Characterization of Torque-Related Activity in Primary Motor Cortex During a Multijoint Postural Task

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Herter TM, Kurtzer I, Cabel DW, Haunts KA, Scott SH. Characterization of torque-related activity in primary motor cortex during a multijoint postural task. J Neurophysiol 97: 2887–2899, 2007. First published January 31, 2007; doi:10.1152/jn.00757.2006. The present study examined neural activity in the shoulder/elbow region of primary motor cortex (M1) during a whole-limb postural task. By selectively imposing torques at the shoulder, elbow, or both joints we addressed how neurons represent changes in torque at a single joint, multiple joints, and their interrelation. We observed that similar proportions of neurons reflected changes in torque at the shoulder, elbow, and both joints and these neurons were highly intermingled across the cortical surface. Most torque-related neurons were reciprocally excited and inhibited (relative to their unloaded baseline activity) by opposing flexor and extensor torques at a single joint. Although coexcitation/coinhibition was occasionally observed at a single joint, it was rarely observed at both joints. A second analysis assessed the relationship between single-joint and multijoint activity. In contrast to our previous observations, we found that neither linear nor vector summation of single-joint activities could capture the breadth of neural responses to multijoint torques. Finally, we studied the neurons’ directional tuning across all the torque conditions, i.e., in joint-torque space. Our population of M1 neurons exhibited a strong bimodal distribution of preferred-torque directions (PTDs) that was biased toward shoulder-extensor/elbow-flexor (whole-limb flexor) and shoulder-flexor/elbow-extensor (whole-limb extensor) torques. Notably, we recently observed a similar bimodal distribution of PTDs in a sample of proximal arm muscles. This observation illustrates the intimate relationship between M1 and the motor periphery.

INTRODUCTION

It is known that primary motor cortex (M1) is an important region for executing volitional motor tasks (Hepp-Reymond 1988; Porter and Lemon 1993), although its specific role remains an area of active investigation. One key issue that remains unresolved is what portion of the motor periphery is reflected in the activity of individual neurons (Scott 2000). Specifically, is neural activity related to relatively localized motor patterns at a single joint or distributed motor patterns across multiple joints?

A number of complementary approaches have provided insight into this issue. One set of approaches examined relationships between the neural and muscle activity. Spike-triggered averaging techniques demonstrated that some M1 neurons (corticomotoneurons) synapse directly onto pools of motoneurons that innervate one or more muscles acting at multiple joints of the limb (Buys et al. 1986; Fetz and Cheney 1980; McKiernan et al. 1998). However, corticomotoneurons are relatively rare and spike-triggered averaging examines patterns of connectivity with muscles but does not inherently address whether the activity of individual neurons reflects a similar, more focal, or broader representation of the motor periphery. Another approach relates the pattern of neural activity to the pattern of muscle activity during behavior. Several previous studies showed that neural activity correlates with the activity of individual or groups of muscles acting at a single joint or across multiple joints (Bennett and Lemon 1996; Holdefer and Miller 2002) and reflect details on the timing and magnitude of muscle activity (Drew 1993; Scott 1997; Smith et al. 1975).

A second set of approaches related neural activity to kinesthesiological parameters such as joint motion, joint torque, or forces applied to the limb. Because the motor system contains many more muscles than mechanical degrees of freedom (df), such kinesthesiological parameters provide a simpler parameter space to examine the relationship between M1 activity and the motor periphery. By design, single-joint studies describe how neural activity correlates with motor patterns at a single joint (Cheney and Fetz 1980; Crutcher and Alexander 1990; Evarts 1968, 1969; Evarts et al. 1983; Fromm 1983; Kakei et al. 1999; Thach 1978), but cannot address how neural activity reflects motor patterns at multiple joints. Furthermore, most studies of volitional whole-arm control correlated neural activity to hand-based parameters (e.g., Caminiti et al. 1990; Georgopoulos et al. 1982, 1992; Kalaska et al. 1989; Moran and Schwartz 1999; Scott and Kalaska 1997; Sergio and Kalaska 2003) and thus they were not designed to identify whether neural activity is related to the shoulder, elbow, or both joints.

Perhaps the most extensive analysis of neural activity related to motor patterns at different joints was conducted by Schieber and colleagues, who studied neural activity related to individual finger movements (Poliakov and Schieber 1999; Schieber and Hibbard 1993). They found that individual neurons were generally related to independent movements of more than one digit, suggesting that neurons may reflect a substantive portion of the motor periphery, at least for the hand. However, the activity of intrinsic and extrinsic finger muscles was often modulated by movements of unspanned digits (Schieber 1995); thus neural processing could reflect motion of many digits/joints or motor patterns of a small, select group of muscles.

We introduced a planar, whole-limb paradigm that uses robotic technology to both monitor and perturb the mechanics of the shoulder and elbow joints independently (Scott 1999).
Compared with the complex musculoskeletal organization of the hand, this whole-limb paradigm is relatively simple because most proximal arm muscles are monoarticular (spanning only the shoulder or elbow) with only four biarticular muscles representing about 19% of the total physiological cross-sectional area of all shoulder and elbow muscles (Cheng and Scott 2000). The objective of this whole-limb paradigm is to facilitate exploring linkages between behavior, limb mechanics, muscle activity, and neural processing.

The present study examined how neural activity in M1 reflects torques applied to the shoulder, elbow, or both joints during a whole-limb postural task. This behavioral task permitted us to examine torque-related activity, commonly recorded in previous single-joint studies, at two mechanical df spanning two joints. We directly compared neural responses to single-joint torques applied to each joint separately and show that most M1 neurons respond reciprocally to opposing torques at one or both joints. Furthermore, nearly all neurons that are coactivated or coinhibited by opposing torques at one joint nevertheless exhibit unimodal directional tuning.

A second value of this paradigm was revealed in our parallel study of EMG activity recorded from proximal arm muscles during this postural task (Kurtzer et al. 2006a). The behavioral goal of this task was to maintain the hand at a spatial target while counteracting mechanical torques applied to the shoulder and/or elbow. Across all torque conditions, this task sampled a uniform distribution of torques at the shoulder and elbow (i.e., in joint-torque space). However, the maximal activity of proximal arm muscles was biased toward either whole-limb flexor or whole-limb extensor torques, thereby creating a bimodal distribution of preferred-torque directions (PTDs) in joint-torque space. If neural processing mirrors the behavioral requirements inherent in a task, then an equal proportion of M1 neurons should have represented each joint torque in this postural task. Alternatively, if neural activity reflects the output patterns of muscles, then a greater proportion of neurons should have represented whole-limb flexor and whole-limb extensor torques in this postural task. Here we demonstrate that the maximal activity of M1 neurons exhibits the same bias toward whole-limb flexor and whole-limb extensor torques that was observed in proximal arm muscles.

The current study extends and elaborates on observations that we previously reported (Cabel et al. 2001).

METHODS

Apparatus and task

Four male rhesus monkeys (Macaca mulatta, 6 to 12 kg) were used in this study following procedures approved by the Queen’s University Animal Care Committee. They were trained to perform motor tasks with their right arm while wearing KINARM (KIN Technologies, Kingston, Canada), a robotic exoskeleton that supports the arm, permits planar shoulder and elbow motion, and can apply mechanical torques at the shoulder and/or elbow (Scott 1999). A virtual reality system presented visual targets within the limb’s movement plane while permitting the monkeys to view their entire limb.

The current task was designed to examine neural activity related to static joint torques at constant limb geometry. At the beginning of each trial a constant torque was applied at the shoulder, elbow, both, or neither joint. After a short delay a visual target (6-mm radius) was displayed near the center of the arm’s workspace (angles of about 30° at the shoulder and 90° at the elbow) where passive viscoelastic forces are relatively small (Graham et al. 2003). The monkeys were required to maintain their hand within an acceptance window (8-mm radius) centered on the visual target for 3,000 to 4,000 ms. The task incorporated nine torque conditions including four single-joint (shoulder flexion, SF; shoulder extension, SE; elbow flexion, EF; and elbow extension, EE), four multijoint (SF + EF; SF + SE, SE + EF, and SE + EE), and an unloaded baseline condition (Cabel et al. 2001; Kurtzer et al. 2005). Torques of ±0.12 Nm were applied to each joint in Monkeys A–C and torques of ±0.32 Nm were used in Monkey D because of his larger size. These torque conditions were presented in a pseudorandom block design with each block repeated five times for a total of 45 trials. A fixed magnitude of torque was always applied at each joint such that the total torque magnitude for multijoint conditions was $\sqrt{2}$ greater than single-joint conditions. This design feature was important because it permitted us to treat shoulder and elbow torques as independent factors.

Data collection

Neural data were collected using standard extracellular recording techniques following surgical implantation of a cylindrical recording chamber over the shoulder/ elbow representation of the left M1 (Scott and Kalaska 1997). Microelectrodes were advanced through M1 until neural activity was observed in response to active or passive movements of the shoulder and/or elbow. Single neurons were then isolated and neural activity was recorded from all neurons that were related to active or passive movements of the shoulder and/or elbow, but not the wrist or fingers.

Joint angles, velocities, and torques applied by the robot were recorded at 1 kHz (Monkeys A–C) or 4 kHz (Monkey D). Cartesian hand positions and tangential hand velocity were calculated from joint angles and velocities. The equations of motion for a two-joint, two df system that included the influence of the mechanical properties of the arm and robotic device were used to calculate the instantaneous torques exerted by the monkey at the shoulder and elbow joints (Cheng and Scott 2000; Scott 1999). These were used to verify that the motors were properly functioning and the monkeys were adequately maintaining static posture. Data sets were excluded from analyses if the mean torque exerted at each joint was not within ±0.02 Nm (and opposite in sign) of the commanded torque.

Data analyses

All analyses examined neural activity with respect to the joint torques that counteracted the mechanical torques applied in each condition. Specifically, we studied torque-related activity, defined as changes in neural activity during loaded conditions relative to the unloaded baseline condition. For example, $\Delta$SF refers to the change in neural activity relative to baseline when a shoulder-flexor torque was generated by the monkey to compensate for an applied shoulder-extensor torque.

Visual analysis of tangential hand velocity indicated that the hand decelerated for $\leq 1,000$ ms after entering the target’s acceptance window (Fig. 1). These movements appeared to influence neural activity because the mean and SD of neural activity also decreased during this period (Fig. 1B). All data were therefore analyzed by using their mean values obtained during the period from 1,000 to 3,000 ms after the hand entered the target’s acceptance window.

By treating shoulder and elbow torques as independent factors, we were able to use a two-way ANOVA (see Cabel et al. 2001) to coarsely identify neurons that were related to torques at the shoulder ($P < 0.01$ for main effect of shoulder) and elbow ($P < 0.01$ for main effect of elbow) in our task. All analyses were restricted to these torque-related neurons.

M1 TOPOGRAPHY. Three-dimensional reconstructions of M1 recording sites were created for Monkeys A–C. Postmortem examination of
the cortical surface was used to determine the angle of orientation of the central sulcus relative to recording chamber in each monkey. The stereotaxic coordinates of each neuron were then rotated to view the data relative to the orientation of the central sulcus. The center of mass of recorded neurons was then identified for each monkey and used to align the medial–lateral axes across monkeys. This permitted group analyses of the medial–lateral distribution of neurons related to the torques at the shoulder and/or elbow.

SINGLE-JOINT ANALYSES. These analyses uncovered important relationships between single-joint torques and torque-related activity. A series of t-tests identified neurons that were significantly modulated by their respective flexor and extensor torques, relative to the unloaded baseline condition \( P < 0.05 \). We also created three scores ranging continuously from −1 to 1.

Reciprocal–comodulation (R-C) scores were calculated for the shoulder and elbow

\[
R-C_{\text{Sh}} = \frac{\text{sign}(\Delta SF + \Delta SE) \times \min(|\Delta SF|, |\Delta SE|)}{\max(|\Delta SF|, |\Delta SE|)} \tag{1}
\]

\[
R-C_{\text{Elb}} = \frac{\text{sign}(\Delta EF + \Delta EE) \times \min(|\Delta EF|, |\Delta EE|)}{\max(|\Delta EF|, |\Delta EE|)} \tag{2}
\]

These scores identified whether neurons that responded to flexor and extensor torques exhibited reciprocal modulation (i.e., equal in magnitude and opposite in direction, R-C Score \( = -1 \)), unidirectional activity (i.e., related to flexor torque only or extensor torque only, R-C Score \( = 0 \)), or coexcitation/coinhibition (equal in magnitude and direction, R-C Score \( = 1 \)).

Flexor–extensor (F-E) scores were also calculated for the shoulder and elbow

\[
F-E_{\text{Sh}} = \frac{|\Delta SF| - |\Delta SE|}{|\Delta SF| + |\Delta SE|} \tag{3}
\]

\[
F-E_{\text{Elb}} = \frac{|\Delta EF| - |\Delta EE|}{|\Delta EF| + |\Delta EE|} \tag{4}
\]

These scores established whether torque-related activity was related to extensor torque only (F-E Score \( = -1 \)), extensor and flexor torques equally (F-E Score \( = 0 \)), or flexor torque only (F-E Score \( = 1 \)).

A shoulder–elbow (S-E) score was calculated across both joints

\[
S-E = \frac{(|\Delta SF| + |\Delta SE|) - (|\Delta EF| + |\Delta EE|)}{|\Delta SF| + |\Delta SE| + |\Delta EF| + |\Delta EE|} \tag{5}
\]

This score determined whether torque-related activity was related to the elbow only (S-E Score \( = -1 \)), both joints equally (S-E Score \( = 0 \)), or the shoulder only (S-E Score \( = 1 \)).

PREDICTING MULTIJOINT ACTIVITY. Our preliminary report based on two monkeys (Cabel et al. 2001) found that changes in neural activity related to multijoint torques could be accurately predicted by vector summation of constituent single-joint activities. We reexamined this issue in our sample of directionally tuned neurons (bootstrap statistic, \( P < 0.01 \)). Changes in activity at the shoulder (\( \Delta S \)) and elbow (\( \Delta E \)) were used to predict multijoint activity using linear (\( \Delta MJ_1 \)) and vector (\( \Delta MJ_v \)) summation models

\[
\Delta MJ_1 = \Delta S + \Delta E \tag{6}
\]

\[
\Delta MJ_v = (\Delta S^2 + \Delta E^2)^{1/2} \tag{7}
\]

DIRECTIONAL TUNING IN JOINT-TORQUE SPACE. We examined issues related to multijoint control by calculating directional tuning properties in joint-torque space. For this particular coordinate frame, neural activities related to the joint torques exerted across the shoulder and elbow joints are represented along the x and y axes, respectively. This contrasts with the mechanical torques applied by the robot across the shoulder and elbow joints, which are equal and opposite the joint torques exerted by the monkey in our static postural task. Using flexor torque as positive and extensor torque as negative, trigonometric convention yields \( SF = 0^\circ \), \( EF = 90^\circ \), \( SE = 180^\circ \), and \( EE = 270^\circ \). Directional tuning features were calculated with the plate method, which describes several features of directional tuning without assuming an underlying tuning function (Gribble and Scott 2002). This method characterized the “mass distribution” of torque-related activity by assuming that activity changes linearly between sampled torque directions and that torque magnitude is equal for each torque direction. By maintaining constant torques at the shoulder and elbow, the overall torque magnitude was greater in the multijoint conditions (see Apparatus and tasks). Multijoint activity was consequently divided by \( \sqrt{2} \) to normalize torque-related activity across all torque conditions; normalization was carried in this specific analysis with only the plate method. The lowest activity across all trials was then subtracted so that all values were \( \geq 0 \).

The location of the center of mass, or centroid, in joint-torque space was used to calculate four directional tuning features. 1) Preferred-torque direction (PTD) describes the angle associated with the greatest increase in activity in joint-torque space. This was calculated as the direction of the centroid relative to the origin in joint-torque space. Importantly, PTDs were calculated as the average of two separate PTDs, one obtained from the four single-joint conditions and the other from the four multijoint conditions (Cabel et al. 2001). Because the multijoint PTD of each neuron was identical irrespective of whether multijoint activity was normalized, the overall PTD was unaffected by normalization. 2) Ratio of inertia (Ir) conveys information analogous to tuning widths calculated with model-based functions such as the von Mises function. This was calculated as the ratio of torque-related activity perpendicular to the PTD axes versus torque-related activity along the PTD axes yielding values ranging from 0 to 1. A cosine obtains an Ir value of 0.44, whereas smaller values denote sharper tuning and larger values denote broader tuning. 3) Torque-slope expresses the change in torque-related activity per unit torque along the PTD. This was calculated by normalizing the magnitude of the centroid (Cr), defined as the radial distance between the centroid and origin, by the torque magnitude (0.12 or 0.32 Nm). 4) Excitation–inhibition score (E-I score) describes the relationship between increases in torque-related activity at the PTD and decreases in torque-related activity opposite the PTD. Torque-related activities at and
opposite the PTD (ΔPTD and ΔOPP, respectively) were obtained using linear interpolation and the E-I score was then calculated

$$E-I = \frac{\text{ΔPTD} + \text{ΔOPP}}{\text{ΔPTD} - \text{ΔOPP}}$$

E-I scores typically range from −1 to 1. Positive (negative) E-I scores occur when the magnitude of excitation at the PTD is greater (lesser) than the magnitude of inhibition opposite the PTD. Values near 0 arise when the magnitudes of excitation and inhibition are similar. E-I scores could go beyond 1 (−1) if both ΔPTD and ΔOPP exhibited excitation (inhibition).

The preceding measures were examined for those neurons with only statistically significant directional tuning as determined with a nonparametric “bootstrapping” test (Scott and Kalaska 1997). This statistic was calculated by comparing the actual value of Cr with bootstrap values of Cr obtained after the torque-related activity was randomly reassigned across all trials. A neuron was considered to have significant directional tuning if fewer than 100 of 10,000 bootstrap values of Cr were greater than the actual value of Cr (P < 0.01). This method produced results that were similar to those obtained from bootstrap methods using mean vector length (Cabel et al. 2001; Scott and Kalaska 1997) and F-tests from planar regression models (similar proportions (85, 89, and 90%) of torque-related units exhibited significant directional tuning).

Reliability of the plate method was verified by comparing its results with those obtained from planar regression models that did not require normalization of data. In brief, the mean values of neural activity and actual torques exerted at the shoulder and elbow (obtained from the equations of motion) were used to calculate planar regression models for each neuron. The shoulder and elbow coefficients from these models were used to calculate PTDs and torque-slopes for each neuron (see Kurtzer et al. 2005). Directly comparing the two methods indicated that they produced similar PTDs (mean absolute difference = 4°) and torque-slopes (r = 0.96).

**RESULTS**

**Categorization and topography**

In all, 359 M1 neurons were recorded in four monkeys (Monkeys A–D: 89, 61, 84, and 125, respectively). The activity of some neurons was modulated by torques at one joint only (Fig. 2A), whereas the activity of other neurons was modulated by torques at both joints (Fig. 2B).

For didactic purposes, we used a two-way ANOVA (see Cabel et al. 2001) to coarsely identify neurons related to torques at the shoulder (P < 0.01 for main effect of shoulder) and elbow (P < 0.01 for main effect of elbow). Within our population of 359 M1 neurons, 146 (41%) were significantly related to the shoulder (shoulder neurons) and 140 (39%) were significantly related to the elbow (elbow neurons). Many of these were classified as multijoint neurons (n = 76, 36%) because they were related to both the shoulder and elbow. Other neurons were identified as shoulder-only neurons (n = 70, 33%) or elbow-only neurons (n = 64, 30%) because they were flagged by a main effect at only one of the two joints. In total, 210 of the 359 neurons recorded in this task (58%) were flagged as torque-related neurons.

The relationship between the different categories of torque-related neurons and their anatomical location within M1 was investigated using three-dimensional reconstructions of M1 in Monkeys A–C (Fig. 3A). Across the three monkeys, neurons related to torques at the shoulder only (red circles), elbow only (green circles), both joints (blue circles), or neither joint (black circles) were largely intermingled across the cortical surface (Fig. 3, B–D). The only evidence of anatomical segregation was observed in Monkey B, where shoulder-only neurons were located medial to elbow-only (Kolmogorov–Smirnov (K-S) test, P < 0.001) and multijoint neurons (K-S test, P = 0.02). In Monkeys A and C, each category exhibited a similar distribution along the medial–lateral axes of M1 (K-S tests, P > 0.1). Furthermore, there was no evidence of anatomical segregation along the medial–lateral axes of M1 when data were grouped across all three monkeys (Fig. 3E) (K-S tests, P > 0.1).

**Neural activity associated with single-joint torques**

Of the 146 shoulder neurons, 44 (30%) were significantly modulated by flexor torque only, 30 (21%) by extensor torque...
only, and 26 (18%) by both flexor and extensor torques (t-test comparing single-joint flexor and extensor torques with unloaded baseline, $P < 0.05$). Of the 140 elbow neurons, 25 (18%) were significantly modulated by flexor torque only, 35 (25%) by extensor torque only, and 22 (16%) by both flexor and extensor torques (t-test, $P < 0.05$). The remaining 46 (32%) shoulder and 58 (41%) elbow neurons exhibited similar patterns of torque-related activity but failed to reach statistical criteria because of the weaker statistical power of the t-test ($df = 8$) compared with the ANOVA ($df = 2, 36$).

Relative to baseline activity in the unloaded condition, flexor and extensor torques at the shoulder (Fig. 4A) and elbow (Fig. 4B) were associated with increases and decreases in activity that ranged from −20 to 28 spikes/s at 0.12 Nm in Monkeys A–C and from −35 to 28 spikes/s at 0.32 Nm in Monkey D. Notably, the magnitude of changes in activity appears to be relatively independent of baseline activity, except that overall activity (with baseline) cannot drop below zero spikes/s (Fig. 4, A and B). As a result, changes in torque-related activity were broadly distributed with mean activities near zero (Fig. 4, C–F).

Figure 5 compares the changes in activity associated with flexor and extensor torques at the shoulder (A) and elbow (D). Most neurons exhibited reciprocal activity (quadrants 2 and 4) and few neurons exhibited coexcitation or coinhibition (quadrants 1 and 3, respectively) ($\chi^2$ test, $P < 0.001$). A number of neurons also exhibited unidirectional activity, as indicated by their presence near the two primary axes. Accordingly, R-C scores for shoulder and elbow neurons (Fig. 5, B and E, respectively) exhibited a significant bias toward a reciprocal pattern of activity (median shoulder R-C score = −0.26; median elbow R-C score = −0.27; Wilcoxon signed-rank test, $P < 0.001$). Comparison of changes in activity associated with flexor and extensor torques also illustrates that some neurons responded similarly to both flexor and extensor torques, whereas other neurons responded stronger to flexor or extensor torques (Fig. 5, A and D). As a result, F-E scores for shoulder and elbow neurons were broadly distributed (Fig. 5, C and F, respectively). Elbow neurons did not exhibit a preference for flexor or extensor torques (median elbow F-E score = −0.06; Wilcoxon signed-rank test, $P > 0.1$), whereas shoulder neurons were marginally more sensitive to flexor torques (median shoulder F-E score = 0.09; Wilcoxon signed-rank test, $P = 0.02$).

Figure 6A compares reciprocal changes in neural activity related to single-joint torques at the shoulder ($\Delta$S$\Phi$ − $\Delta$S$\Theta$) and elbow ($\Delta$EF − $\Delta$EE). There was a significant bias in this relationship ($\chi^2$ test, $P < 0.001$) such that disproportionately more neurons were sensitive to whole-limb flexor torque (quadrant 2; expected = 40, observed = 58) or whole-limb extensor torque (quadrant 4; expected = 67, observed = 85) compared with flexor torques at both joints (quadrant 1; expected = 54, observed = 36) or extensor torques at both joints (quadrant 3; expected = 49, observed = 31). There was also considerable overlap between neurons that were categorized as shoulder-only (red), elbow-only (green), and multijoint (blue).

S-E scores (Fig. 6B) examined whether changes in neural activity (reciprocal or coexcitation/coinhibition) were related to the shoulder (1), elbow (−1), or both joints equally (0). Most neurons were influenced by torques at both joints, although elbow-only (green), multijoint (blue), and shoulder-only (red) neurons were appropriately biased toward −1, 0, and 1, respectively. Surprisingly, a number of shoulder-only and elbow-only neurons exhibited S-E scores that were biased...
Predicting multijoint activity

Our initial report found the multijoint activity could be predicted from vector summation of constituent single-joint activities (Cabel et al. 2001). Here we reinvestigated this issue and found that neither linear nor vector summation models accurately predicted multijoint activity across our entire sample of directionally tuned neurons (Fig. 7, A and B). On average, linear summation overestimated multijoint activity (mean residual error = 2.6 spikes/s; t-test, \( P < 0.001 \)) and vector summation underestimated multijoint activity (mean residual error = \(-1.6 \) spikes/s; t-test, \( P < 0.001 \)).

To verify that single-joint neurons did not create this conflicting result, we repeated our analysis on the subset of directionally tuned neurons that were flagged as multijoint neurons by the ANOVA (\( n = 74 \)). Again, neither model accurately predicted multijoint activity across the entire subset of multijoint neurons (Fig. 7, C and D). Linear summation marginally overestimated multijoint activity (mean residual error = 1.8 spikes/s; t-test, \( P = 0.06 \)) and vector summation appreciably underestimated multijoint activity (mean residual error = \(-4.5 \) spikes/s; t-test, \( P < 0.001 \)). A series of t-tests were subsequently used to directly compare the predicted activity of linear and vector summation models with the actual multijoint activity. Of the 74 neurons, 16 (22%) were categorized as “linear summation” neurons (linear, \( P \geq 0.05 \); vector, \( P < 0.05 \)), eight (11%) were classified as “vector summation” neurons (linear, \( P < 0.05 \); vector, \( P \geq 0.05 \)), and four (5%) could not be labeled as either “linear summation” or “vector summation” neurons (linear, \( P < 0.05 \); vector, \( P < 0.05 \)). Linear and vector summation models could not be differentiated from each other in the other 46 (62%) neurons (linear, \( P \geq 0.05 \); vector, \( P \geq 0.05 \)).

Tuning properties in joint-torque space

Of the 210 torque-related neurons flagged by the ANOVA, 178 (85%) exhibited significant directional tuning in joint-torque space (plate method bootstrap statistic, \( P < 0.01 \)). The various directional tuning properties in joint-torque space (see METHODS) are illustrated with four exemplar neurons in Fig. 8. Figure 8A illustrates neuron 11531b (see also Fig. 2A), which was maximally active during torque conditions that involved shoulder-flexor torque and minimally active during torque conditions that engaged shoulder-extensor torque. The pattern of torque-related activity across all joint-torque directions gave rise to a PTD of 6°, cosine-like sensitivity to changes in joint-torque direction (\( Ir = 0.42 \) compared with 0.44 for a cosine) and a torque-slope of 129 spikes s\(^{-1}\)Nm\(^{-1}\) (\( Cr = 15.5 \) spikes/s, torque = 0.12 Nm). Furthermore, the magnitude of excitation at the PTD was similar to the magnitude of inhibition opposite the PTD (E-I score = \(-0.02 \)).

The other exemplar neurons in Fig. 8 illustrate divergent directional tuning properties. Relative to its baseline activity, Neuron 33171b (B) exhibited far greater inhibition opposite its PTD than excitation at its PTD (E-I score = \(-0.72 \)). Neuron 32441a (C) was sharply tuned (\( Ir = 0.21 \)) relative to a cosine and showed strong excitation at its PTD and weak excitation relative to baseline opposite its PTD (E-I score = 1.11). Neuron 12811a (D) was broadly tuned relative to a cosine (\( Ir = 0.82 \)) and displayed greater inhibition opposite its PTD than...
excitation at its PTD (E-I score = −0.54). Furthermore, each of these neurons was associated with a different PTD and a lower torque-slope than that of neuron 11531b.

Figure 8 also illustrates the importance of removing baseline activity before calculating Ir. Neuron 11531a (A) exemplifies a case where the minimum overall activity including baseline was near 0 spikes/s (torque direction = 180°), resulting in similar values of Ir for the overall activity (middle plot) and torque-related activity (right plot) in joint-torque space (Ir values of 0.43 and 0.42, respectively). In contrast, neurons 33171b (B) and 12811a (D) had minimum overall activities that were well above 0 spikes/s (torque direction values of 0 and 180°, respectively) resulting in broader tuning for their overall activity (Ir values of 0.72 and 0.94, respectively) compared with their torque-related activity (Ir values of 0.50 and 0.82, respectively).

A number of interesting results were observed across the entire population of directionally tuned neurons. Most notably, PTDs exhibited a significant bimodal distribution (bimodal Rayleigh test, mean vector = 0.26, P < 0.001) oriented along the axes of 141–321° (Fig. 9A). Although PTDs also exhibited a significant, albeit weaker, unimodal distribution (unimodal Rayleigh test, mean vector = 0.17, P < 0.01), the mean vector for the bimodal distribution was consistently greater for each individual monkey. Furthermore, this bimodal distribution confirms the preference for whole-limb flexor and whole-limb extensor torques that we observed when single-joint torques were compared across the shoulder and elbow (Fig. 6A).

We found that torque-slopes, Ir values, and E-I scores were all broadly distributed (Fig. 9, B, C, and D, respectively). Torque-slopes were spread over a range of 4 to 129 spikes·s⁻¹·Nm⁻¹ and a mean of 38 spikes·s⁻¹·Nm⁻¹ (Fig. 9B). Notably, torque-slopes were higher at 0.12 Nm in Monkeys A–C than at the 0.32 Nm in Monkey D (mean torque-slopes of 46 and 24 spikes·s⁻¹·Nm⁻¹, respectively; t-test, P < 0.001). This agrees with previous single-joint studies that observed smaller changes in torque-related activity at higher torque magnitudes (Evarts et al. 1983; Werner et al. 1990). Ir values were distributed over a range of 0.08 to 0.99 (Fig. 9C), but unlike torque-slopes, Monkeys A–D had similar median Ir values of 0.37, 0.44, 0.41, and 0.42, respectively. E-I scores were spread over a range of −2.5 to 2.4 (Fig. 9D) and had a significantly positive mean of 0.25 (t-test, P < 0.001), indicating that increases in torque-related activity at the PTD were significantly greater than decreases opposite the PTD.

Because values of torque-slope and Ir were broadly distributed, we speculated that neurons with PTDs near 45 and 225° may exhibit higher torque-slopes or different tuning to compensate for their diminutive numbers. However, neither torque-slopes nor tuning widths (Ir) varied significantly between
sparsely and densely populated regions of joint-torque space (Wilcoxon rank-sum tests, \( P > 0.1 \)). In fact, a negative correlation between Ir and E-I scores (\( r = -0.49; t\)-test for correlation, \( P < 0.001 \)) was the only significant relationship that we observed between the various properties of directional tuning (Fig. 9E). The presence of this relationship indicates that neurons with greater excitation than inhibition were sharply tuned at their PTD, whereas neurons with greater inhibition than excitation were sharply tuned opposite their PTD (sharp tuning opposite the PTD necessitates broad tuning at the PTD).

Because neural activity cannot decrease below zero spikes/s, we speculated that neurons with low baseline activity may account for the observation that increases in torque-related activity at the PTD were greater than decreases opposite the PTD (Fig. 9D). Accordingly, the mean E-I score of neurons with low baseline activity (<10 spikes/s) was not different from zero (mean E-I score = 0.04; \( t\)-test, \( P > 0.1 \)). As a result of the relationship between Ir and E-I scores (Fig. 9E), the mean Ir of neurons with low baseline activities was significantly sharper than a cosine (median Ir = 0.32; Wilcoxon signed-rank test, \( P < 0.001 \)), whereas the mean Ir of neurons with higher baseline activities was not different from a cosine (median Ir = 0.45; Wilcoxon signed-rank test, \( P > 0.1 \)).

**Discussion**

A major goal of this study was to examine what portion of the motor periphery is reflected in the activity of individual M1 neurons by characterizing how neural activity is modulated by variations in torque exerted at two separate joints. Our approach provides a direct extension of studies that examine neural processing during single-joint motor tasks to consider multiple joints. Our methodology also shares certain similarities to previous studies that correlate load-related activity to hand-based parameters. We therefore included complementary analyses reflective of previous single-joint and hand-based studies. Furthermore, the detailed descriptions of torque-related activity provide an important foundation for developing and assessing computational models of M1 processing.

In summary, we observed that many neurons in the shoulder/elbow region of M1 were quantitatively related to joint torques at the shoulder only (33%), elbow only (30%), or both joints (36%) and that these neurons were highly intermingled across the cortical surface. Relative to their unloaded baseline activity, most torque-related neurons were reciprocally modulated by opposing flexor and extensor torques at a single joint (Fig. 5, B and E). A small number of neurons were coexcited or coinhibited.
coinhibited by opposing torques at one joint, but these neurons generally exhibited reciprocal modulation at the other joint (Fig. 6C). Notably, our population of M1 neurons exhibited a bimodal distribution of PTDs that was biased toward whole-limb flexor and whole-limb extensor torques (Fig. 9A). Other properties of directional tuning (torque-slope and tuning width) exhibited broad distributions (Fig. 9, B and C) that were unrelated to this bias. These observations have several implications regarding the neural basis of multijoint control, which are discussed in the following text.

**M1 topography**

Classical studies of M1 in humans (Penfield and Rasmussen 1950) and monkeys (Woolsey et al. 1952) observed that movements of body parts evoked by stimulation were broadly segregated along the medial–lateral axes. Specifically, the legs, trunk, arms, face, and mouth were found to be represented within anatomically distinct subregions of M1. It is debated, however, whether there is a functional organization within these major regions (reviewed in Sanes and Schieber 2001; Schieber 2001). In the arm representation, for example, some studies observed a random organization (Donoghue et al. 1992; Gould et al. 1986), whereas other studies observed that the proximal arm (shoulder–elbow) is represented within a horseshoe-shaped region surrounding the distal arm (wrist–hand) (Kwan et al. 1978; Park et al. 2001).
The current study addressed whether neurons within the shoulder–elbow region of M1 exhibit an orderly topography. Although our study was limited to neurons within the medial branch of the horseshoe organization (hand/wrist-related neurons were found laterally), we found that neurons related to the shoulder only, elbow only, or both joints were intermingled across the surface of M1 and did not exhibit distinct segregation along the medial–lateral axes of M1. Similar results were reported for the hand representation, in which single neurons are generally related to movements of multiple digits and do not exhibit an obvious somatotopic organization (Polikov and Schieber 1999; Schieber and Hibbard 1993). These observations support the notion that M1 possesses only a broad segregation of body parts. Substantive overlap in the neural representations of the shoulder and elbow may reflect the behavioral requirements of many motor tasks in which these joints are coordinated together to move the hand in space (Sanes and Schieber 2001; Schieber 2000).

Is cocontraction reflected in a small population of torque-related neurons?

In everyday life, common motor behaviors may be affected by random mechanical perturbations. For example, our arms randomly experience clockwise and counterclockwise perturbations while driving over rough terrain. Coactivation of antagonistic muscles (i.e., cocontraction) is one strategy to reduce the influence of limb perturbations that may occur while trying to maintain a static posture (e.g., Darainy et al. 2004; Franklin and Milner 2003; Gomi and Osu 1998; McIntyre et al. 1996).

Surprisingly little is known about the neural basis of cocontraction because few studies examined neural activity during tasks that promote cocontraction. At the level of the cortex, Humphrey and Reed (1983) examined the responses of M1 neurons during slow and fast wrist perturbations that respectively produced reciprocal activation and cocontraction of opposing wrist muscles. They found two distinct populations of neurons: one that was modulated only during rapid perturbations and one that was modulated only during slow perturbations. This finding suggests that reciprocal activation and cocontraction of opposing wrist muscles might be represented by distinct neural processes in M1. However, muscles of the elbow and shoulder were also more active during rapid perturbations than slow perturbations and thus it is possible that one population was related to the wrist, whereas the other was related to the shoulder and elbow.

Indirect evidence for distinct representations of reciprocal activation and cocontraction may also be interpreted from single-joint studies of torque-related activity in M1 (Evarts et al. 1983; Werner et al. 1991). These studies found that most torque-related M1 neurons exhibited a reciprocal pattern of activity in response to opposing torques; i.e., they were excited by torques applied in one direction and inhibited by torques applied in the opposing direction. However, they also found that a considerable number of torque-related neurons were excited or inhibited by both opposing torques. Because opposing torques primarily activate antagonistic muscle groups, these results suggest that this population of neurons may be related to cocontraction.

If neurons with similar responses to opposing single-joint torques are related to cocontraction, then neural correlates of cocontraction should also be observed in whole-limb studies. Specifically, one might expect to find neurons that exhibit bimodal or uniform changes in force- or torque-related activity relative to unloaded baseline. However, two comprehensive whole-limb studies, one postural and one isometric, did not report bimodal or uniform changes in force-related activity relative to baseline (Kalaska et al. 1989; Sergio and Kalaska 2003). The current study may explain why these whole-limb studies did not report such correlates of cocontraction. We found that a sizable proportion of multijoint neurons (28/76, 37%) showed coexcitation/coinhibition at one of the two joints. If these neurons were related to cocontraction of antagonist muscles, one would expect that many would exhibit coexcitation/coinhibition at both joints and few would exhibit unimodal tuning. Contrary to these expectations, few of these neurons (6/28, 21%) exhibited coexcitation/coinhibition at both joints (Fig. 6C) and nearly all (26/28, 93%) were unimodally tuned (e.g., Fig. 8C).

Although our results suggest that torque-related M1 neurons are not related to cocontraction, it is important to recognize that our task was not specifically designed to explore the neural basis of cocontraction. Several recent studies of human behavior examined patterns of cocontraction during posture (Darainy et al. 2004; Franklin and Milner 2003) and reaching (Burdet et al. 2001; Milner and Franklin 2005) and may provide a foundation for future studies designed to explore the neural basis of cocontraction.

Relationship between M1 and muscle activations

There are many different parameters or levels of information that can be used to describe the kinetics of forces applied to a limb: 1) contact forces between the limb/hand and load, 2) joint torques representing the combined action of all muscles spanning a given joint, 3) individual muscle forces, and even 4) muscle activation patterns. The difference between these kinetic descriptions reflects how much the properties of the musculoskeletal system are incorporated into the kinetic measure. Contact forces do not consider any aspect of the limb except the site of contact. Joint torques include the influence of limb geometry and intersegmental dynamics. Muscle forces consider the mechanical action of individual muscles. Muscle activation patterns additionally include the mechanical properties of muscle including force–length and force–velocity relationships and excitation–contraction coupling.

Neural activity could be related to any of the above parameters, although it remains unclear which parameters are represented by supraspinal processes. Theoretical frameworks based on sensorimotor transformations (Hollerbach 1982; Kalaska and Crammond 1992; Soechting and Flanders 1992) indicate that all may be represented neurally, whereas other frameworks, such as optimal feedback control (Scott 2004), suggest that such a hierarchy of representations is not required.

In the present experiment, monkeys were trained to counteract a uniform distribution of torques. If neural processing reflected the range of behavioral requirements inherent in a task, one might expect that each torque direction would have been represented by an equal proportion of M1 neurons. In fact, a previous study observed that the activity of M1 neurons can reflect the range of behavioral requirements (Hepp-Reymond et al. 1999). Specifically, force-related activity of indi-
individual neurons was modulated by contextual cues indicating the upcoming range of forces and number of force steps in a grip force task. In the current study, however, we observed a bimodal distribution of PTDs. Furthermore, we did not observe any systematic relationships between PTDs, torque-slopes, and tuning widths, indicating that the relatively small proportion of neurons with PTDs near 45 and 225° did not possess higher torque-slopes or different tuning widths to compensate for the bimodal distribution of PTDs. Taken together, these findings indicate that M1 neurons as a population do not reflect the range of behavioral requirements inherent in our postural task.

Another possibility is that proprioceptive feedback during the task influenced M1 activity. Because many M1 neurons respond strongly to proprioceptive input (Evarts and Tanji 1976; Flament and Hore 1988; Lemon and Porter 1976; Scott and Kalaska 1997; Wolpaw 1980; Wong et al. 1978), one might expect that a greater proportion of neurons would have preferred joint torques that reflected the mechanical action of the shoulder and elbow muscles. Although most shoulder and elbow muscles span only a single joint, the four biarticular muscles combine flexion or extension at both joints. However, these directions in joint-torque space were least represented across our population of M1 neurons.

Notably, our population of torque-related M1 neurons exhibited a bimodal distribution of PTDs that was biased toward whole-limb flexor and whole-limb extensor torques. This mirrored the pattern of torque-related EMG of a sample of proximal arm muscles in the same monkeys in this postural task (Kurtzer et al. 2006a). Other studies also described close relationships between M1 and the motor periphery by comparing patterns of activity across populations of neurons and muscles. Importantly, greater proportions of neurons and muscles are maximally activated when the hand moves toward or away from the body compared with the left or right during planar reaching movements (Kurtzer et al. 2006b; Scott et al. 2001). Biases in their preferred directions of movement (Caminiti et al. 1990; Kakei et al. 1999; Scott and Kalaska 1997) and force (Sergio and Kalaska 2003) undergo similar rotations after changes in limb geometry. Both neurons and muscles exhibit similar temporal changes in their distributions of preferred movement direction (Sergio et al. 2005; Todorov 2000). Finally, both display a coupling between their onset time and magnitude of response (Scott 1997). Each of these findings highlights the intimate relationship between M1 and the motor periphery, but they do not imply a point-to-point mapping in which M1 neurons are merely upper motor neurons. Rather, they suggest that the activities of M1 neurons and peripheral muscles are shaped by similar constraints.

**Biased representations of joint torque: muscle synergies or optimal strategies?**

A fundamental issue in motor control is that the redundancy of the musculoskeletal system requires the CNS to select patterns of muscle activations from an infinite set of possible solutions to execute even the simplest multijoint behaviors. Bernstein (1967) proposed that this problem could be simplified if a broad range of motor behaviors could be produced with a small number of distinct muscle synergies, sets of muscles that are collectively activated to form functional units. Accordingly, motor commands would be accomplished by activating appropriate combinations of muscle synergies.

A number of subsequent studies provided empirical evidence suggesting that the CNS uses muscle synergies. Notably, patterns of muscle activity were decomposed into a small number of muscle synergies across a broad range of tasks and species including postural control and locomotion in humans (Henry et al. 1998; Ivanenko et al. 2004) and cats (Buford and Smith 1990; Macpherson et al. 1986; Ting and MacPherson 2005), and a variety of natural behaviors in frogs (d’Avella et al. 2003). Synergistic patterns of muscle activity were also observed during reflex responses to cutaneous stimulation in spinalized frogs, suggesting that such patterns are reflected in neural circuitry at the spinal level (Hart and Giszter 2004; Tresch et al. 1999).

The present data could be viewed as providing evidence that muscle synergies are expressed by neural processes at supraspinal levels. We found that in our planar task M1 neurons tended to represent torque-related activity in one of two multijoint muscle synergies: whole-limb flexion and whole-limb extension. Because other studies also observed that M1 activity reflects various muscles synergies (Donoghue et al. 1992; Holdefer and Miller 2002; Park et al. 2004), these observations could be viewed as evidence that muscle synergies may form the basis of a common language to create complex motor patterns.

Alternatively, our results are also consistent with motor patterns arising from optimal control strategies that are unrelated to the notion of muscle synergies (Scott 2004). Similar to earlier studies of the monkey wrist (Hoffman and Strick 1999), human forearm (Buchanan et al. 1989; van Zuylen et al. 1988), and human leg (Nozaki et al. 2004), we observed that the pattern of activations of monoarticular and biarticular shoulder and elbow muscles was systematically rotated away from their anatomical action toward whole-limb flexor or whole-limb extensor torques (Kurtzer et al. 2006a). Mathematical models illustrated that minimizing global measures of muscle activity could predict the observed PTD rotations of each group of upper arm muscles: shoulder flexors and extensors, elbow flexors and extensors, and biarticular flexors and extensors (Kurtzer et al. 2006a). These models suggest that M1 may control certain motor behaviors, such as postural maintenance, by producing patterns of neural activity that achieve the task goal by minimizing muscle factors such as output noise. As a result, muscle synergies may not reflect an explicit simplifying strategy for controlling movement. Rather, they may be the appropriate pattern of muscle activities given the physical properties of the musculoskeletal system and the task goals. This raises the problem of what evidence is required to demonstrate whether muscle synergies are an explicit strategy for simplifying motor control or an emergent pattern of muscle activity suitable for optimizing task goals.

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