Hz stimulation, the triceps showed excitation at all elbow angles, whereas for 15-Hz stimulation the triceps showed little or no excitation and a small inhibition at position IV. As in previous examples, the 15-Hz stimulation evoked an excitatory phase followed by an inhibitory phase, whereas the 200-Hz stimulation evoked only an excitatory response.

Example 6

The example in Fig. 6 is similar to the one shown in Fig. 5. For all elbow positions, stimulation evoked greater activity in the biceps than in the triceps. The level of activity evoked in the biceps, and also the difference between biceps and triceps activity was greatest for position I and smallest for position IV. The pattern was similar though not identical for both 200- and 15-Hz

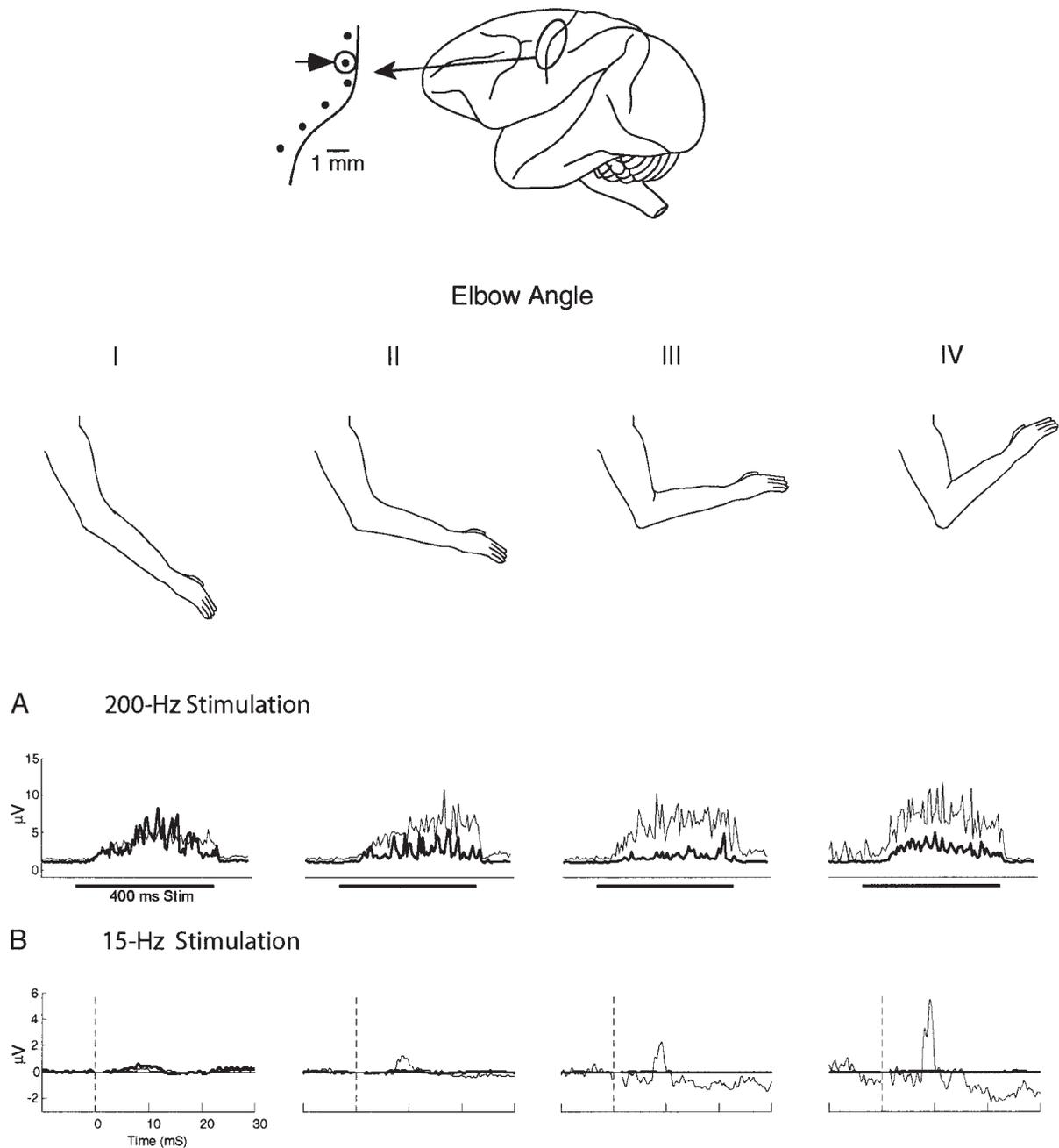


FIG. 2. EMG activity evoked by stimulation of another example site in primary motor cortex. The location of the site is shown in the brain drawing (*top*). See legend to Fig. 1 for details. *A*: for 200-Hz stimulation, activity in both muscles was significantly affected by joint angle (triceps, $F = 6.29$, $P < 0.001$; biceps, $F = 3.12$, $P = 0.032$). *B*: for 15-Hz stimulation, activity in both muscles was significantly affected by joint angle (triceps, $F = 27.47$, $P < 0.001$; biceps, $F = 29.78$, $P < 0.001$).

stimulation. For 200-Hz stimulation, the triceps showed excitation at all elbow angles, whereas for 15-Hz stimulation, the triceps switched from excitation in positions I and II to inhibition in positions III and IV. Note that the pattern obtained in this example is in some ways a reverse of the pattern obtained in Fig. 1.

Group data

The examples given in the preceding text show a gradually shifting pattern from dorsal to ventral sites. In dorsal sites, stimulation evoked more triceps than biceps activity. In ventral sites, stimulation evoked more biceps than triceps activity. In

intermediate sites, stimulation evoked activity that shifted relatively toward the triceps or the biceps depending on elbow angle. Figures 7, 8, and 9 show the mean result for all 35 sites, broken down into dorsal, intermediate, and ventral sites. These mean graphs show a similar change in properties from dorsal to ventral sites.

Figure 7 shows the mean result for 12 sites in the dorsal portion of the studied area. For this set of sites, stimulation evoked on average more triceps activity than biceps activity. This discrepancy was greatest for position IV, the most flexed position tested. In these respects the pattern was

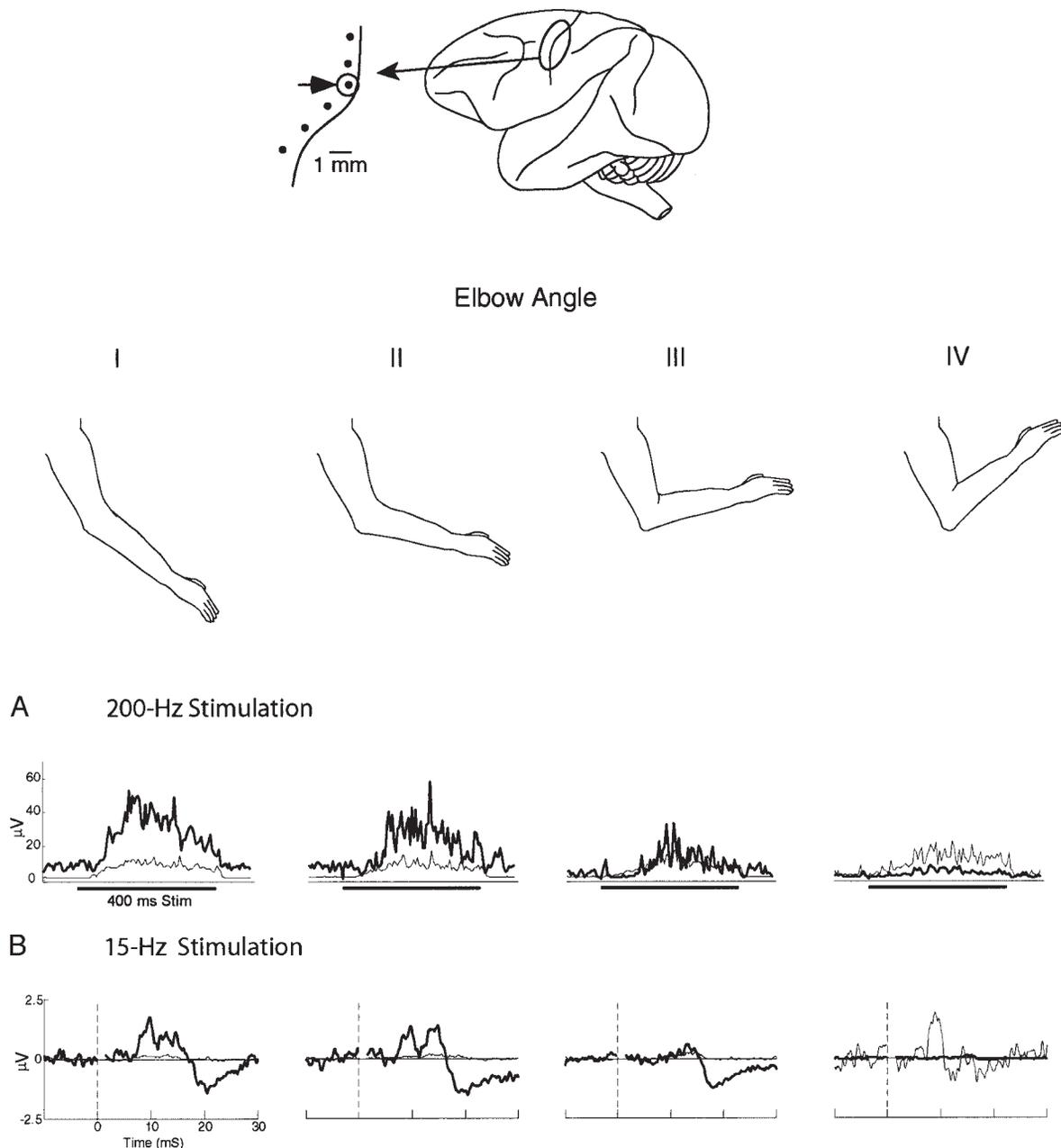


FIG. 3. EMG activity evoked by stimulation of another example site in primary motor cortex. Location of site shown in brain drawing (top). See legend to Fig. 1 for details. *A*: for 200-Hz stimulation, activity in both muscles was significantly affected by joint angle (triceps, $F = 2.96$, $P = 0.039$; biceps, $F = 27.71$, $P < 0.001$). *B*: for 15-Hz stimulation, activity in both muscles was significantly affected by joint angle (triceps, $F = 113.25$, $P < 0.001$; biceps, $F = 178.15$, $t < 0.001$).

similar for both 200-Hz stimulation (Fig. 7A) and 15-Hz stimulation (Fig. 7B).

Figure 8 shows the mean result for 13 sites in the middle portion of the studied area. For this group of sites, stimulation evoked more biceps than triceps activity when the arm was in an extended posture (position I), and more triceps than biceps activity when the arm was in a flexed posture (position IV). This pattern was similar for both 200- and 15-Hz stimulation, but not identical. The elbow angle at which the biceps and triceps activity crossed was different in the two cases.

Figure 9 shows the mean result for 10 sites in the ventral portion of the studied area. For this group of sites, stimulation evoked more biceps than triceps activity, and this

discrepancy was greatest for position I, the most extended position tested. This pattern was similar for both 200- and 15-Hz stimulation.

DISCUSSION

The present experiment used electrical stimulation to examine the mapping between points in cortex and the biceps and triceps muscles. The findings suggest that this mapping can change depending on joint angle. For cortical sites in the dorsal part of the arm and hand representation, stimulation evoked greater triceps activity, consistent with initiating a movement to an extended angle. The amount by which the evoked triceps activity exceeded

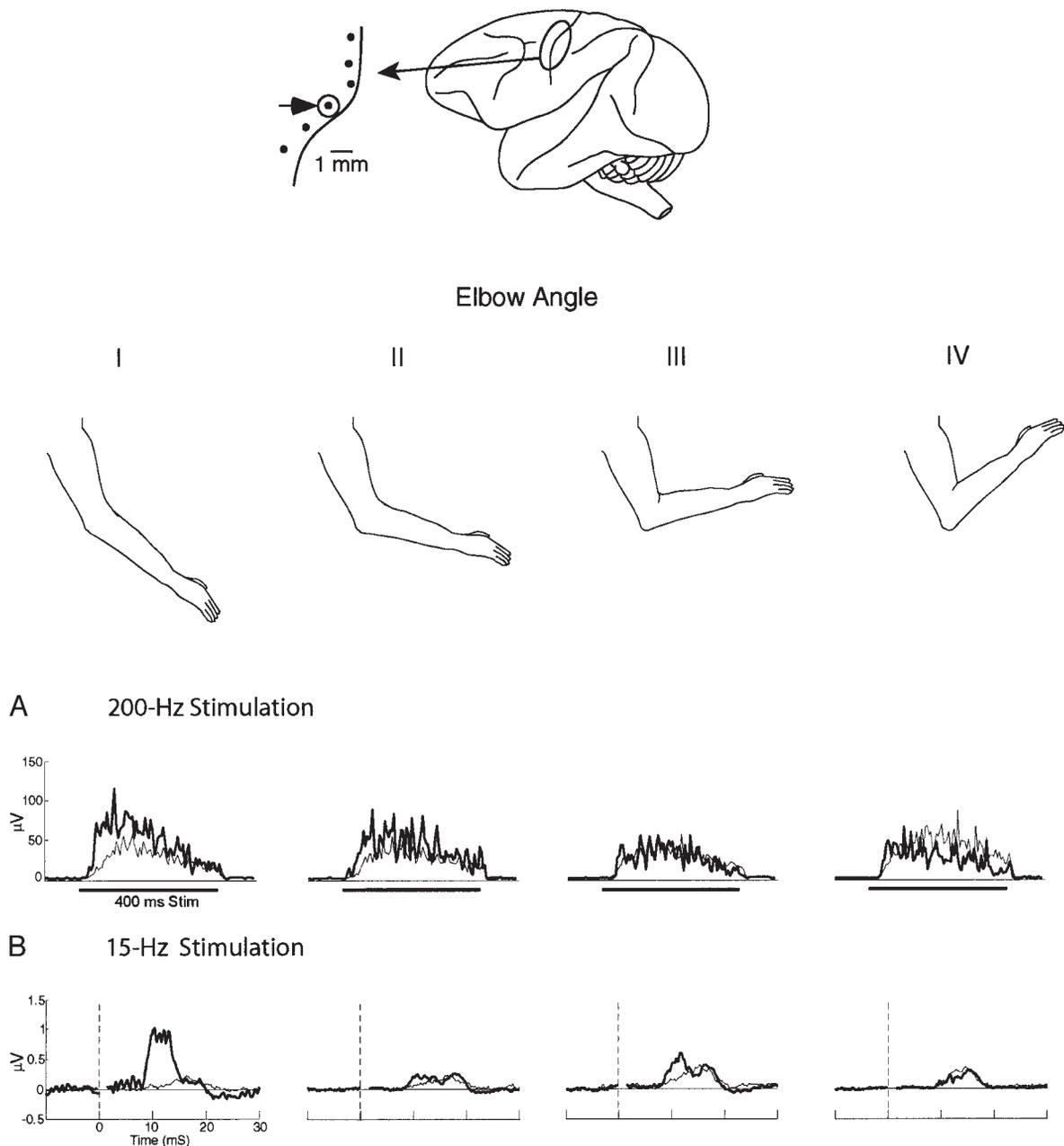


FIG. 4. EMG activity evoked by stimulation of another example site in primary motor cortex. Location of site shown in brain drawing (top). See legend to Fig. 1 for details. *A*: for 200-Hz stimulation, activity in both muscles was significantly affected by joint angle (triceps, $F = 7.40$, $P < 0.001$; biceps, $F = 23.23$, $P < 0.001$). *B*: for 15-Hz stimulation, activity in both muscles was significantly affected by joint angle (triceps, $F = 31.08$, $P < 0.001$; biceps, $F = 110.21$, $P < 0.001$).

the evoked biceps activity depended on elbow angle. When the elbow was fixed in a flexed angle, the discrepancy between the evoked triceps and biceps activity was greatest.

For cortical sites in the ventral part of the arm and hand representation, the opposite result was obtained. Stimulation evoked greater biceps activity than triceps activity, consistent with initiating a movement to a flexed angle. When the elbow was fixed in an extended angle, the discrepancy between the evoked biceps and triceps activity was greatest.

For intermediate cortical sites, the stimulation-evoked activity was not consistently greater in the biceps or triceps; instead, it shifted relatively toward the biceps or triceps depending on elbow angle. When the elbow was fixed in an extended angle,

the evoked activity was typically greater in the biceps. When the elbow was fixed in a flexed angle, the evoked activity was typically greater in the triceps.

These patterns were observed when we averaged the effects of 400-ms long, 200-Hz stimulation trains. They were also observed when we averaged the effects of individual pulses presented at 15 Hz. However, although the same general patterns were observed, the two types of stimulation were not the same in their details. In the case of 15-Hz stimulation, both inhibitory and excitatory effects were observed. Often an excitatory phase of the response was followed by an inhibitory phase. In the case of the 200-Hz stimulation trains, only excitatory effects were ob-

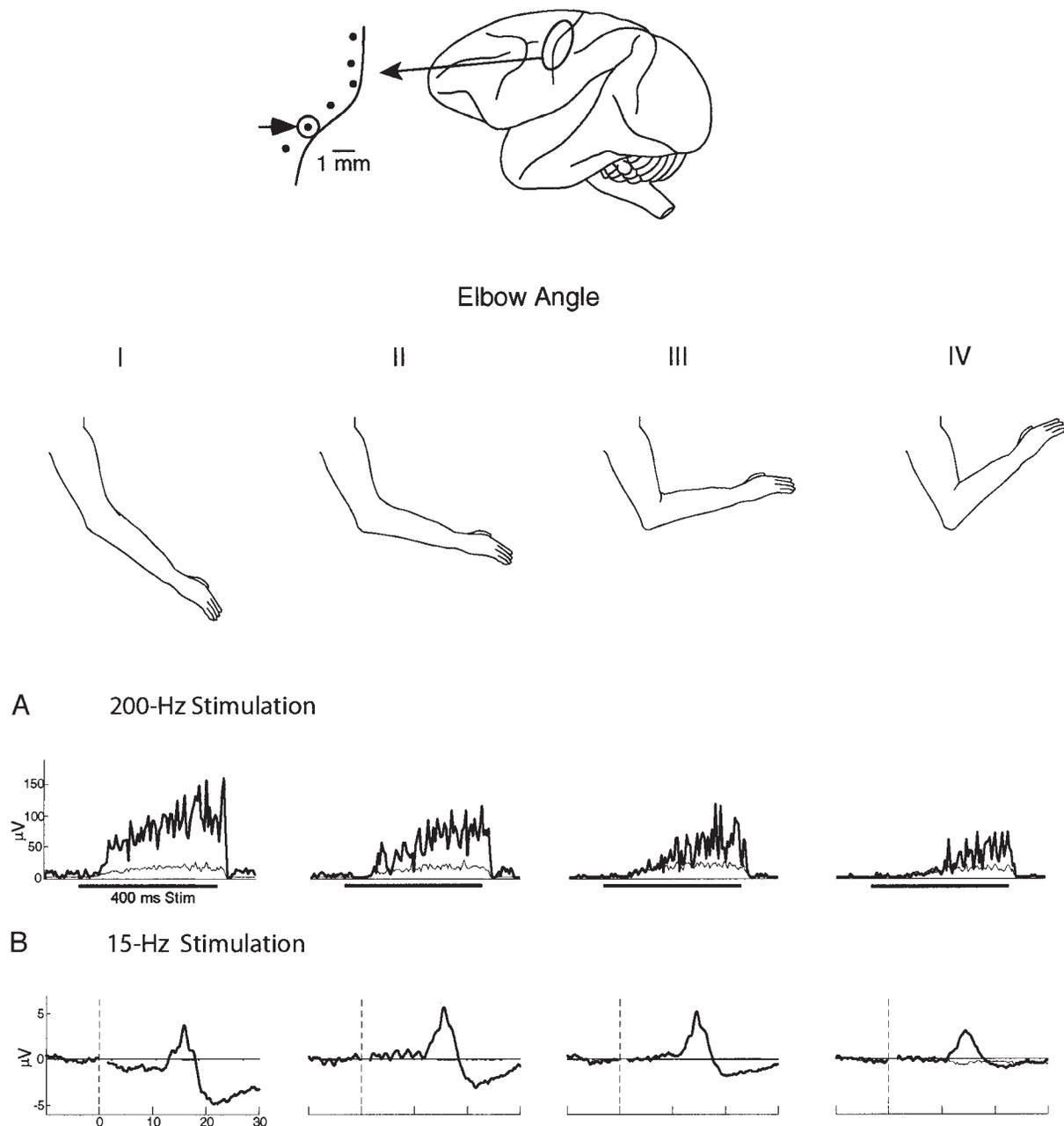


FIG. 5. EMG activity evoked by stimulation of another example site in primary motor cortex. Location of site shown in brain drawing (top). See legend to Fig. 1 for details. *A*: for 200-Hz stimulation, activity in both muscles was significantly affected by joint angle (triceps, $F = 4.0$, $P = 0.011$; biceps, $F = 38.79$, $P < 0.001$). *B*: for 15-Hz stimulation, activity in both muscles was significantly affected by joint angle (triceps, $F = 94.93$, $P < 0.001$; biceps, $F = 46.28$, $P < 0.001$).

served. One possibility is that the 200-Hz stimulation trains resulted in greater signal spread, recruiting more neurons. Because excitatory effects were more common than inhibitory effects, an averaging of effects over a greater pool of tissue might have resulted in an overall preponderance of excitation. It should also be noted that in the present experiment, the arm was relaxed and held passively, thus the baseline level of muscle activity was small. It is possible that in conditions of active movement, with a greater baseline level of muscle activity, more stimulation-evoked inhibitory effects might have been observed.

In the case of the 15-Hz stimulation, the observed effects occurred with a latency as short as 7 ms. This timing suggests

that these shortest-latency effects may have depended on relatively direct pathways and on spinal circuitry. In this hypothesis, proprioceptive signals about muscle stretch and elbow joint angle may have modulated the spinal circuitry in such a way as to alter the strength of the descending connections from cortex to muscles.

Comparison to specific previous stimulation studies

The present results are consistent with previous studies showing that a change in joint angle will change the manner in which cortical stimulation affects muscle activity (e.g., Armstrong and Drew 1985; Lemon et al. 1995; Rho et al. 1999;

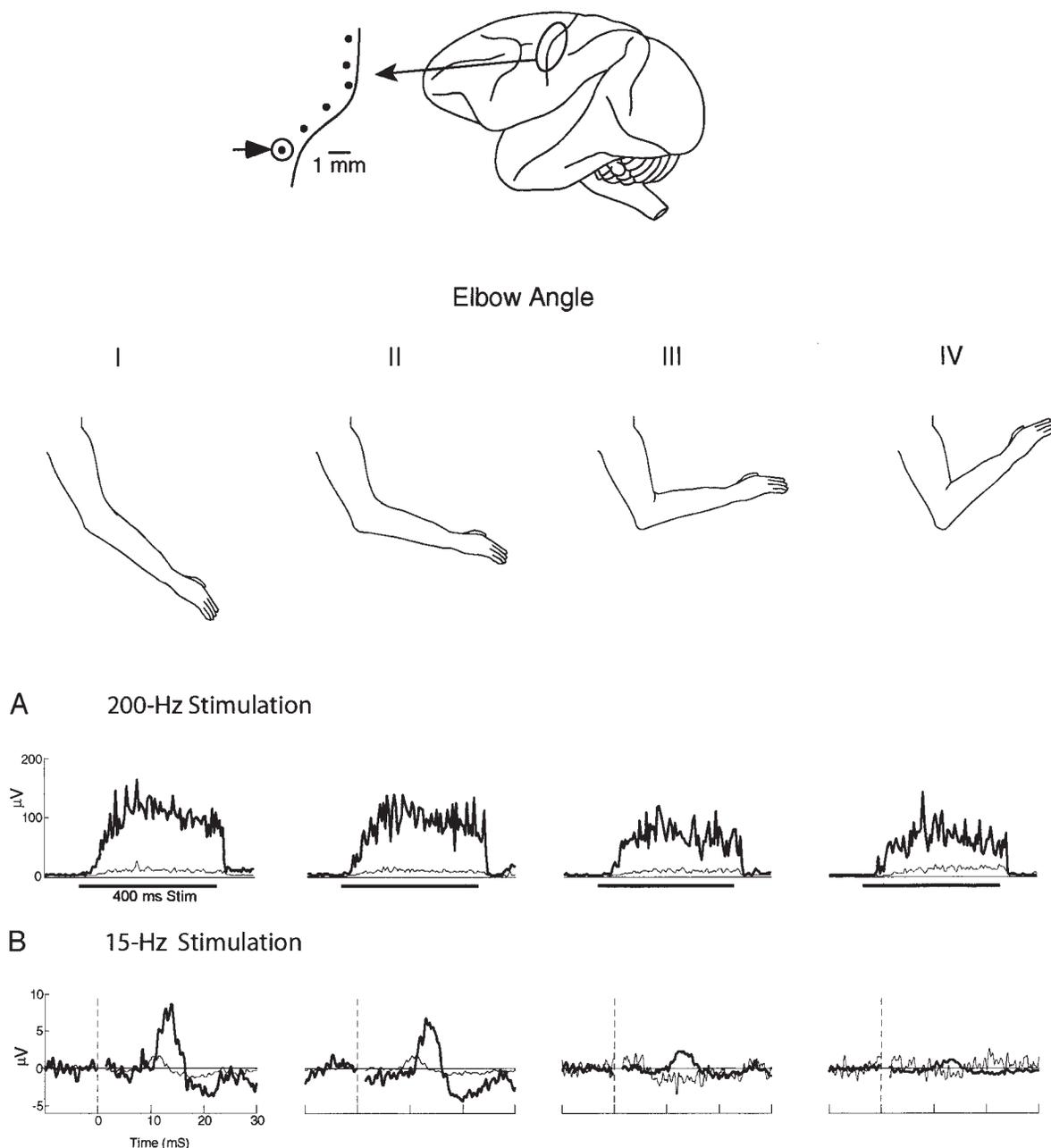


FIG. 6. EMG activity evoked by stimulation of another example site in primary motor cortex. Location of site shown in brain drawing (top). See legend to Fig. 1 for details. A: for 200-Hz stimulation, activity in biceps but not in triceps was significantly affected by joint angle (triceps, $F = 1.03$, $P = 0.388$; biceps, $F = 4.91$, $P = 0.005$). B: for 15-Hz stimulation, activity in both muscles was significantly affected by joint angle (triceps, $F = 65.51$, $P < 0.001$; biceps, $F = 25.86$, $P < 0.001$).

Sanes et al. 1992). For example, one previous study of the rat motor cortex (Sanes et al. 1992) used electrical stimulation to map the muscles of the foreleg. Changing the posture of the foreleg altered the size of the cortical representation of the foreleg muscles. Another study used electrical stimulation in cat motor cortex while the cat was engaged in stepping movements (Armstrong and Drew 1985). The stimulation affected the muscles of the foreleg in a manner that changed when the limb was in different phases of the step cycle. A third study showed that transcranial magnetic brain stimulation in human motor cortex affected the muscles of the forelimb in a manner that was modulated by the posture of the forelimb (Lemon et al. 1995). In these previous studies, as in the present study,

limb posture appeared to influence the mapping from cortex to muscles.

The present results are also consistent with the findings of Park et al. (2001) who used 15-Hz stimulation to study the representation of forelimb muscles in the motor cortex of monkeys. They found that the biceps were generally more represented in ventral sites, and the triceps were generally more represented in dorsal sites. This previous study, however, did not investigate the effect of elbow angle. In the present study, each cortical site did not appear to have a fixed mapping to the biceps and triceps; the mapping could shift relatively toward the biceps or triceps depending on proprioceptive feedback about elbow angle.

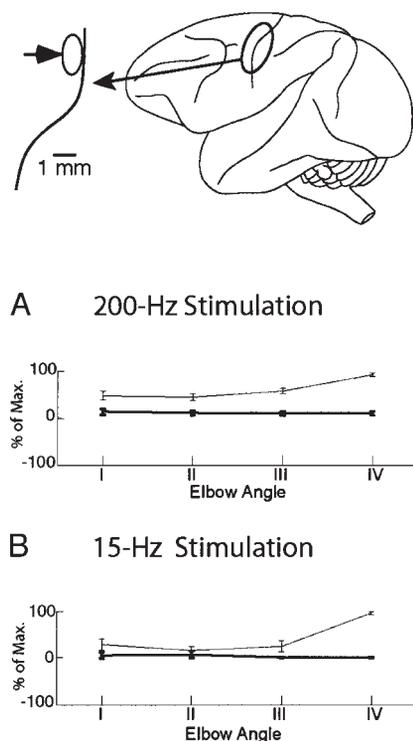


FIG. 7. Mean EMG activity evoked by stimulation of 12 sites in the dorsal portion of the arm and hand representation. Location of these sites is shown in the brain drawing (top). A: mean EMG evoked by 200-Hz stimulation as a function of elbow angle. Thick line shows biceps activity, thin line shows triceps activity. For each site, activity in the 8 conditions was normalized to the maximum of the 8 conditions. All 12 sites were then averaged together. y axis is therefore plotted in percent of maximum. Error bars are SE. B: mean EMG evoked by 15-Hz stimulation as a function of elbow angle.

Map of postures?

On the basis of our previous electrical stimulation studies (Graziano et al. 2002a,b), we proposed that activity at a site in motor cortex acts as a higher-order signal, instructing the limb to move to a certain posture regardless of the initial posture. The view of a postural control of movement was suggested previously in many different versions based on computational modeling, behavioral work in humans and monkeys, and stimulation studies in the spinal cord of the frog and rat (e.g., Bizzi et al. 1984; Feldman et al. 1998; Giszter et al. 1993; Rosenbaum et al. 1995; Tresch and Bizzi 1999). We suggest that the results of the present experiment may reflect a map of desired postures encoded in motor cortex. Our interpretation, however, remains a hypothesis. In the following sections we consider two central questions that remain to be answered. The first question is whether the patterns of muscle activity that occur during the stimulation-evoked movements are similar to the patterns that occur during voluntary movement. The second question is whether the stimulation-evoked movements match the responses of single neurons recorded during voluntary movements.

Muscle activity during stimulation-evoked movement

In the present experiment, we measured muscle activity while the arm was fixed. During isometric conditions, when a steady force is applied by the limb but the limb is restrained

from moving, the agonist and antagonist muscles can be co-active to some degree, but the agonist muscle shows greater activation (e.g., Hebert et al. 1991; Kubo 2004). The activation reaches a plateau during the steady application of the force. This pattern is similar to that found in the present study.

To compare the stimulation-evoked movements to normal movements, however, would require stimulating while the arm is free to move and measuring muscle activity during the evoked movement. This experiment has not been completed. In preliminary tests (Taylor et al. 2002, 2003), we found that in at least some ways the EMG patterns obtained during stimulation-evoked movements were similar to those typical of voluntary movement (e.g., Cooke and Brown 1990; Hallett et al. 1975; Morrison and Anson 1999). We found a variety of stimulation-evoked EMG patterns including initial activation of agonist and suppression of antagonist muscles, biphasic and triphasic patterns during the movement, and tonic co-contraction when the arm had reached its final posture and had stiffened to maintain the posture. We obtained similar patterns during the monkey's voluntary movement. However, these experiments are ongoing, and the degree of similarity between stimulation-evoked and voluntary movement is not yet clear. Although the stimulation-evoked movements appear to resemble voluntary movements in at least some ways, they are unlikely to be identical given that electrical stimulation is fundamentally artificial.

Single-neuron properties

In most brain areas where electrical stimulation has been tested, the effects evoked by stimulation match the single

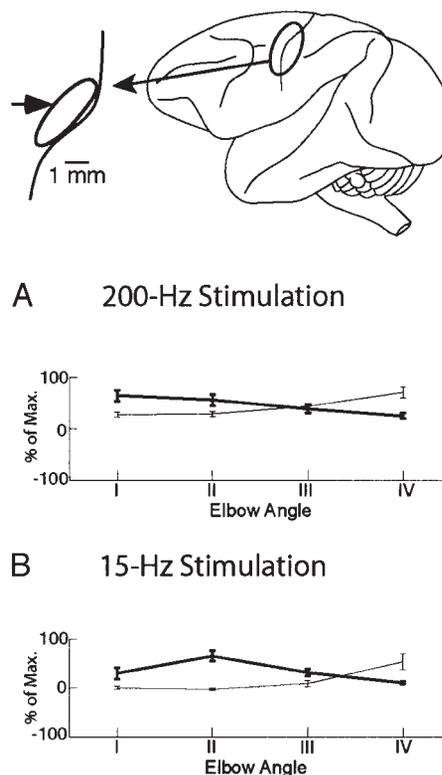


FIG. 8. Mean EMG activity evoked by stimulation of 13 sites in the middle portion of the arm and hand representation. A: mean EMG evoked by 200-Hz stimulation as a function of elbow angle. B: mean EMG evoked by 15-Hz stimulation as a function of elbow angle.

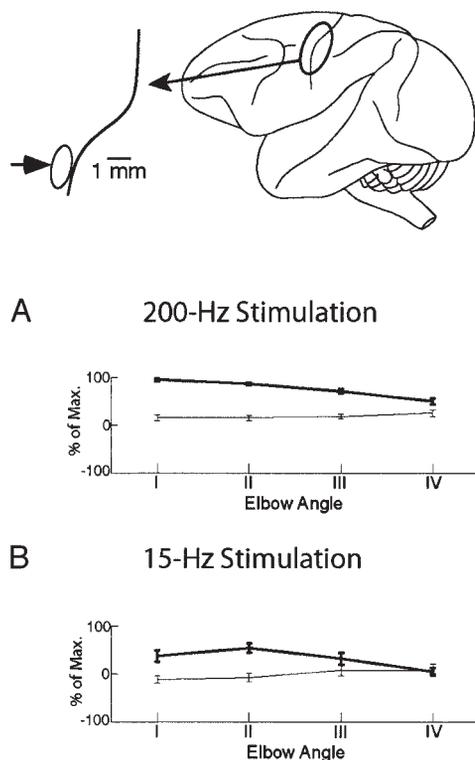


FIG. 9. Mean EMG activity evoked by stimulation of 10 sites in the ventral portion of the arm and hand representation. *A*: mean EMG evoked by 200-Hz stimulation as a function of elbow angle. *B*: mean EMG evoked by 15-Hz stimulation as a function of elbow angle.

neuron properties in some understandable way (e.g., Bruce et al., 1985; Gottlieb et al., 1993; Robinson 1972; Saltzman et al., 1990; Schiller and Stryker 1972). An important question, therefore is how the map of stimulation-evoked postures that we obtained in motor cortex can be related to the single neuron properties. As discussed in this section, the answer to this question is not clear and more experiments will be needed, especially experiments that examine the relationship between neuronal activity and arm posture.

Georgopoulos and colleagues (1986) trained monkeys to reach in various directions from a central starting position and found that neurons in motor cortex were broadly tuned to the direction of reach. Were the neurons tuned specifically to the directional vector of reach or to a spatial location toward which the hand was moving? Because these experiments involved relatively small (~ 10 cm) movements away from a central position, the results may be consistent with both possibilities. Although different initial positions of the hand were tested in some of these experiments, the tests were limited and a full directional tuning curve was not obtained for every initial hand position.

Caminiti et al. (1990) tested motor cortex neurons in a paradigm in which the initial position of the hand was varied over a greater spatial range and the directional tuning of the neurons was systematically tested for each initial position. They found that when the initial position of the hand was changed, the preferred direction of reach rotated in a direction and by an amount that was highly variable from neuron to neuron. In their description, the preferred direction vector was "different in magnitude, orientation, and sometimes even in sign for different cells." Despite the wide distribution among

individual cells, when a mean across cells was computed, the average preferred direction of reach rotated in the same direction as the shoulder and by ~ 60 – 75% of the amount by which the shoulder rotated. One interpretation of these results is that on average, motor cortex neurons are tuned to the direction of reach, and this preferred direction is roughly anchored with respect to the shoulder. However, individual neurons behaved in a variety of ways and this shoulder-centered directional tuning is not a property of every neuron.

More recently, Sergio and Kalaska (2003) recorded from neurons while the monkey applied force in various horizontal directions to a manipulandum under isometric conditions. Each cell was broadly tuned to the direction of applied force. When the manipulandum was placed in different locations in a horizontal plane, the preferred direction of the cells changed. The preferred directions did not change in a manner consistent with the cells coding force aimed toward a final position in space. This result appears to be a clear negative for cells coding an end position of the hand, at least within the constraints of the task.

The studies of Caminiti et al. (1990) and of Sergio and Kalaska (2003) provide a test of the hypothesis of endpoint coding or coding of the final position of the hand in space. It is important to note that endpoint coding is not the same as end-posture coding. This difference arises because of the many degrees of freedom of the arm. Consider a specific posture of the arm in which the hand is located in central space, the shoulder, elbow, and wrist are at particular angles, and the forearm is pronated to a specific degree. It is possible for the hand to move toward central space in Cartesian coordinates, while at the same time, in joint coordinates, the arm moves away from that final posture. Likewise, it is possible for the hand to move away from central space in Cartesian coordinates while the arm moves relatively toward that final posture. To understand how the single neuron properties in motor cortex might relate to the stimulation-evoked map of postures, it will be useful to measure the configuration of the arm in joint space during free, three-dimensional movements and to simultaneously record from motor cortex neurons. In this fashion, the posture of the arm can be tracked and related to neuronal activity. We propose the following two main hypotheses.

First, each electrically evoked posture might be the result of the co-activation of different neurons with diverse properties. In this hypothesis, the neurons affected by the stimulation might be tuned to parameters such as hand direction, velocity, joint rotation, or muscle force (e.g., Evarts 1968; Georgopoulos et al. 1986, 1992; Kakei et al. 1999; Kalaska et al., 1989; Reina et al. 2001; Scott and Kalaska 1995, 1997). The summed action of these neurons might lead to a movement that balances at an intermediate posture. In this case, individual neurons studied at a site in cortex would not show tuning to the posture obtained on stimulation. Instead, the obtained posture would be a result of the average properties of the local population of neurons, and this average would vary across cortex to result in an apparent map of stimulation-evoked effects.

Second, each individual neuron might be tuned to movement toward a specific posture. In this hypothesis, the neurons would become active as the arm approached or reached a specific joint configuration, and electrical stimulation of the site would evoke the same joint configuration. If this hypothesis is correct—if there is postural coding in motor cortex—it is impor-

tant to consider that the degree of tuning may depend on the part of motor cortex under study. In our stimulation study, the precision with which the arm reached its final posture varied among stimulation sites. For example, when stimulation evoked a hand-to-mouth movement, the final posture was highly repeatable and the hand moved to the mouth with an accuracy of a few centimeters. When stimulation evoked a movement of the hand to the area of central space in front of the chest, the final posture was more variable and the terminal position of the hand ranged among trials within an area as broad as 10 cm. Thus the degree and nature of the postural tuning might depend on the recording site.

We are currently investigating these hypotheses by recording the multi-joint posture of the arm and, simultaneously, the activity of single neurons in motor cortex. In this fashion we hope to understand the reasons behind the systematic effects of electrical stimulation in motor cortex.

ACKNOWLEDGMENTS

We thank C. Gross, D. Cooke, T. Mole, and M. Muscat for invaluable help.

GRANTS

This work was supported by Burroughs Wellcome Grant 992817 and National Eye Institute Grant EY-11347.

REFERENCES

- Armstrong DM and Drew T.** Forelimb electromyographic responses to motor cortex stimulation during locomotion in the cat. *J Physiol* 367: 327–351, 1985.
- Bizzi E, Accornero N, Chapple W, and Hogan N.** Posture control and trajectory formation during arm movement. *J Neurosci* 4: 2738–2744, 1984.
- Bruce CJ, Goldberg ME, Bushnell MC, and Stanton GB.** Primate frontal eye fields. II. Physiological and anatomical correlates of electrically evoked eye movements. *J Neurophysiol* 54: 714–734, 1985.
- Caminiti R, Johnson PB, and Urbano A.** Making arm movements within different parts of space: dynamic aspects in the primate motor cortex. *J Neurosci* 10: 2039–2058, 1990.
- Cheney PD, Fetz EE, and Palmer SS.** Patterns of facilitation and suppression of antagonist forelimb muscles from motor cortex sites in the awake monkey. *J Neurophysiol* 53: 805–820, 1985.
- Cooke JD and Brown SH.** Movement-related phasic muscle activation. II. Generation and functional role of the triphasic pattern. *J Neurophysiol* 63: 465–472, 1990.
- Cooke DF and Graziano MSA.** Sensorimotor integration in the precentral gyrus: polysensory neurons and defensive movements. *J Neurophysiol* 91: 1648–1660, 2004.
- Evarts EV.** Relation of pyramidal tract activity to force exerted during voluntary movement. *J Neurophysiol* 31: 14–27, 1968.
- Feldman AG, Ostry DJ, Levin MF, Gribble PL, and Mitnitski AB.** Recent tests of the equilibrium-point hypothesis (λ model). *Motor Control* 2: 189–205, 1998.
- Freedman EG, Stanford TR, and Sparks DL.** Combined eye-head gaze shifts produced by electrical stimulation of the superior colliculus in rhesus monkeys. *J Neurophysiol* 76: 927–952, 1996.
- Georgopoulos AP, Ashe J, Smyrnis N, and Taira M.** The motor cortex and the coding of force. *Science* 256: 1692–1695, 1992.
- Georgopoulos AP, Schwartz AB, and Kettner RE.** Neuronal population coding of movement direction. *Science* 233: 1416–1419, 1986.
- Giszter SF, Mussa-Ivaldi FA, and Bizzi E.** Convergent force fields organized in the frog's spinal cord. *J Neurosci* 13: 467–491, 1993.
- Gottlieb JP, Bruce CJ, and MacAvoy MG.** Smooth eye movements elicited by microstimulation in the primate frontal eye field. *J Neurophysiol* 69: 786–799, 1993.
- Graziano MSA, Cooke DF, Taylor CSR, and Moore T.** Distribution of hand location in monkeys during spontaneous behavior. *Exp Brain Res* 155: 30–36, 2004.
- Graziano MSA, Taylor CSR, and Moore T.** Complex movements evoked by microstimulation of precentral cortex. *Neuron* 34: 841–851, 2002a.
- Graziano MSA, Taylor CSR, Moore T, and Cooke DF.** The cortical control of movement revisited. *Neuron* 36: 349–362, 2002b.
- Hallett M, Shahani BT, and Young RR.** EMG analysis of stereotyped voluntary movements in man. *J Neurol Neurosurg Psychiatry* 38: 1154–1162, 1975.
- Hebert LJ, De Serres SJ, and Arsenault AB.** Cocontraction of the elbow muscles during combined tasks of pronation-flexion and supination-flexion. *Electromyogr Clin Neurophysiol* 31: 483–488, 1991.
- Kekei S, Hoffman D, and Strick P.** Muscle and movement representations in the primary motor cortex. *Science* 285: 2136–2139, 1999.
- Kalaska JF, Cohen DA, Hyde ML, and Prud'homme MA.** Comparison of movement direction-related versus load direction-related activity in primate motor cortex, using a two-dimensional reaching task. *J Neurosci* 9: 2080–2102, 1989.
- Kubo K, Tsunoda N, Kanehisa H, and Fukunaga T.** Activation of agonist and antagonist muscles at different joint angles during maximal isometric efforts. *Eur J Appl Physiol* 91: 349–352, 2004.
- Lemon RN, Johansson RS, and Westling G.** Corticospinal control during reach, grasp, and precision lift in man. *J Neurosci* 15: 6145–6156, 1995.
- Morrison S and Anson JG.** Natural goal directed movements and the triphasic EMG. *Motor Control* 3: 346–371, 1999.
- Park MC, Belhaj-Saif A, Gordon M, and Cheney PD.** Consistent features in the forelimb representation of primary motor cortex in rhesus macaques. *J Neurosci* 21: 2784–2792, 2001.
- Reina GA, Moran DW, and Schwartz AB.** On the relationship between joint angular velocity and motor cortical discharge during reaching. *J Neurophysiol* 85: 2576–2589, 2001.
- Rho MJ, Lavoie S, and Drew T.** Effects of red nucleus microstimulation on the locomotor pattern and timing in the intact cat: a comparison with the motor cortex. *J Neurophysiol* 81: 2297–2315, 1999.
- Robinson DA.** Eye movements evoked by collicular stimulation in the alert monkey. *Vision Res* 12: 1795–1808, 1972.
- Rosenbaum DA, Loukopoulos LD, Meulenbroek RG, Vaughan J, and Engelbrecht SE.** Planning reaches by evaluating stored postures. *Psychol Rev* 102: 28–67, 1995.
- Salzman CD, Britten KH, and Newsome WT.** Cortical microstimulation influences perceptual judgements of motion direction. *Nature* 346: 174–177, 1990.
- Sanes JN, Wang J, and Donoghue JP.** Immediate and delayed changes of rat cortical output representation with new forelimb configurations. *Cereb Cortex* 2: 141–152, 1992.
- Schiller PH and Stryker M.** Single-unit recording and stimulation in superior colliculus of the alert rhesus monkey. *J Neurophysiol* 35: 915–924, 1972.
- Scott SH and Kalaska JF.** Changes in motor cortex activity during reaching movements with similar hand paths but different arm postures. *J Neurophysiol* 73: 2563–2567, 1995.
- Scott SH and Kalaska JF.** Reaching movements with similar hand paths but different arm orientations. I. Activity of individual cells in motor cortex. *J Neurophysiol* 77: 826–852, 1997.
- Sergio LE and Kalaska JF.** Systematic changes in motor cortex cell activity with arm posture during directional isometric force generation. *J Neurophysiol* 89: 212–228, 2003.
- Strick PL.** Stimulating research on motor cortex. *Nat Neurosci* 5: 714–715, 2002.
- Taylor CSR, Cooke DF, and Graziano MSA.** Complex mapping from precentral cortex to muscles. *Soc Neurosci Abstr* 28, 2002.
- Taylor CSR, Cooke DF, and Graziano MSA.** The EMG signature of complex movement is evoked within 20 ms by microstimulation of motor cortex. *Soc Neurosci Abstr* 29, 2003.
- Tehovnik EJ and Lee K.** The dorsomedial frontal cortex of the rhesus monkey: topographic representation of saccades evoked by electrical stimulation. *Exp Brain Res* 96: 430–442, 1993.
- Tresch MC and Bizzi E.** Responses to spinal microstimulation in the chronically spinalized rat and their relationship to spinal systems activated by low threshold cutaneous stimulation. *Exp Brain Res* 129: 401–416, 1999.