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Three-dimensional tuning profile of motor cortical activity during arm movements

[Running Head] motor cortical activity during arm movements

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Abstract

The neural firing activity in the primary motor cortex was modulated to the direction of hand movement. In contradiction to previous reports, a recent study found a non-uniform distribution of preferred directions of neurons while monkeys made center-out reaching movements in a horizontal plane. To re-examine the distribution of preferred directions in three-dimensional space, we recorded the activity of 117 arm-related neurons in the primary motor cortex and electromyographic signals of shoulder and upper arm muscles of a monkey while it performed center-out reaching movements towards 26 target points placed on a sphere-shaped workspace. We found that the distribution of preferred directions of neurons was non-uniform and that it was correlated to muscle activity and arm joint rotations.

Keywords: primary motor cortex, arm movement, directional tuning, preferred direction, electromyography, neural coding, spherical distribution, shoulder and upper arm muscles

Introduction

The interpretation of the activity of arm-related cells in the primary motor cortex (M1) has been discussed for several decades. The correlation between neural firing and the direction of hand movement observed by Georgopoulos et al. [1] implied i) the activity of motor cortical cells represents a higher-level parameter of hand movement rather than a lower-level parameter related to muscle activity, ii) the M1 activity during arm reaching movement is broadly tuned to the direction of hand movement, iii) each neuron has a preferred direction in which its activity is maximal. The tuning curve of neural firing is described by a cosine function, and the preferred directions are distributed uniformly throughout three-dimensional space [2]. Based on these findings, subsequent studies showed many parameters were correlated to M1 activity during reaching. In contrast, Todorov [3] hypothesized that M1 activity represents the activity of the muscle groups directly and that the higher-order parameters related to the activity of M1 cells is an epiphenomenon of the musculoskeletal system. Recently, Scott [4] found a non-uniform distribution of preferred directions of neurons and a correlation between this non-uniform distribution and peak joint power at the shoulder and elbow in two-dimensional arm movements.

To distinguish between these paradigms, we re-examined precisely the tuning profile of M1 activity during three-dimensional arm movements. Previous studies analyzed the three-dimensional tuning profile during arm movements in eight directions at most. In contrast, we recorded the neural activity during center-out reaching in 26 directions placed on a sphere. In the present study we found, i) the distribution of preferred directions of neurons was not uniform throughout three-dimensional space, ii) the spatial distribution of preferred directions was correlated with the EMG activity of arm muscles and the joint rotations of the elbow and shoulder.

Materials and Methods

Behavioral task

Prior to the experiment, a female rhesus monkey (*Macaca mulatta*; body weight 4.0 kg) was trained to perform a simple reaching task. It was cared for in the manner described in the Guiding Principles in the Care and Use of Animals in the American Physiological Society. The monkey sat on a chair in front of two industrial robots (A255, CRS Robotics, Burlington, Ontario, Canada) in the dark. Each robot had a single hand equipped with a push button with an LED (a red circle 3 mm in diameter) that indicated the start position or goal position in three-dimensional space. The position of the robot hand was controlled through a personal computer. The start position was placed in the midsagittal plane at eye level 17 cm in front of the monkey. The goal position was any one of 26 positions on an imaginary sphere of 12 cm radius centered at the start position (Fig. 1A).

The reaching task started with the movement of the robots. With both LEDs turned off, the hand of one robot moved to a start position while the hand of the other robot moved to a goal position. Once the robots had completed their respective movements, the LED of the start position was turned on. The illumination of the start position was not strong enough for the monkey to see the goal position. The monkey had been trained to push the button with its right hand within one second after the appearance of the start position. A variable length of time after the monkey pushed the button (1-1.5 sec.), the LED of the goal position was turned on and the LED of the start position was turned off simultaneously. In order to receive the goal of a little juice, the monkey was required to move her right hand to the goal position within 1 second after the goal was illuminated. After the reaching movement, the monkey must keep pushing the goal button for a variable period of time (1-1.5 sec.). Her left hand was strapped to the chair and her head was prevented from moving by a head holder implanted in the skull. Although her eye position was recorded using an implanted scleral search coil, the findings on her eye movements are not described in this paper. Her eye movement was not bound at all during the task. The reaching movements toward the 26 directions were repeated eight times in a randomized-block design. One block of recording consisted of 208 trials lasting about 35 minutes in total.

Neural recording

The activity of single neurons in the proximal arm region of the primary motor cortex of the left hemisphere was recorded extracellularly using a seven-channel multi-electrode recording system (System-Eckhorn, Thomas Recording, Marburg, Germany). The electrodes were glass-coated tungsten-platinum wires. To assess the related area of each neuron, we checked the cell activity while an experimenter moved the monkey's joints (hand, elbow and shoulder) after every recording session. All spike data were checked carefully after each recording, and noise and irregular spike data were removed offline.

EMG recording

After the neural recording sessions, the EMGs of nine muscles (*Triceps lateralis, Triceps longus, Biceps longus, Teres major, Pectoralis major, Trapezius par caudalis, Trapezius par rostralis, Spinodeltoideus and Cleidodeltoideus*) were recorded during the execution of the 3-D motor task. Signals were acquired by using Teflon-coated multistrand stainless steel intramuscular electrodes. Electromyographic activity was preamplified and recorded with a sampling rate of 100 Hz. The recorded data were rectified online.

Hand path recording

To record the arm positions online, infrared markers were attached to the wrist, the center of the forearm, the elbow and the center of the upper arm. The positions of the infrared markers were recorded by Optotrak (Northern Digital Inc., Waterloo, Ontario, Canada) every 20 msec. The hand position, elbow joint angle and three shoulder joint angles (horizontal, vertical and inner/outer rotation angles of the upper arm) were calculated geometrically by the positions of the markers, assuming that the arm is a two-link model.

Statistics

The mean firing rates of neurons from the time the peripheral target appeared to the time the monkey pushed the button (RMT, reaction time + movement time) were calculated in each direction for each trial. The mean length of the mean firing rates was analyzed by a nonparametric "bootstrapping" test [5] to identify whether or not the neural firing rates were tuned directionally. The extent of directional tuning in three-dimensional space was assessed using the standard cosine function [2].

The standard cosine function has the general form

$$f = b + k \cos \theta_{CM}$$

where f is the mean firing rate and b, k are regression coefficients, θ_{CM} is the angle formed by the cell's preferred direction and the direction of hand movement. The degree of fitness was assessed by the multiple regression F-test.

Results

The monkey moved her hand almost straight from the starting position to the targets (Fig. 1B). The average time it took the monkey to react to the target and push the button was 877 msec. The activity of each of 117 cells was recorded from M1 of the contralateral hemisphere. Through passive movement of the arm, we identified the areas of the body to which 68 of the 117 cells were related. The activity of 61 of the 68 cells (90%) was related to the shoulder and/or elbow. The activity of the remainder (7 cells, 10%) was related to wrist rotation or stimulus to the back, chest or lateral side of the trunk. Although these 7 cells were not purely arm-related, we included them in the data analysis to clarify the properties of all recorded cells.

As in previous studies, the activity of most cells (106/117, 91%) was modulated directionally during RMT (Bootstrapping test, $P < 0.01$), and most directional cells (89/106, 84%) showed a good fit to the cosine tuning model (F-test, $p < 0.05$). These findings coincide with those of previous studies [2][6]. In contrast with those two studies, however, the distribution of preferred directions of neurons was non-uniform (Rayleigh test, $P < 0.05$; Fig. 2B). Most of the preferred directions of neurons were placed in the upper hemisphere (61/89, 69%; chi-square test, $P < 0.05$). A small percentage of the preferred directions of neurons (9/89, 10%; chi-square test, $P < 0.05$) were placed in the lower-right quadrant.

The EMG activities of all muscles during RMT were directionally modulated (Bootstrapping test, $P < 0.01$) and showed a good fit to the cosine tuning model (F-test, $p < 0.05$). Fig. 2B shows the preferred directions of all muscles. The distribution was not uniform (Rayleigh test, $P < 0.01$). The contour plot in Fig. 2B shows the average of the standardized activity of all muscles. The muscular activity in the lower-right quadrant was significantly smaller than in the other quadrants (Wilcoxon-Mann-Whitney test, $P < 0.05$). The non-uniform distribution of the muscular activity was similar to that of the preferred directions of neurons.

To examine the correlation between neural activity and the joint rotations of the elbow and shoulder, we calculated the joint angles rotated during arm movements. Fig. 2C shows the summations of the elbow joint and three shoulder joint angles in each direction. The summation of joint rotation angles in the lower-right quadrant was significantly smaller than those in the other areas (Wilcoxon-Mann-Whitney test, $P < 0.05$). The distribution was similar to those shown for EMG and neural activity.

Discussion

The purpose of this study was to re-examine the tuning profile of the neural activity in the primary motor cortex related to arm movement during the execution of a three-dimensional task. In contradiction to previous studies, the non-uniform distribution of the preferred directions of neurons, found recently in two-dimensional experiments, was also observed in three-dimensional experiments. Analysis of the data showed that the distribution of neural activities was correlated to EMG activities of the shoulder and upper arm muscles. This contradiction to previous studies could be attributed to the different location of the workspace with respect to the position of the monkey. In fact, we placed the starting position at eye level, whereas a previous study [2] placed it at shoulder level. Another study reported that the distribution of preferred directions varies with the location of the workspace [6]. Tanaka [7] suggested that this observation was due to the dependence of the movement direction, represented in one of the joint-related coordinate systems, on the posture of the arm. The similarity between the distribution of cell activity, EMG activity and joint rotation angles, observed in the present experiments, suggests the effect of muscle action in M1 cell activity. The effect of gravity may explain why most preferred directions of neurons were placed in the upper hemisphere. However, the lack of neurons in the lower-right quadrant coincides with the distribution of joint rotation angles acquired regardless of the effects of gravity. The kinematic structure of the arm was an important factor in determining the non-uniform distribution of preferred directions of neurons. These findings could support the hypothesis that the firing of M1 cells represents the activity of the muscle groups directly and that the higher-order parameters related to the activity of M1 cell are an epiphenomenon of the musculoskeletal system [3].

In the present experiment, the EMG activity and the neural firing activity were not recorded simultaneously because the animal could have experienced stress if it had had to work for several days with electrodes implanted under its skin. However, no significant difference in the performance of the tasks appeared, and a clear correlation between the EMG activity and the joint angles showed the consistency in performance.

Similarities between cell activity, EMG activity and joint rotation angles were found at the population level of analysis. No correlation was found between joint angle or EMG with individual cell activity. Various types of temporal patterns of cell activity were found, as in many previous studies [8]. The temporal patterns of these findings should be examined in future studies.

Conclusion

In contradiction to previous studies, the distribution of preferred directions of neurons in primary motor cortex was not uniform throughout three-dimensional space. The spatial distribution of preferred directions was correlated with the EMG activity of arm muscles and the joint rotations of the elbow and shoulder. These findings suggest that the directional tuning of activity of motor cortical cells is attributed to a lower-level parameter related to muscle activity rather than a higher-level parameter of hand movement.

References

1. Georgopoulos AP, Kalaska, JF, Caminiti R et al. J Neurosci 2, 1527-1537 (1982).
2. Schwartz AB, Kettner RE, Georgopoulos AP. J Neurosci 8(8), 2913-2927 (1988).
3. Todorov E. Nature Neurosci 3(4), 391-398 (2000).
4. Scott SH, Gribble PL, Graham KM et al. Nature 413, 161-165 (2001).
5. Crammond DJ, Kalaska JF. Exp Brain Res 108, 45-61 (1996).
6. Caminiti R, Johnson PB, Urbano A. J Neurosci 10(7), 2039-2058 (1990).
7. Tanaka S. Neurosci Lett 180, 83-86 (1994).
8. Kalaska JF, Cohen DAD, Hyde ML et al. J Neurosci 9(6), 2080-2102 (1989).

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Figure legends

Fig. 1

(A) Perspective view of target arrangements and the Mercator projection. The target labeled 0 is the starting position of arm movement, and the other targets are the goal positions. The origin of the coordinate system (X=Y=Z=0) is the midpoint of the plane between the monkey's eyes. **(B)** Hand paths during arm reaching movements.

Fig. 2

(A) Mercator projection of the peripheral targets.

(B) Spatial distribution of preferred directions of neural activity in the primary motor cortex. The contour plot represents the average of standardized activities of all muscles. The bright intensity indicates high activity and the dark one indicates low activity. The indices represent the preferred directions of arm-related muscles. (*A Triceps lateralis; B Triceps longus; C Biceps longus; D Teres major; E Pectoralis major; F Trapezius par caudalis; G Trapezius par rostralis; H Spinodeltoideus; I Cleidodeltoideus*).

(C) Directional change of arm joint rotation angles during arm reaching movements. The contour plot represents the summation of the angles of elbow joint rotation and shoulder joint rotation.

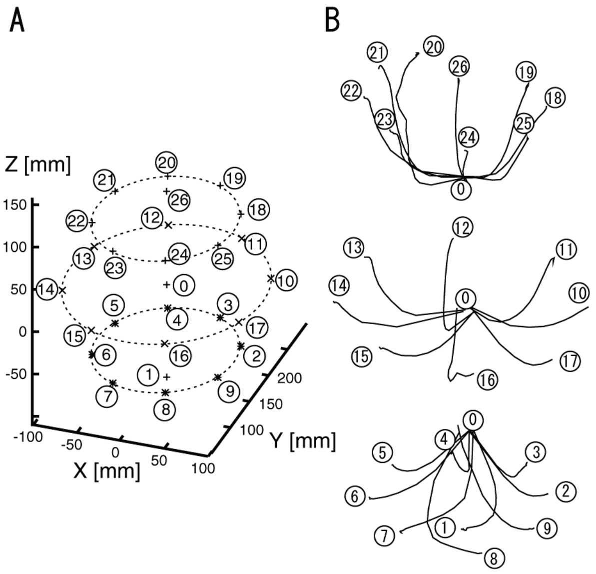
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Fig.1

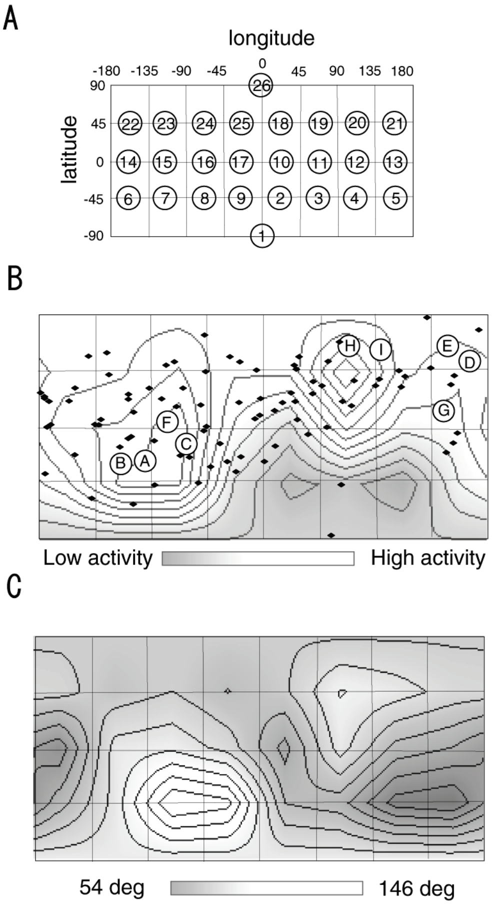
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Fig.2