Published in final edited form as:

Science. 2015 November 6; 350(6261): 667–670. doi:10.1126/science.aaa8035.

Corticomotoneuronal cells are “functionally tuned”

Darcy M. Griffin^{1,2}, Donna S. Hoffman^{1,2,3}, and Peter L. Strick^{1,2,3,*}

¹University of Pittsburgh Brain Institute, Center for the Neural Basis of Cognition and Systems Neuroscience Institute, Pittsburgh, PA, USA

²Department of Neurobiology, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA

³Research Service, Department of Veterans Affairs Medical Center, Pittsburgh, PA, USA

Abstract

Corticomotoneuronal (CM) cells in the primary motor cortex (M1) have monosynaptic connections with motoneurons. They are one of the few sources of descending commands that directly influence motor output. We examined the contribution of CM cells to the generation of activity in their target muscles. The preferred direction of many CM cells differed from that of their target muscles. Some CM cells were selectively active when a muscle was used as an agonist. Others were selectively active when the same muscle was used as a synergist, fixator, or antagonist. These observations suggest that the different functional uses of a muscle are generated by separate populations of CM cells. We propose that muscle function is one of the dimensions represented in the output of M1.

Even simple movements are produced by complex patterns of muscle activity. For example, during wrist flexion, some muscles function as agonists to generate force in the direction of flexion. Other muscles function as fixators to prevent joint motion in the radial and ulnar direction, and still others serve as antagonists to brake movement and assist in speed control (1). Movement dexterity depends on the central control over the precise timing and amplitude not only of agonist muscle activity but also of the activity of muscles performing other functions.

We examined the contribution of corticomotoneuronal (CM) cells in the primary motor cortex (M1) to the generation and control of different patterns of muscle activity. CM cells are output neurons in M1 that have monosynaptic connections with motoneurons in the spinal cord. CM cells are located in a distinct caudal portion of M1 that is both phylogenetically and ontogenetically new (2, 3). We identified 41 CM cells and their target muscles using spike-triggered averaging (SpTA) of electromyographic (EMG) activity from 12 to 13 forearm muscles (4). We examined the directional tuning of CM cells and their target muscles while a monkey performed wrist movements in eight directions with the limb

*Corresponding author. strickp@pitt.edu.

SUPPLEMENTARY MATERIALS

www.sciencemag.org/content/350/6261/667/suppl/DC1

Materials and Methods

Figs. S1 to S3

References (7–16)

in three different postures (5). Twenty CM cells (~49%) were directionally tuned for all three wrist postures. Nearly all of these CM cells (19 of 20) were considered to be “muscle-like,” and none were considered to be “extrinsic-like” [see the supplementary materials (fig. S1)]. We compared the preferred direction of these CM cells (i.e., the direction of cell’s maximal activity) with that of their target muscles.

We found a marked disparity between the preferred directions of many CM cells and the preferred directions of their target muscles. Only 6 of 20 (30%) directionally tuned CM cells had preferred directions that matched or were within $\pm 45^\circ$ of their target muscles. An equal number of directionally tuned CM cells (6 of 20, 30%) had preferred directions that were opposite to or differed by $\pm 135^\circ$ from the preferred direction of their target muscles. The preferred directions of the remaining 8 CM cells were intermediate (i.e., differed by $\pm 46^\circ$ to $\pm 134^\circ$ from the preferred direction of their target muscles). Overall, the majority of the directionally tuned CM cells (14 of 20) had preferred directions that were distinctly different ($\pm 46^\circ$) from the average preferred direction of their target muscles.

One example of a disparity between the preferred direction of a CM cell and that of the single wrist muscle it facilitated [palmaris longus (PL)] is illustrated in Fig. 1 (CM cell 96). This CM cell also suppressed two digit muscles [flexor digitorum profundus (FDP) and extensor digitorum communis (EDC)] (Fig. 1A). When the limb was pronated (Pro), this CM cell was most active for movements to the 45° target, whereas the wrist muscle (PL) facilitated by this CM cell was most active for movements to the 180° target (compare Fig. 1B-Pro with Fig. 1D-Pro; also compare Fig. 1C-Pro, top, with Fig. 1C-Pro, bottom).

CM cell 96 displayed orderly shifts in its maximal activity to the 90° and 135° targets as the limb posture was rotated to Mid (midway between pronation and supination) and Sup (supination) (Fig. 1B-Mid and Fig. 1B-Sup; see also Fig. 1C-Mid, bottom, and Fig. 1C-Sup, bottom). The same rotation in limb posture also resulted in orderly shifts in the maximal activity of its target muscle (PL), but to the 225° and 270° targets (Fig. 1D-Mid and Fig. 1D-Sup; see also Fig. 1C-Mid, top, and Fig. 1C-Sup, top). Thus, the disparity between the preferred direction of CM cell 96 and that of the target muscle it facilitated was maintained across shifts in limb posture.

These observations make it unlikely that the activity of CM cell 96 contributed to the generation of the initial agonist bursts of activity in the muscle it facilitated. Instead, the activity of this CM cell was consistent with it contributing to the generation of antagonist bursts of activity in the muscle it facilitated (PL) (Fig. 1E). The cell’s activity also was consistent with its contributing to the prompt termination of activity in the muscles it inhibited (FCU and EDC) (Fig. 1E).

Another example of an extreme disparity between the preferred direction of a CM cell and that of its target muscles is shown in Fig. 2 (CM cell 200). This CM cell facilitated eight muscles: one wrist extensor [extensor carpi ulnaris (ECU)], three digit extensors [extensor digiti secundi et tertii proprius (ED23), extensor digiti quinti proprius (ED45), and EDC], one wrist flexor [flexor carpi ulnaris (FCU)], one digit flexor (FDP), one thumb abductor [abductor pollicis longus (APL)], and one elbow flexor [brachioradialis (BR)] (Fig. 2A).

When the limb was in Pro, CM cell 200 was most active for movements to the 180° target (Fig. 2B-Pro and Fig. 2C-Pro, bottom). Under the same conditions, the most strongly facilitated target muscle (ECU) was most active for movements to the 90° target (Fig. 2D-Pro and Fig. 2C-Pro, top). The other four directionally tuned muscles that were facilitated by CM cell 200 also had preferred directions that differed from the CM cell by more than 45° (Fig. 2C-Pro, top, and fig. S2).

CM cell 200 displayed orderly shifts in its maximal activity when the limb posture was rotated to Mid and Sup (Fig. 2B-Mid and Fig. 2B-Sup; see also Fig. 2C, bottom). The same rotations in the limb position also resulted in orderly shifts in ECU's maximal activity, but to different targets (Fig. 2D-Mid and Fig. 2D-Sup; see also Fig. 2C, top). CM cell 200 was most active for movements to the 225° target in Mid and to the 270° target in Sup. In contrast, ECU was most active for movements to the 135° target in Mid and to the 180° target in Sup. The other target muscles of CM cell 200 displayed similar shifts in their maximal activity associated with changes in limb position (Fig. 2C, top, and fig. S2). Thus, the disparity between the CM cell's preferred direction and the preferred directions of its target muscles was maintained across shifts in limb posture. Here again, our observations make it unlikely that the activity of CM cell 200 contributed to the generation of the initial agonist bursts of activity in the muscles it facilitated. Instead, the activity of this CM cell was consistent with its contributing to the generation of increases in activity that occurred when its target muscles were used as fixators or antagonists (Fig. 2E)

We examined the angular relationship between the preferred directions of individual CM cells and the preferred directions of their target muscles. We normalized the preferred direction of each facilitated muscle to 0° (Fig. 3, dashed gray line). Then, we plotted the preferred direction of each CM cell in relation to the normalized preferred direction of the muscle (Fig. 3, black lines). Because we examined neuron and muscle activity in three postures, this analysis resulted in three vectors for each CM cell-target muscle combination. The broad distribution of the vectors (Fig. 3) suggests that the agonist, synergist, fixator and antagonist functions of target muscles are each well-represented by the activity of individual CM cells.

This conclusion is supported by an examination of the angular relationships between individual CM cells and the specific target muscles they facilitated (Fig. 4). Nine muscles were the target of facilitation for more than one of the 20 directionally tuned CM cells in our sample. For eight of these muscles, the multiple CM cells facilitating the same muscle displayed different functional relationships. For example, FCR was facilitated by two different CM cells (Fig. 4I). The preferred direction of cell 115 was consistent with its contributing to the agonist function of the muscle, whereas the preferred direction of cell 103 was consistent with its contributing to the antagonist function of the muscle. Another compelling example is EDC, which was facilitated by five different CM cells in our sample (Fig. 4B). Agonist, synergist, fixator, and antagonist functions of EDC were represented by the preferred direction of at least one of the five CM cells in our sample that facilitated it. These results support the concept that the different functional uses of muscles are represented by separate populations of CM cells. This concept is further supported by the timing differences between CM cells that contribute to the agonist function of the muscles

they facilitated versus those that contribute to the antagonist function of the muscles they facilitated (fig. S3). CM cells that facilitated agonists were active before CM cells that facilitated antagonists. The greater delay between the onset of CM cell facilitation and the onset of antagonist activity may be due the arrival of the facilitation at a time when the antagonist motoneuron pool is relatively inactive and perhaps suppressed.

The key result of the present study is that for many CM cells there is a major disparity between the cell's preferred direction and the preferred directions of its target muscles. We interpret this result as indicating that individual CM cells are functionally tuned. Indeed, we provide evidence that some CM cells specifically contribute to the agonist function of a muscle, whereas other CM cells specifically contribute to the synergist, fixator, or antagonist function of the same muscle. From this perspective, the multiple functions of a target muscle are represented by the activity of separate populations of CM cells. The concept of functional tuning is supported by Muir and Lemon's (6) observation that some CM cells were more active during a precision grip, whereas others were more active during a power grip, even though both types of CM cells facilitated the same target muscles. In their case, like ours, CM cell activity was linked to the functional use rather than the magnitude of muscle activity.

A major question raised by our results concerns the origin of the functional tuning that we observed. It is possible that the functional tuning reflects an explicit representation of different motor functions in New M1, just as orientation and ocular dominance are explicitly represented in primary visual cortex. In this sense, the different motor functions of CM cells would be either categorically (e.g., agonist, fixator, and antagonist) or continuously represented. The results shown in Fig. 3 support a continuous representation. However, the broad directional tuning of CM cells and their target muscles could obscure a categorical representation if it exists.

It is also possible that functional tuning is an emergent property of New M1. The wrist movements and patterns of muscle activity required by our task are not part of the animal's natural repertoire. Thus, skilled performance of the task requires an animal to generate new patterns of muscle activity that are acquired through extensive practice. We have previously argued that "the direct access to motoneurons afforded by CM cells enables New M1 to bypass spinal cord mechanisms and sculpt novel patterns of motor output that are essential for highly skilled movements" (3). Thus, functional tuning of CM cells may emerge as part of the sculpting process during extended practice on the task. In any event, functional tuning, whether explicitly represented or an emergent property, reflects a clear expansion of the known motor dimensions that M1 generates and controls.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

We thank R. Dum for surgical assistance; M. Watach and K. Thiel for technical assistance; K. Reinert for statistical assistance; and M. Page (Great Island Software, Chatham, MA) and S. Hoffman (Reflective Computing, Olympia,

WA) for development of custom computer programs. This work was supported by funds from the Department of Veterans Affairs, Medical Research Service (P.L.S.) and NIH grants R01NS24328 (P.L.S.), P30NS076405 (P.L.S.), and FNS070366A (D.M.G.). The contents do not represent the views of the Department of Veterans Affairs or the United States Government. The supplementary materials contain additional data. All other data are available upon request from the corresponding author.

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Fig. 1. Disparity between the preferred direction of a CM cell (approximate extension) and its target muscle (approximate flexion)

(A) Spike-triggered averages of EMG activity triggered on spikes of CM cell 96 ($n > 27,000$ spikes). Horizontal lines show the baseline mean (center) and ± 2 SD of the mean (top and bottom). PL shows post-spike facilitation (red); EDC and FDP show post-spike suppression (blue). Asterisks indicate size of effect: *, 2 to 3.9 SD; **, 4 to 5.9 SD. (B) CM cell activity aligned on movement onset ($n = 13$ trials). Large black arrows indicate the target close to the neuron's preferred direction. Small black arrows and numbers to the right indicate the movement direction. (C) Preferred directions of the CM cell (black) and its target muscles. (D) Activity of PL during movement ($n = 13$ trials). Large red arrows indicate the target close to PL's preferred direction. (E) Activity of the CM cell and its target muscles in the MID posture aligned on movement onset for movements to the 90° target ($n = 37$ trials). Left dotted line is aligned with the peak of CM cell activity. Right dotted line is aligned with the peak of PL's activity.

Fig. 2. Disparity between the preferred direction of a CM cell (approximate flexion) and its target muscles (approximate extension)

See Fig. 1 legend for description. **(A)** Spike-triggered averages of EMG activity triggered on spikes of CM cell 200 ($n > 33,000$ spikes). ***, 6 to 8.9 SD; ****, 9 SD. **(B)** CM cell activity aligned on movement onset ($n = 8$ trials). **(C)** Preferred directions of the CM cell (black) and its target muscles. **(D)** Activity of ECU during movement ($n = 8$ trials). **(E)** Activity of the CM cell and its target muscles in the MID posture aligned on movement onset ($n = 26$ trials). Movements were to the 225° target. Left dotted line is aligned with the peak of CM cell activity. Right dotted line is aligned with the peak of ECU's activity.

Fig. 3. Spatial relationship between CM cells and their target muscles
 Preferred directions of 20 directional CM cells (black lines with arrows) in three postures. We normalized the preferred direction of each facilitated muscle to the 0° target (dashed vertical gray line with arrow). We plotted the preferred directions of each CM cell for the three postures (black lines with arrows) in relation to their target muscle.

Fig. 4. Preferred directions of different CM cells (colored arrows) that facilitated the same target muscle

Each numbered arrow is the average of three different postures for a single CM cell. The target muscles are (A) APL, $n = 6$ CM cells; (B) EDC, $n = 5$ CM cells; (C) ECU, $n = 6$ CM cells; (D) extensor carpi radialis brevis (ECRB), $n = 3$ CM cells; (E) extensor carpi radialis longus (ECRL), $n = 3$ CM cells; (F) ED23, $n = 3$ CM cells; (G) PL, $n = 3$ CM cells; (H) ED45, $n = 2$ CM cells; (I) flexor carpi radialis (FCR), $n = 2$ CM cells.