Partial Reconstruction of Muscle Activity From a Pruned Network of Diverse Motor Cortex Neurons

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INTRODUCTION

Primary motor cortex (M1) neurons traditionally have been viewed as “upper motor neurons,” conveying the notion that M1 output neurons directly drive the activity of particular spinal (lower) motoneuron pools (Phillips and Landau 1990). M1 neurons with direct connections to motoneuron pools can be identified physiologically by the postspike effects they produce in spike-triggered averages (SpikeTAs) of rectified electromyographic (EMG) activity. During voluntary movements—such as reach and prehension (McKiernan et al. 2000), wrist flexion and extension (Fetz and Cheney 1980), or precision pinch and power grasp (Lemon et al. 1986)—many M1 neurons that produce postspike effects show discharge modulation similar to the EMG activity of their target muscles, supporting the view that the activity patterns of lower motoneurons follow those of their upper motor neurons in M1.

In similar studies, however, other M1 neurons have shown discharge modulation distinctly different from that of their target muscles. During alternating wrist movements, for example, many M1 neurons discharged an initial phasic burst not apparent in the EMG activity of target muscles (Cheney and Fetz 1980). Other instances have been observed in which an M1 neuron was active without EMG activity in one or more of its target muscles (Bennett and Lemon 1996; Buys et al. 1986; Fetz and Cheney 1987). Conversely, a target muscle could be active when its M1 corticomotoneuronal cell was not. Such instances of neuron–muscle dissociation suggest that the activity of motoneuron pools may not simply follow the inputs received directly from M1 neurons.

The upper motor neuron notion received additional support from studies showing that the discharge patterns of M1 neuron ensembles can be used to reconstruct the EMG activity patterns of muscles or the time course of movement parameters (Humphrey et al. 1970; Moran and Schwartz 1999; Morrow and Miller 2003; Taylor et al. 2002; Westwick et al. 2006). These M1 populations typically have been selected for movement-related discharge, however, and may have included many neurons—corticocortical, corticostriatal, corticorubral, corticothalamic, and local interneurons—with little direct influence on motoneuron pools. Moreover, variable time lags generally have been allowed to optimize the fit between M1 neuron activity and EMG or movement parameters. Although such reconstructions demonstrate that the information needed to generate the EMG is present in M1 neurons, a substantial fraction of this information therefore may reach the motoneuron pools over routes less direct than monosynaptic corticomotoneuronal connections. Rubrospinal neurons and spinal interneurons, for example, that receive input from M1, are active in relation to finger movements, and produce SpikeTA effects in forearm muscles, may contribute substantially to control of finger movements along with the crucial corticomotoneuronal connections (Fetz et al. 2002; Houk et al. 1988; Kuypers 1987; Mewes and Cheney 1994).

Here we used SpikeTAs to identify M1 neurons with short-latency correlational linkages to the motoneuron pools of finger and wrist muscles during 12 individuated flexion/extension finger and wrist movements. We examined the degree of similarity between the discharge patterns of these M1 neurons and the EMG activity patterns of their target muscles. We then explored the extent to which simple summation of the M1 neuron activity patterns, acting only at short latency through...
those linkages indicated by SpikeTA effects, could account for the EMG activity patterns of muscles across the 12 movements.

**METHODS**

Many of the methods used in the present study for behavioral training, data collection, and initial analyses were described in previous reports (Poliakov and Schieber 1999; Schieber 1991, 2002; Schieber and Rivlis 2005) and are summarized here as needed.

**Animals and behavioral procedures**

All care and use of these purpose-bred monkeys complied with the USPHS Policy on Humane Care and Use of Laboratory Animals and were approved by the University Committee on Animal Resources at the University of Rochester. Each monkey was trained to perform visually cued individuated flexion and extension movements of the right-hand fingers and/or wrist (Schieber 1991). As the monkey sat in a primate chair, the right elbow was held in a molded cast and the right hand was placed in a pistol-grip manipulandum that separated each finger into a different slot. At the end of each slot, the fingertip lay between two microswitches. By flexing or extending the digit a few millimeters, the monkey closed the ventral or dorsal switch, respectively. The manipulandum, in turn, was mounted on an axis that permitted flexion and extension wrist movements. Each monkey viewed a display on which each digit (and the wrist) was represented by a row of five light-emitting diodes (LEDs). When the monkey flexed or extended a digit, closing a microswitch, the central yellow LED went out and a green LED to the left or right, respectively, came on, cueing the monkey as to which switch(es) had been closed. Red LEDs to the far left or right were illuminated one at a time, under microprocessor control, instructing the monkey to close that one switch (or move the wrist). If the monkey closed the instructed switch within the 700 ms allowed after illumination of the red instruction LED, and held it closed for a 500-ms final hold period without closing any other switches, the monkey received a water reward. After each rewarded trial, the movement to be instructed for the next trial was rotated in a pseudorandom order. We abbreviate each instructed movement with the number of the instructed digit (1 = thumb through 5 = little finger, W = wrist) and the first letter of the instructed direction (f, flexion; e, extension), for example, “4f” indicates instructed flexion of the ring finger.

**Data collection**

After training, aseptic surgery under isoflurane anesthesia was used to open a craniotomy over the left central sulcus at the level of the hand representation, to implant a rectangular Lucite recording chamber over the craniotomy and to implant head-holding posts. Once the monkey had recovered from this procedure and had become accustomed to performing the finger-movement task with its head held stationary, EMG electrodes made of 32-gauge, Teflon-insulated, multistranded stainless steel wire (Cooner AS632, Chatsworth, CA) were implanted percutaneously using aseptic technique in eight to 16 forearm and hand muscles under ketamine anesthesia, using techniques adapted from those of Cheney and colleagues (McKiernan et al. 2000). For forearm muscles, each wire was stripped of insulation for 1 mm and passed retrograde for 2 mm into a 23-gauge hypodermic needle, after which the needle was passed percutaneously into the muscle belly, and then the needle was withdrawn, leaving the wire tip fish-hooked in the muscle belly. To implant intrinsic muscles of the hand, wires were tunneled separately for each muscle from a 5-mm incision on the dorsal aspect of the forearm to a 5-mm incision on the dorsal aspect of the hand, wire tips were stripped and inserted into the muscle belly using hypodermic needles, and then the incisions were closed with subcuticular, absorbable suture. For both forearm and intrinsic muscles, two wires were placed 5–10 mm apart in the long axis of each muscle belly to provide a bipolar recording configuration. Four bipolar pairs were led to a single external connector. Appropriate location of each bipolar pair was confirmed by observing the movements evoked with intramuscular stimulation (1-s trains of 100-Hz biphasic, constant-current pulses, 200 μs per phase, 10–1,000 μA). Externally, the wires and connectors were held in place with elastic adhesive tape (Elastikon, Johnson & Johnson), covered with a self-adhesive wrap (Vetrap, 3M) and the monkey was placed in a jacket (Alice King Chatham, Hawthorne, CA) with heavy Cordura sleeves to prevent removal of the electrodes. During subsequent recording sessions the sleeve and self-adhesive wrap were removed, exposing the connectors held in the elastic adhesive tape. Implanted electrodes typically functioned well for 6–8 wk, after which they were removed by loosening the elastic adhesive tape with acetone and then gently pulling each wire out through the skin. After 2 wk, another set of EMG electrodes was implanted.

The present data were collected using three sets of EMG electrode implantations in monkey C and four sets in monkey G. Muscles implanted in each set typically included eight to 16 of the following: thenar eminence (Thenar); first dorsal interosseus (FDI); hypothenar eminence (Hypoth); flexor digitorum profundus, radial region (FDPr); flexor digitorum profundus, ulnar region (FDPu); flexor digitorum profundus, proximal ulnar region (FDPpu); flexor digitorum superficialis (FDS); flexor carpi radialis (FCR); palmaris longus (PL); flexor carpi ulnaris (FCU); abductor pollicis longus (APL); extensor pollicis longus (EPL); extensor digitii secundii et tertii (ED23); extensor digitorum communis (EDC); extensor digiti quinti et quarti (ED45); extensor carpi radialis (ECR); extensor carpi ulnaris (ECU); and supinator (Sup). We previously showed that in a given monkey these muscles produce distinct, reproducible patterns of EMG activity across the 12 individuated finger and wrist movements, although the pattern for any given muscle may vary among monkeys (Poliakov and Schieber 1999; Schieber 1995). The present EMG recordings therefore were accepted as originating from a given muscle only if off-line analysis showed the pattern of EMG activity characteristic of that muscle.

Thereafter in daily recording sessions conventional techniques were used to record single M1 neurons simultaneously with EMG activity from the implanted forearm and hand muscles (EMG amplification 2,000–100,000×, band-pass 0.3–3 kHz, sampling frequency about 4 kHz per channel) as the monkey performed individuated finger and wrist movements. The present data were collected in 165 microelectrode penetrations performed over 13 mo in monkey C and in 83 microelectrode penetrations performed over 6 mo in monkey G. During each recording session, one data acquisition interface was used to store data to disk on one host PC, which also provided a scrolling display of all neuron and EMG recordings (Power1401 interface, Spike2 software, Cambridge Electronic Design, Cambridge, UK). A second identical data acquisition interface and host PC running AVE software (courtesy LE Shupe, EE Fetz, and PD Cheney) were used concurrently to form initial on-line averages of rectified EMG for each channel using data segments extending ±50 ms from the time of all neuron spikes. As more segments are averaged, EMG activity that is not time-locked to the neuronal spike evens out toward a baseline, whereas EMG activity that is time-locked to the spike accumulates progressively, forming a facilitatory peak or suppression trough (Fetz and Cheney 1980). M1 neurons that had produced no effect in the on-line averages after accumulating 4,000 spike triggers were recorded further only long enough to obtain 10 correctly performed trials of each instructed movement. M1 neurons that produced an effect evident in the on-line average of at least one muscle were recorded until 10,000 spikes had accumulated or as long as satisfactory isolation could be maintained.
Data analysis

To summarize the activity pattern of each M1 neuron during the 12 individuated finger and wrist movements, we compiled for each instructed movement a separate histogram (20-ms binwidth) of spike discharge times during all correctly performed trials, aligning the data at the end of the movement (time of switch closure) in each trial (e.g., Fig. 1). The activity pattern of each EMG similarly was summarized by averaging the full-wave-rectified waveform during exactly the same correctly performed trials of each instructed movement used to generate the histograms of neuron activity, again aligned at the end of the movement. For this purpose, EMGs were initially averaged at a binwidth corresponding to the sampling frequency and the average subsequently was downsamples to a binwidth of 20 ms. In comparing the activity patterns of neurons and EMGs, we focused on a 700-ms period (from 500 ms before to 200 ms after the end of each movement) that included the vast majority of modulation in both M1 neuron and EMG activity.

Off-line, spike-triggered averages (SpikeTAs) were formed for each EMG channel using custom software to average segments of rectified EMG activity from 30 ms before to 50 ms after each spike of the M1 neuron. Significant effects in SpikeTAs were identified with multiple-fragment statistical analysis (Poliakov and Schieber 1998). This approach divides the spike train into multiple fragments, forms a triggered average using the spikes in each fragment, and subtracts from the mean value of the average in a 10-ms test window (6–16 ms after the trigger) the mean in immediately preceding and succeeding 10-ms control windows. If this difference on average is significantly different from 0 across all the fragments, the peak (or trough) in the test window is statistically significant. Because previous studies showed that the peaks and troughs of postspike effects in SpikeTAs typically occur at latencies from 6 to 16 ms after the M1 neuron spike (Cheney and Fetz 1985; Fetz and Cheney 1980; Kasser and Cheney 1985; Lemon et al. 1986; McKiernan et al. 1998), statistically significant peaks (or troughs) were identified in that fixed temporal window. Potentially significant effects occurring at other latencies were not examined in the present analysis.

Initial SpikeTAs were formed using all spikes recorded from a given M1 neuron. If any muscle showed a peak (or trough) still significant at the \( P < 0.05 \) level after Bonferroni correction for testing multiple EMG channels, the neuron was accepted as producing effects. Then each EMG in that recording with a peak (or trough) significant at \( P < 0.05 \) without correction was submitted to the following analysis. To eliminate contributions of sweeps containing only noise, a second, filtered average was formed, using spikes as triggers only if the root-mean-square (RMS) value of the EMG from 30 ms before to 50 ms after the trigger was \( > 0.05 \text{ V} \), i.e., greater than the typical noise level of 0.3–0.4 V after amplification \( \times 2,000 \)–100,000 (McKiernan et al. 1998). If the peak (or trough) in this filtered average remained significant at \( P < 0.05 \) (without Bonferroni correction), the effect was retained for further analysis. Any baseline ramp in the filtered average was subtracted and the filtered average was smoothed with a flat five-point finite impulse response filter. When significant effects were identified in multiple muscles in the same recording, one of any pair of effects potentially resulting from cross talk between EMG recordings was eliminated (Buys et al. 1986; Kasser and Cheney 1985).

A computer algorithm then performed the following computations for each EMG-filtered, ramp-subtracted, smoothed SpikeTA (Schieber 2002; see also Fig. 1 of Schieber and Rivlis 2005). The mean and SD were calculated over a baseline period from 30 to 10 ms

![Fig. 1. Electromyographic (EMG) activity compared with that of primary motor cortex (M1) neurons producing spike-triggered average (SpikeTA) effects in flexor digitorum profundus, ulnar region (FDPu). Rows: patterns of electromyographic (EMG) activity in FDPu (top) and in 35 M1 neurons that each produced a SpikeTA effect in FDPu, during 12 different finger and wrist movements (columns) denoted at top by the abbreviations 1f (thumb flexion) through We (wrist extension). Each of these traces is the multiple-trial average histogram of activity recorded during a given instructed movement, from 500 ms before to 200 ms after the end of each movement (switch closure), at which point trials were aligned. Second row (MPI-weighted sum): sum of all 35 neuron activity patterns, each weighted by the mean percent increase (MPI) of the SpikeTA effect produced by that neuron in FDPu. Identifying number of each neuron is given at the left of its row. Additional features of each neuron shown here are given in Table 2. Calibration bars at bottom right represent 700 ms (horizontal) and 150 spikes/s (vertical) and apply to all 35 neurons. Vertical scale of FDPu EMG and of the MPI-weighted sum is arbitrary. Trace at the far right of each row shows each neuron’s SpikeTA of FDPu EMG, from 30 ms before to 50 ms after the trigger time (vertical line). SpikeTAs are expanded vertically such that the height from minimum to maximum is the same for each trace.](http://jn.physiology.org/content/97/1/72/F1.large.jpg)
before the trigger. The maximum value of the peak (or minimum of the trough) was identified and the average was followed backward and forward until it fell within 2 SD of the baseline mean. These times were defined as the onset and offset, respectively, of the SpikeTA effect and their latencies were corrected for the time from spike onset to the trigger pulse used for averaging. We then computed two standard measures of the strength of each SpikeTA effect, the mean percent increase (MPI), and peak percent increase (PPI) (Cheney and Fetz 1985; Lemon et al. 1986; McKiernan et al. 2000). MPI was calculated as MPI = [(A - B)/B] × 100, where A is the mean amplitude of the peak (or trough) from its onset to offset and B is the mean amplitude of the SpikeTA during the baseline period from 30 to 10 ms before the trigger. PPI was calculated as PPI = [(P - B)/B] × 100, where P is the maximum (for a peak, or minimum for a trough) of the SpikeTA waveform between the onset and offset of the peak or trough and B is the same baseline mean used to calculate the MPI above. We also computed a third measure of the strength of each SpikeTA effect, the normalized area, which was calculated by multiplying the MPI by the duration of the peak or trough, from onset to offset. Finally, the peak width at half-maximum (PWHM) of the SpikeTA effect was determined by computing half the height of the peak above (or trough below) the baseline mean and measuring the width of the peak (or trough) at this level. The analyses above were performed using custom Spike2 scripts (Cambridge Electronic Design). Subsequent analyses described later in RESULTS were accomplished in MATLAB (The MathWorks, Natick, MA).

In the RESULTS we used MPI as our default measure of the strength of SpikeTA effects because MPI expresses the strength across the entire duration of the effect, rather than only at the instant of the peak, which is expressed by the PPI. We also examined a third measure of the strength of SpikeTA effects, the normalized area, which integrates the amplitude of peak (or trough) from onset to offset, again expressed as a percentage of the baseline mean. Because absolute levels of EMG activity cannot be compared directly across different electrodes, all three of these measures normalize the strength of the SpikeTA effect by dividing by the mean of the SpikeTA during a baseline period preceding the peak or trough.

As described elsewhere in detail (Schieber and Rivlis 2005), although our data show a continuous spectrum of SpikeTA effects, for purposes of exposition we used onset latency and PWHM criteria to divide SpikeTA effects from monkeys C and G into four categories: pure postspike effects (onset latency >5 ms, PWHM <9 ms), pure + synchrony effects (onset latency <5 ms, PWHM <9 ms), late-widening effects (onset latency >5 ms, PWHM >9 ms), and synchrony effects (onset latency <5 ms, PWHM >9 ms). Whereas pure postspike facilitation effects indicate monosynaptic excitation (and pure postspike suppressions disynaptic inhibition) from the M1 trigger neuron to the motoneuron pool, pure + synchrony effects indicate some degree of direct input from the trigger neuron combined with additional inputs to the same motoneuron pool from other neurons synchronized with the trigger neuron. Late-widening effects similarly may indicate direct input from the trigger neuron combined with additional late-arriving inputs from other synchronized cortical or subcortical neurons or, alternatively, may result from the motor unit action potentials of various motoneurons with various waveform durations occurring in the muscle at slightly different latencies after the arrival of synaptic input from the trigger neuron in the motoneuron pool (Palmer and Fetz 1985). Inputs from neurons synchronized with the trigger neuron dominate synchrony SpikeTA effects, which then may or may not include direct input from the trigger neuron. All four types of SpikeTA effects nevertheless show that synaptic inputs arrived in the motoneuron pool at a relatively short latency, time-locked to spikes discharged by the trigger neuron. Whereas in the case of pure and pure + synchrony effects, every spike discharged by trigger neuron can be assumed to have produced synaptic input in the motoneuron pool, late-widening and synchrony effects may have involved no direct input from the trigger neuron, and thus not every spike may have signaled synaptic input. Nevertheless, because pure + synchrony, late-widening, and synchrony effects often were larger than pure effects, the spikes discharged by these M1 neurons provide a surrogate signal for the arrival of more input to the motoneuron pools than the spikes of M1 neurons that produced pure postspike effects. For these reasons, and because they constituted large fractions of the populations of SpikeTA effects obtained from monkeys C and G, we have included M1 neurons that produced pure + synchrony, late-widening, and synchrony effects along with those that produced pure postspike effects in the present study.

RESULTS

One hundred fifty-nine neurons with a significant SpikeTA effect in at least one muscle were recorded in monkey C and 83 in monkey G. Certain aspects of these neurons and their SpikeTA effects were previously described (Poliakov and Schieber 1999; Schieber 2002; Schieber and Rivlis 2005). From these recordings, we collected the set of EMGs recorded from a given muscle and examined histograms showing the average pattern of EMG activity during the 12 individuated finger and wrist movements for each recording. We rejected from further analysis any recordings in which the pattern of EMG activity across the 12 movements differed substantially from the stereotyped pattern characteristic of that muscle. (Such atypical recordings presumably resulted from migration of the electrode tips over the latter days of the electrode implant because the recorded pattern of EMG activity shifted gradually day by day.) For each muscle, the EMG recordings retained for analysis thus were selected to have a relatively consistent pattern characteristic of a particular motoneuron pool.

To have a reasonable sample of M1 neurons to compare with each muscle, for the present study we arbitrarily required that ≥10 M1 neurons with SpikeTA effects be available in the retained set of consistent EMG recordings. This requirement resulted in 10 muscles from monkey C and seven muscles from monkey G being selected for study. One hundred forty neurons from monkey C and 45 from monkey G therefore were included in the present analysis because they produced a SpikeTA effect in at least one of the selected muscles. Numbers of neurons with SpikeTA effects in each of the muscles selected for study are listed in Table 1. Concerning neuron–muscle pairs, 295 from monkey C and 124 from monkey G showed a significant SpikeTA effect in a selected muscle.

Limited similarity between M1 neuron and EMG activity patterns

M1 neurons that produce pure postspike effects in rectified EMG are thought to drive their target motoneuron pools directly, particularly during voluntary finger movements. The spikes of M1 neurons that produce pure + synchrony, late-widening, and synchrony SpikeTA effects also signal the arrival, at short latency, of time-locked input in the target motoneuron pool (Schieber and Rivlis 2005). Given the rather short latencies with which these neurons produce effects in EMG, peaking between 6 and 16 ms after the cortical spike, the discharge pattern of M1 neurons might be expected to resemble the EMG activity pattern of the muscles in which they produced SpikeTA effects, with little temporal difference (<20 ms). The top row of Fig. 1 shows rectified EMG averaged across 35 separate recordings from FDPs for each of the 12 instructed
movements. To quantify the similarity between these 35 FDPu recordings, the coefficient of variation ($R^2$) for the correlation between each individual EMG recording and the average of all 35 was computed using the data from all 12 movements. The lowest of these $R^2$ values was 0.8397, confirming that the pattern of EMG activity was consistent among these FDPu recordings.

These 35 FDPu recordings each were made simultaneously with a different M1 neuron that produced a significant SpikeTA effect in FDPu. The bottom rows of Fig. 1 show the activity patterns of these 35 M1 neurons (C0033–C0526). Traces in each row represent spike-frequency histograms during each of the 12 movements. Traces at the far right show the SpikeTA effect produced by that neuron in FDPu. The vertical scales were adjusted to fill the same vertical height for each of these 35 SpikeTA effects. Large effects therefore appear as distinct peaks or troughs compared with an apparently low noise level, whereas smaller effects have less clearly defined peaks and an apparently larger noise level. To incorporate as many neurons as possible in the present analysis, we systematically included all SpikeTA effects with a peak or trough amplitude relative to noise level, regardless of the peak or trough amplitude relative to other features in the SpikeTA. The $P$ value for each of these SpikeTA effects is given in Table 2.

To quantify the similarity between the 12-movement activity pattern of each M1 neuron and the average EMG activity pattern of FDPu, the coefficient of variation ($R^2$) between these two patterns was calculated. Whereas other studies quantified neuron–muscle similarity using continuous data (Holdefer and Miller 2002; McKiernan et al. 2000; Miller et al. 1993), we chose to compute $R^2$ between these multiple-trial averages specifically to minimize trial-by-trial variability and to evaluate instead the average pattern of activity underlying the 12 individuated finger and wrist movements. Individual neuron–EMG $R^2$ values for these 35 recordings are given in Table 2. The highest was 0.431 for neuron C0242. Although all 35 neurons produced SpikeTA effects in FDPu, none had an activity pattern particularly similar to that of the average EMG.

For some neurons, the degree of neuron–EMG similarity appeared consistent with the SpikeTA effect. C0107, for example, produced a pure postspike facilitation in FDPu with an MPI of 9.0% and discharged bursts with FDPu during movements 4f, 4e, and 5e, resulting in an $R^2$ of 0.326. The discharge of C0107 thus appeared to contribute directly to activation of FDPu.

In contrast, neuron C0221 produced a pure postspike suppression with an MPI of −4.2%. C0221 discharged bursts during 2f, 3f, 2e, and 3e when FDPu was relatively inactive, and this dissimilarity between neuron C0221 and FDPu EMG was reflected in an $R^2$ of 0.016. C0221 also discharged bursts concurrently with FDPu during 4f, 4e, and 5e, however. Rather than simply having a discharge pattern negatively correlated with that of FDPu in an agonist/antagonist fashion, during certain movements C0221 thus appeared to limit ongoing FDPu activity.

However, for other neurons the degree of neuron–EMG similarity appeared inconsistent with the SpikeTA effect. C0130, for example, produced a late-widening SpikeTA effect (onset latency 8.7 ms, PWHM 12 ms) with an MPI of 10.8%. C0130 was most active during 2f when FDPu was relatively silent, however, resulting in an $R^2$ value of 0.070. Although spikes discharged by C0130 were associated with strong, short-latency facilitation of FDPu, EMG in FDPu was not always generated during discharge of C0130. Thus some of these 35 M1 neurons had patterns of activity across the 12 movements that partially resembled that of FDPu EMG, whereas others had quite dissimilar patterns. Indeed, examin-

### Table 1. EMG reconstruction summary

<table>
<thead>
<tr>
<th>Muscle</th>
<th>Neurons with SpikeTA Effect</th>
<th>$R^2$ of MPI-Weighted Sum</th>
<th>Bootstrap $P$ (out of 5,000)</th>
<th>Exponential Asymptote</th>
<th>Highest $R^2$ Using up to 5 Neurons</th>
<th>Neurons Used for highest $R^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>APL</td>
<td>34</td>
<td>0.2567</td>
<td>0.0060</td>
<td>0.2927</td>
<td>0.5554</td>
<td>5</td>
</tr>
<tr>
<td>ECU</td>
<td>35</td>
<td>0.3844</td>
<td>0.0008</td>
<td>0.3882</td>
<td>0.6587</td>
<td>5</td>
</tr>
<tr>
<td>ED23</td>
<td>58</td>
<td>0.2662</td>
<td>0.1046</td>
<td>0.2720</td>
<td>0.7016</td>
<td>5</td>
</tr>
<tr>
<td>ED45</td>
<td>39</td>
<td>0.1697</td>
<td>0.0590</td>
<td>0.1848</td>
<td>0.7139</td>
<td>5</td>
</tr>
<tr>
<td>EDC</td>
<td>25</td>
<td>0.1529</td>
<td>0.0868</td>
<td>0.1779</td>
<td>0.3719</td>
<td>5</td>
</tr>
<tr>
<td>FDI</td>
<td>10</td>
<td>0.3088</td>
<td>0.0014</td>
<td>0.3273</td>
<td>0.4639</td>
<td>4</td>
</tr>
<tr>
<td>FDPu</td>
<td>35</td>
<td>0.3261</td>
<td>0.0084</td>
<td>0.3463</td>
<td>0.5958</td>
<td>5</td>
</tr>
<tr>
<td>PL</td>
<td>28</td>
<td>0.3564</td>
<td>0.0004</td>
<td>0.3675</td>
<td>0.6319</td>
<td>5</td>
</tr>
<tr>
<td>Sup</td>
<td>17</td>
<td>0.0444</td>
<td>0.2406</td>
<td>bad fit</td>
<td>0.4001</td>
<td>5</td>
</tr>
<tr>
<td>Thenar</td>
<td>14</td>
<td>0.1000</td>
<td>0.2088</td>
<td>0.0996</td>
<td>0.3911</td>
<td>3</td>
</tr>
</tbody>
</table>

For each muscle studied here, the table gives the following values: the number of neurons studied that produced a significant SpikeTA effect in the muscle; $R^2$ for the correlation between the muscle’s average EMG activity pattern during the 12 movements and the MPI weighted sum of the neurons’ activity patterns; a bootstrapped value of $P$ for the hypothesis that the value obtained for $R^2$ could have resulted from chance alone; the asymptote for an exponential fit estimating the highest $R^2$ achievable by including larger numbers of neurons; the maximum $R^2$ achieved using up to five best neurons; and the number of neurons used to achieve that $R^2$. Each of these values is described in detail in RESULTS.
TABLE 2. Neurons with SpikeTA effects in FDPu

<table>
<thead>
<tr>
<th>Neuron</th>
<th>Neuron-EMG R</th>
<th>Neuron-EMG R²</th>
<th>MPI of SpikeTA Effect</th>
<th>P value of SpikeTA Effect</th>
<th>FDPu Effect: Pure (1)</th>
<th>Total EMGs</th>
<th>Pure Effects</th>
<th>Synchrony Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>C0033</td>
<td>0.451</td>
<td>0.203</td>
<td>5.5</td>
<td>0.000</td>
<td>1</td>
<td>9</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>C0077</td>
<td>−0.538</td>
<td>0.290</td>
<td>−5.8</td>
<td>0.001</td>
<td>1</td>
<td>9</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>C0086</td>
<td>0.044</td>
<td>0.002</td>
<td>−10.2</td>
<td>0.006</td>
<td>1</td>
<td>9</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>C0094</td>
<td>0.620</td>
<td>0.384</td>
<td>9.7</td>
<td>0.000</td>
<td>1</td>
<td>9</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>C0106</td>
<td>−0.094</td>
<td>0.009</td>
<td>5.0</td>
<td>0.028</td>
<td>0</td>
<td>9</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>C0107</td>
<td>0.571</td>
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<td>9.0</td>
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For each of the 35 neurons from monkey C with SpikeTA effects in FDPu (shown in Fig. 1), the table provides the following values: the correlation coefficient (R) of the correlation between the multiple trial average activity patterns of the neuron and FDPu; the coefficient variation (R²) of that correlation; the MPI of the SpikeTA effect; the P value of the SpikeTA effect (0.000 indicates P ≤ 0.000049); an indication of whether the SpikeTA effect was pure (1) or reflected synchrony (0); the total number of those muscles in which the neuron produced a pure postspike effect; or a synchrony SpikeTA effect. Each of these values is described in detail in RESULTS.

Synchrony (0); the total number of those muscles in which the neuron produced a pure postspike effect; or a synchrony SpikeTA effect. Each of these values is described in detail in RESULTS.

Sign and strength of the SpikeTA effects

M1 neurons that facilitate a given pool of motoneurons might be expected to have discharge patterns similar to the EMG produced by the motoneuron pool, whereas M1 neurons that suppress the EMG might be expected to be quite dissimilar. These two contrasting relationships cannot be distinguished readily using MPI. We therefore used R to examine relationships between neuron–EMG activity pattern similarity and 1) the sign and strength of the SpikeTA effect, 2) whether the effect was pure or included synchrony, and 3) the number of muscles influenced by the neuron.

Factors that might influence neuron–EMG similarity

The lack of overall similarity between the activity patterns of M1 neurons and the muscles in which they produced SpikeTA effects might have resulted in part from inclusion of many M1 neurons with relatively weak effects in particular motoneuron pools. We therefore explored possible relationships between neuron–EMG activity pattern similarity and 1) the sign and strength of the SpikeTA effect, 2) whether the effect was pure or included synchrony, and 3) the number of muscles influenced by the neuron.

Figure 2 shows a scatterplot of neuron–muscle R versus MPI for each of the 35 M1 neurons from monkey C that produced...
a SpikeTA effect in FDPu. In general, M1 neurons that facilitated FDPu (positive MPI) tended to be active when FDPu was active (positive R), whereas neurons that suppressed FDPu (negative MPI) tended to be active when FDPu was inactive (negative R). Although a few neurons with positive MPI had negative R, and vice versa, neuron–muscle R and MPI were correlated significantly for FDPu in monkey C (P < 0.00001; r = 0.6775).

Overall correlations between neuron–muscle R and MPI were significant, however, for only four of the 17 muscles studied (P < 0.05 after Bonferroni correction for 17 tests). These four significant correlations resulted entirely from the signs of R and MPI and not from their magnitudes. If only neuron–muscle pairs with positive MPI were included, or if only those with negative MPI were included, or if points representing pairs with negative MPI were reflected through the origin such that all neuron–muscle pairs could be included, no muscle showed a significant correlation between neuron–muscle R and MPI. Similar analyses performed with other measures of SpikeTA effect amplitude (PPi or normalized area) likewise provided no evidence of a relationship with neuron–EMG similarity. These observations are consistent with other studies in which only a nonsignificant tendency for the magnitude of PSpF to correlate with the amplitude of long-term temporal cross-correlations between spike frequency and EMG was found in a reach and prehension task (McKer- nan et al. 2000). M1 neurons that produced larger SpikeTA effects in a given muscle thus did not have activity patterns systematically more similar to that of the muscle than neurons with smaller SpikeTA effects.

Pure versus synchrony SpikeTA effects

Whereas a pure postspike effect indicates relatively direct synaptic connections from the M1 neuron to the motoneuron pool, other SpikeTA effects—pure + synchrony, late-widening, and synchrony—indicate that in addition to any direct connections, inputs time-locked to the spikes of the M1 neuron arrived at short latency in the motoneuron pool over less-direct routes as well (Baker and Lemon 1998; Fetz et al. 1989; Schieber and Rivlis 2005). Because of these less-direct inputs, neuron–EMG activity pattern similarity might be lower for M1 neurons that produced SpikeTA effects with features of synchrony than for those that produced pure effects. We therefore compared the distributions of R² values for neuron–EMG pairs with pure versus synchrony (here including pure + synchrony, late-widening, and synchrony) SpikeTA effects using Kolmogorov–Smirnov (KS) tests.

When such comparisons were made for each of the 10 muscles studied in monkey C, only for Supinator did R² distributions show a significant difference (P = 0.0409), depending on whether the SpikeTA effect was pure or synchrony, and this difference would not have been considered significant after Bonferroni correction for 10 tests. When R² values were pooled from all 10 muscles in monkey C, the distributions of R² values were significantly different (P = 0.0125); however, the R² values on the whole were slightly larger for neuron–muscle pairs with synchrony effects (mean R² = 0.1120, median R² = 0.0713) than for those with pure effects (mean R² = 0.1012, median R² = 0.0391). In monkey G, sample sizes were too small to apply KS tests to individual muscles. When SpikeTA effects from all seven muscles were pooled, the distributions of R² values were not significantly different for neuron–EMG pairs with pure versus synchrony effects (P = 0.6271). The activity patterns of neuron–EMG pairs with pure SpikeTA effects thus were not more similar than the activity patterns of pairs with synchrony effects.

Muscle field size

The function of many M1 output neurons is complicated by the branching of individual corticospinal axons to influence multiple spinal motoneuron pools (Buys et al. 1986; Fetz and Cheney 1980; Shinoda et al. 1979, 1981). During movements for which all the muscles receiving input from a given M1 neuron show similar patterns of EMG activity, the number of target muscles would not be expected to affect the similarity of activity patterns in an M1 neuron and its target muscles. However, given that each of the present muscles had a relatively distinct activity pattern during the present repertoire of individuated movements (Poliakov and Schieber 1999; Schieber 1995), neuron–EMG similarity might depend in part on the number of muscles influenced by the neuron. A neuron producing a SpikeTA effect in only one muscle, for example, might have an activity pattern more similar to that muscle than would be possible for a neuron that produced SpikeTA effects in five additional muscles. Because we were unable to record from every upper extremity muscle, we have no exact measurement of the number of muscles receiving SpikeTA effects from each M1 neuron. Nevertheless, neurons for which we found SpikeTA effects in multiple muscles were likely to have had larger muscle fields on average than neurons for which we identified only one SpikeTA effect.

For each of the M1 neurons studied here, we therefore counted the number of simultaneously recorded EMGs in which independent SpikeTA effects were identified (muscle field size of the neuron). For this count we included not only EMGs of the muscles selected for the more detailed analyses...
here, but rather all EMGs recorded simultaneously with the M1 neuron. In monkey C, 51 of the present M1 neurons produced SpikeTA effects in only one muscle, 44 neurons in two muscles, 23 in three, 27 in four, 14 in five, 11 in six, and one neuron produced effects in seven muscles. We formed separate distributions of neuron–EMG $R^2$ values for neurons with one, two, three, four, and six SpikeTA effects (excluding the one neuron with seven effects from further analysis), and performed pairwise comparisons of these $R^2$ distributions with KS tests. The only significant differences found were for neurons with muscle field size of six. At the $P < 0.05$ level, this distribution was significantly different from that for each of the other muscle field sizes—one, two, three, four, and five—although only the six versus three and six versus five comparisons remained significant after Bonferroni correction for 15 tests. Contrary to expectation, however, $R^2$ values for neurons with muscle field size of six were on the whole higher than those for neurons in any other group. In monkey G, 27 of the present M1 neurons had SpikeTA effects in one muscle, 18 in two, seven in three, eight in four, three in five, four in six, six in seven, and one neuron had effects in eight muscles. Excluding the one neuron with effects in eight muscles, pairwise KS test showed $R^2$ distributions different at $P < 0.05$ comparing neurons only with a muscle field size of seven to those with one, four, or six effects. None of these remained significant after Bonferroni correction for 21 tests, although $R^2$ values for neurons with seven effects on the whole were higher than those in other groups. M1 neurons with large muscle fields thus may tend to have activity patterns somewhat more similar to those of the muscles they influence than do neurons with small muscle fields.

Reconstruction of EMG activity patterns from M1 neurons

Although the degree of similarity between the activity patterns of M1 neurons and the muscles in which they produced SpikeTA effects was limited, the presence of a significant SpikeTA effect indicates that the EMG activity of that muscle on average was facilitated or suppressed at a consistent latency relative to many if not all of the action potentials discharged by that M1 neuron. We therefore explored the extent to which the activity patterns of M1 neurons, acting simply through the inputs to a neuron indicated by their SpikeTA effects, could be combined to reconstruct the EMG activity pattern of that muscle.

The amplitude of SpikeTA effects may depend on several factors, including the range of conduction times from M1 neurons to motoneurons and from motoneurons to muscle, temporal facilitation at corticomotoneuronal synapses, persistent inward currents in motoneuron dendrites, the proportion of motoneurons facilitated or suppressed, the recorded waveforms of contributing motor unit action potentials (MUAPs), the number of motor units recorded by the EMG electrodes, cancellation of some MUAPs by superimposition with others, and the general background EMG level (Baker and Lemon 1995; Bennett and Lemon 1994; Botteron and Cheney 1989; Fetz and Cheney 1980; Hultborn et al. 2003; Lemon and Mantel 1989; Muir and Porter 1973; Palmer and Fetz 1985). Although the relationship between synaptic input strength and SpikeTA effect amplitude may be complex, in general more synaptic input would be expected to lead to discharge of more motoneurons and a larger SpikeTA effect. Indeed, a recent computer simulation indicated that once a substantial number of synapses become active, additional inputs to motoneurons sum linearly, albeit at reduced gain (Cushing et al. 2005). For the present reconstructions, we therefore used the MPI of each SpikeTA effect as an empirical measure of the relative strength of inputs to the motoneuron pool time-locked to the spikes of each M1 neuron.

Although each neuron in the present population was recorded at a different time, the pattern of EMG activity of each muscle across the 12 finger and wrist movements, averaged over multiple trials of each movement, was highly stereotyped across recording sessions. Therefore rather than convolving the spike train of each M1 neuron with its SpikeTA effect on a trial-by-trial basis to reconstruct the EMG activity pattern of a given muscle, we multiplied the average activity pattern of each neuron by the MPI of its SpikeTA effect in the target muscle (cf. Bennet and Lemon 1996) and these MPI-weighted neuron activity patterns then were summed.

The second row of Fig. 1 shows the MPI-weighted sum of the activity of all 35 neurons from monkey C that produced SpikeTA effects in FDPu. Although the pattern of this summed activity did not exactly match the average EMG pattern, the MPI-weighted sum did capture many features of the variation in FDPu EMG across the 12 movements. During extension movements, the MPI-weighted sum, like FDPu EMG, showed the largest bursts of activity during 4e and 5e, less during 1e, still less during 2e and 3e, and little if any activity during We. During flexion movements, an obvious mismatch was apparent during 2f, the MPI-weighted sum showing considerable activity when there was virtually none in the EMG; otherwise, however, the MPI-weighted sum, like the EMG, showed activity during 4f and 5f and less during Wf and 1f. During 3f the MPI-weighted sum showed suppression below 0, which would not be apparent in the EMG.

To quantify the degree of similarity between the MPI-weighted sum of M1 neuron activity and the average FDPu EMG, $R^2$ was computed for the correlation between the two waveforms during the 500 ms before and 200 ms after the end of movement (switch closure) across all 12 movements. For the example shown in Fig. 1, $R^2$ was 0.3261, a value greater than the mean of the individual neuron–average EMG $R^2$ values (0.1352), but not greater than the maximum individual neuron–EMG $R^2$ of 0.4312.

The modest $R^2$ for the correlation between the MPI-weighted sum of neuron activity and the average FDPu EMG activity might have arisen by chance alone. To examine this possibility, we reshuffled the neuronal activity patterns randomly among the 12 movements and 35 neurons (for example, the activity pattern of neuron C0106 during movement 3f might be reassigned to represent the activity pattern of neuron C0115 during movement 5e), formed a new MPI-weighted sum, and recomputed $R^2$. This process was repeated 5,000 times. Only 42 of the 5,000 (42/5,000 = 0.0084) resulting $R^2$ values were $>0.3261$, indicating that the $R^2$ value of 0.3261 would not have occurred by chance alone at the $P < 0.01$ level.

For each of the 17 muscles studied, $R^2$ was computed for the correlation between the MPI-weighted sum of M1 neuronal activity patterns and the average EMG activity pattern and the significance of the $R^2$ was estimated by bootstrapping as described above for FDPu (values given in Table 1). For no
muscle did $R^2$ for the MPI-weighted sum exceed the maximal $R^2$ value for an individual neuron. Nevertheless, for eight of the ten muscles studied in monkey C, $R^2$ values for the MPI-weighted sum were higher than the mean $R^2$ value for individual neurons and five of these eight were significantly different from chance by bootstrap ($P < 0.05$). In monkey G, $R^2$ values for the MPI-weighted sum were higher than the mean $R^2$ value for individual neurons for three of the seven muscles, although only one was significant. Because individual neuron $R^2$ values were not correlated with MPIs (Fig. 2), these significant reconstructions in six of the 17 (35%) muscles were unlikely to have resulted simply from heavily weighting a few neurons with activity patterns most similar to that of the EMG. Rather, these results suggest a tendency for the MPI-weighted sum to be more similar to the EMG than the activity pattern of the average individual neuron, consistent with the general observation that a population of neural responses, when summed, gives a more accurate reconstruction than single neurons.

To explore further the contributions of similar versus dissimilar neurons, $R^2$ was recomputed stepwise as progressively more neurons were incorporated in the MPI-weighted sum of activity patterns. The dot–dash line in Fig. 3 shows $R^2$ as the 35 neurons that produced SpikeTA effects in FDPu in monkey C were incorporated stepwise in the original order in which they were actually recorded (top to bottom of Fig. 1). Rather than rising steadily as more neurons were incorporated, this curve shows multiple rises and falls, indicating that whereas incorporating some of the 35 neurons increased the similarity between the MPI-weighted sum and the actual EMG, incorporating other neurons reduced the similarity. This is consistent with the observation that whereas some of the M1 neuron activity patterns resembled that of FDPu EMG activity, others did not.

To examine whether incorporating more neurons on average tended to increase $R^2$, we calculated the stepwise change in $R^2$ as the MPI-weighted sum was computed using the same 35 neurons in 1,000 randomly chosen orders. Additional curves in Fig. 3 show the mean ± SD, maximum, and minimum of $R^2$ as a function of the number of neurons incorporated for these 1,000 permutations. All these curves converge at the value of 0.3261, once all 35 neurons had been incorporated. The mean $R^2$ value (solid line) rose steadily as more neurons were incorporated, indicating that adding more neurons on average increased the similarity to FDPu EMG. An exponential fit to this mean curve approached an asymptote of $R^2 = 0.3543$, only slightly higher than 0.3261 obtained with 35 neurons. Similar exponential asymptotes for other muscles likewise were only slightly higher than the $R^2$ value obtained with the recorded neurons (Table 1). Consistent with prior observations that relatively small numbers of M1 neurons can predict motor output (Georgopoulos et al. 1999; Humphrey et al. 1970; Morrow and Miller 2003), the present observations suggest that simply incorporating a much larger number of neurons would not have substantially improved this type of reconstruction.

Following the minimum curve in Fig. 3 shows that 13 neurons could be incorporated without moving $R^2$ appreciably above 0. Adding in the remaining 22 neurons, however, moved $R^2$ from 0 toward 0.3261. Following the maximum curve shows that the highest $R^2$ (0.5429) was obtained when nine neurons had been incorporated. Adding more neurons thereafter lowered the maximum $R^2$ to 0.3261. A minority of M1 neurons that produced SpikeTA effects in FDPu thus had discharge patterns that made a relatively linear contribution to reconstruction of the FDPu EMG pattern. Other M1 neurons, although not having discharge patterns that closely resembled that of FDPu EMG, did represent some facilitation or suppression that contributed to sculpting a pattern that partially resembled the EMG. Still other neurons had activity patterns that did not contribute to reconstructing a pattern like that of the EMG, even though these M1 neurons also produced SpikeTA effects in FDPu.

Given that the MPI-weighted sum of activity patterns from a relatively small number of neurons could more closely resemble the EMG than a sum incorporating all neurons with SpikeTA effects in the muscle, we searched the pool of neurons with SpikeTA effects in a given muscle for the combination of up to five neurons whose MPI-weighted sum gave the highest $R^2$ value. (We limited our search to five neurons because of the long computational time required to search all possible combinations of larger numbers of neurons.) For each of the 17 muscles, the highest $R^2$ value using up to five neurons was substantially higher than the value obtained using all neurons (Table 1). Thus the set of M1 neurons with SpikeTA effects in a given muscle generally included some neurons that contributed to the similarity between the MPI-weighted sum and EMG activity pattern and other neurons that detracted from this similarity.

**Time shifts**

The SpikeTA effects used in the present study provide evidence of inputs arriving in the motoneuron pools at short latency relative to the spikes discharged by M1 neurons. All the present SpikeTA effects had a significant peak or trough falling within a window 6–16 ms after the triggering spikes.
We therefore considered it unlikely that the influence of these M1 neurons on EMG activity would show an appreciable time lag at the 20-ms resolution used here.

To examine this possibility, however, we shifted the EMG pattern of each muscle relative to the MPI-weighted sum of neuron activity patterns by one to four bins (±20, 40, 60, or 80 ms) and then recomputed $R^2$ for the relationship between the MPI-weighted sum and the time-shifted EMG pattern. As shown in Fig. 4, for all muscles studied in monkey C except Supinator (Sup), $R^2$ values decreased progressively as the EMG pattern was shifted to ±20, 40, 60, and 80 ms. For negative time shifts, however, $R^2$ increased substantially, reaching a maximum for each muscle at −40 to −60 ms. For FDPu, $R^2$ increased from 0.3261 with no shift to 0.4997 with a −60-ms shift. These observations suggest that in monkey C the discharge of M1 neurons that produced SpikeTA effects showed a time lead of 40–60 ms relative to EMG activity. A lesser tendency for $R^2$ to decrease with positive time shifts of the EMG pattern and to increase with negative time shifts could also be seen for some of the muscles studied in monkey G, although the changes were less dramatic and similar maxima with −40- to −60-ms shifts were not evident. These time shifts increased $R^2$ values largely by improving the temporal alignment between the bursts of neuron activity and the subsequent bursts of EMG that produced the finger and wrist movements.

These effects of time lead, particularly in monkey C, are beyond those attributable to the conduction and synaptic delays that contribute to the latency of the SpikeTA effects per se and are consistent instead with previous observations of time lead in the discharge of M1 neurons (Everts 1968; Humphrey et al. 1970; Morrow and Miller 2003; Schwartz and Adams 1995). The effects of time lead also are double those attributable to the 20- to 30-ms width of the synchrony SpikeTA effects included in the present reconstructions. We thus infer that M1 neurons that produce short-latency SpikeTA effects through mono-, di-, or oligosynaptic routes may also influence the same motoneuron pools at longer latencies. This additional time may be required for the integration of synaptic inputs needed to bring motoneurons to threshold as well as to recruit additional synaptic inputs that arrive by more indirect pathways.

DISCUSSION

How similar is the activity of motor cortex neurons and that of the muscles they control?

M1 neurons that produce SpikeTA effects in a given muscle often show discharge frequency modulation similar to the temporal modulation of the muscle’s EMG activity (Fetz and Cheney 1980; McKiernan et al. 2000). Studies showing such similarity typically have selected M1 neurons that discharge concurrently with muscles activated in one or two movements because spikes must occur concurrently with EMG activity for a SpikeTA effect to be detected. Other movements for which the M1 neuron might be active while the muscle is quiescent, or vice versa, may not be performed. M1 neurons that are inactive during the one or two movements examined might also produce SpikeTA effects in a particular muscle, although these effects will not be detected unless the neuron artificially is made to discharge concurrently with EMG activity (Kasser and Cheney 1983).

In the present study, recording each M1 neuron during 12 movements provided ample opportunity to observe instances of such neuron–muscle dissociation, which lowered the overall similarity between the activity patterns of M1 neurons and those of the muscles in which they produced SpikeTA effects. We considered the possibilities that including neurons with weak SpikeTA effects, with synchrony effects, and/or with projections that diverged to a large number of muscles, might have reduced the overall level of neuron–muscle similarity, but we found no systematic relationships between neuron–muscle

FIG. 4. Time shifts. For each muscle studied in each monkey, the similarity ($R^2$) between the MPI-weighted sum of M1 neuron activity patterns and the EMG activity pattern of the muscle was recomputed as the EMG pattern was shifted in time relative to the summed neuron pattern. Negative time shifts of the EMG pattern tended to increase $R^2$, indicating that the summed neuron pattern led the EMG. In monkey C, $R^2$ peaked at shifts of −60 to −40 ms, longer than the delay attributable to conduction delays in the pathways mediating SpikeTA effects.
similarity and any of these factors. We therefore conclude that the partial neuron–muscle similarity found here reflects the normal physiology of control from M1 during a relatively large repertoire of individuated finger and wrist movements. During such movements, M1 neurons, even those with relatively direct connections to spinal motoneuron pools, do not drive muscles to be active in patterns that simply follow the activity of M1 neurons. Rather, our results suggest that M1 neurons act as a network of diverse elements in controlling muscles during individuated movements.

Reconstruction of EMG activity from a pruned network

In general, the difficulty of obtaining physiological data on a mammalian neural network complicates examination of how such a network actually functions. The network between M1 neurons and spinal motoneuron pools provides an opportunity to approach this problem, however, because spike-triggered averaging (SpikeTA) of rectified EMG activity can provide evidence of inputs that arrive in a motoneuron pool at short latency relative to many or all of the spikes discharged by single M1 neurons. Whether such SpikeTA effects represent monosynaptic, disynaptic, or oligosynaptic connections between the M1 neuron and the motoneuron pool, these SpikeTA effects provide a measure of the sign and strength of the relationship between discharge of the neuron and time-locked, short-latency activation of the muscle. Furthermore, the same simultaneous recording of M1 neuronal discharge and EMG activity used to form the SpikeTA also documents the concurrent modulations of activity in the M1 neuron and the EMG activity generated by the motoneuron pool.

Our reconstruction approach was highly constrained. Every neuron that produced a significant SpikeTA effect in a given muscle was incorporated and every neuron that produced no SpikeTA effect was excluded. The weight of the network connection between each neuron and each muscle was assigned to be the MPI of their SpikeTA effect, with no adjustment of weights. In all but the final section of results, time lags between neuron and EMG activity were assumed to be <20 ms, based on the latency of SpikeTA effects. Even with these constraints, we were able to partially reconstruct the EMG activity patterns of multiple muscles from a simple network of M1 neurons, pruned of all neuron–muscle connections not documented by a SpikeTA effect, as illustrated schematically in Fig. 5. Although each neuron was recorded at a different time, the activity of all neurons recorded from a given monkey was summed as if they had been active simultaneously. For simplicity, we have dealt with the reconstruction of EMG activity in each muscle separately. However, because most of the individual M1 neurons had independent SpikeTA effects in multiple muscles and because in such cases the same pattern of neuron activity was used in the reconstruction of multiple EMGs, the present results represent the reconstruction of multiple EMGs from a network of M1 neuron inputs.

The overall performance of this pruned network can be summarized by the average $R^2$ of the correlations between the EMG activity of each muscle and the MPI-weighted sum of the M1 neuron population. With no time shifts, this average $R^2$ (from Table 1) was 0.2031 for all 17 muscles studied or 0.3426 for the six muscles with $R^2$ greater than that expected by chance alone (bootstrap $P < 0.05$). Using values after a −40-ms time shift, however, gives an average $R^2$ of 0.2638 for all 17 muscles or 0.4644 for the six muscles with significant $R^2$. The present reconstructions, pruned by the features of empirically measured SpikeTA effects, thus attained only a modest degree of similarity to the actual EMG patterns.

Beyond the pruned network

In contrast to our highly constrained pruned network, less-constrained reconstructions have achieved substantially higher degrees of similarity (Morrow and Miller 2003). Beyond the short-latency inputs to motoneuron pools represented by SpikeTA effects, what factors might contribute to the control of motoneuron pools from M1?

First, the present reconstructions were based solely on inputs from M1 neurons. Yet inputs from other sources—e.g., descending rubrospinal neurons (Mewes and Cheney 1991; Miller et al. 1993), spinal interneurons (Perlmutter et al. 1998), and peripheral afferents (Flament et al. 1992)—were also likely to have modulated EMG activity. M1 provides descending input to many of these other sources of input to motoneu-

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**FIG. 5.** Pruned network from M1 to muscles. Functional connections from each of 10 M1 neurons to the 10 muscles studied in monkey C are shown schematically. These 10 neurons were selected arbitrarily to illustrate the diversity of the 140 neurons from monkey C incorporated in the present analysis. Ellipses at either end of the row of M1 neurons emphasize that these 10 are only a sample of the population of M1 neurons included in the present analysis, which in turn is only a small sample of the active M1 neuron population. Ellipses at either end of the row of motoneuron pools emphasize that many more muscles are being influenced concurrently by the same population of M1 neurons. Thickness of each line is scaled to the MPI of the SpikeTA effect documented for that neuron–muscle pair. Any network connections not documented by a significant SpikeTA effect have not been drawn, effectively pruning the network of undocumented connections. Filled circles indicate facilitatory SpikeTA effects, open circles suppressive effects. Although the present study reconstructed the EMG of each muscle separately, because the same activity pattern of a given neuron was used in reconstructing all the EMGs to which it contributed, the results effectively examine the entire pruned network.
rons and may act in part by influencing them (Kuypers 1987; Lemon and Griffiths 2005).

Second, based on the short latency of SpikeTA effects, our reconstructions initially assumed a time lag of <20 ms between the discharge of M1 neurons and reconstructed EMG. M1 neurons, however, often show a substantial time shift relative to EMG activity (McKierman et al. 2000; Morrow and Miller 2003; Schwartz and Adams 1995). Indeed, shifting the MPI-weighted sum of neuron activity to lead the EMG by 40–60 ms increased $R^2$ for all but one of the muscles studied in monkey C. This temporal delay is two- to threefold longer than that attributable to conduction and synaptic delays in the pathways mediating SpikeTA effects. The addition of a few synaptic delays, each on the order of 0.5 ms, to allow for conduction through pathways including rubrospinal neurons and spinal interneurons would fall substantially short of accounting for a 40- to 60-ms lead. Much of this lead therefore may represent time required for integration of synaptic inputs to bring motoneurons to threshold. In addition, time may be required for M1 outputs to recruit rubrospinal neurons, spinal interneurons, and others, which in turn then provide additional inputs to the motoneurons.

Third, our approach assumes that the effects of different M1 neurons on the motoneuron pool are linear. Several previous studies of feline motoneurons showed that the effects on motoneuron firing produced by stimulating different pairs of premotor input populations do sum approximately linearly (Binder et al. 2002; Cushing et al. 2005; Powers and Binder 2000). However, many potential factors, such as active dendritic conductances that produce persistent inward currents (Hultborn et al. 2003; Lee and Heckman 2000; Prather et al. 2001), might produce nonlinear input/output relationships, contributing to discrepancies between the MPI-weighted sums of M1 neuron activity and the actual EMGs. Furthermore, when the muscle is quiescent much more synaptic input may be required to bring motoneurons initially to threshold than to produce further increases in EMG activity (Cheney and Fetz 1980).

Fourth, and finally, we used MPI as a constant measure of the average effect of each M1 neuron on the EMG activity of a given muscle, although the effect of an M1 neuron on a given motoneuron pool may vary depending on a number of factors including the level of activity both in the M1 neuron and in the motoneuron pool (Bennett and Lemon 1994; Fetz and Cheney 1987; Muir and Porter 1973; Schwartz and Adams 1995). Furthermore, the contribution to the MPI of an action potential from a motor unit may be greater when only a few other motor units are active than when numerous active motor units are generating a full interference pattern (Baker and Lemon 1995). Use of a constant MPI—which cannot account for such fluctuations in the relationship between the activity of an M1 neuron and the EMG it influences—thus may have limited the similarity between the present reconstructions and the actual EMG.

Control of skilled finger movements requires normal function of M1 and its direct corticomotoneuronal projections (Lawrence and Kuypers 1968; Porter and Lemon 1993; Schieber and Poliaakov 1998). Our findings suggest, however, that monosynaptic corticomotoneuronal connections that produce pure postspike effects and other relatively direct functional connections that produce pure + synchrony, late-widening, and synchrony SpikeTA effects, together account for only part of this control. The same M1 neurons that produce these short-latency effects may both exert substantial influence at longer latencies required for synaptic integration, and have additional influence that arrives in the motoneuron pools at longer latencies after integration in rubrospinal neurons and spinal interneurons. Such nonlinear effects in the process of integrating synaptic inputs, some of which arrive by other pathways, may in part dissociate the activity of motoneuron pools from that of the M1 neurons that participate in their control.

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References


