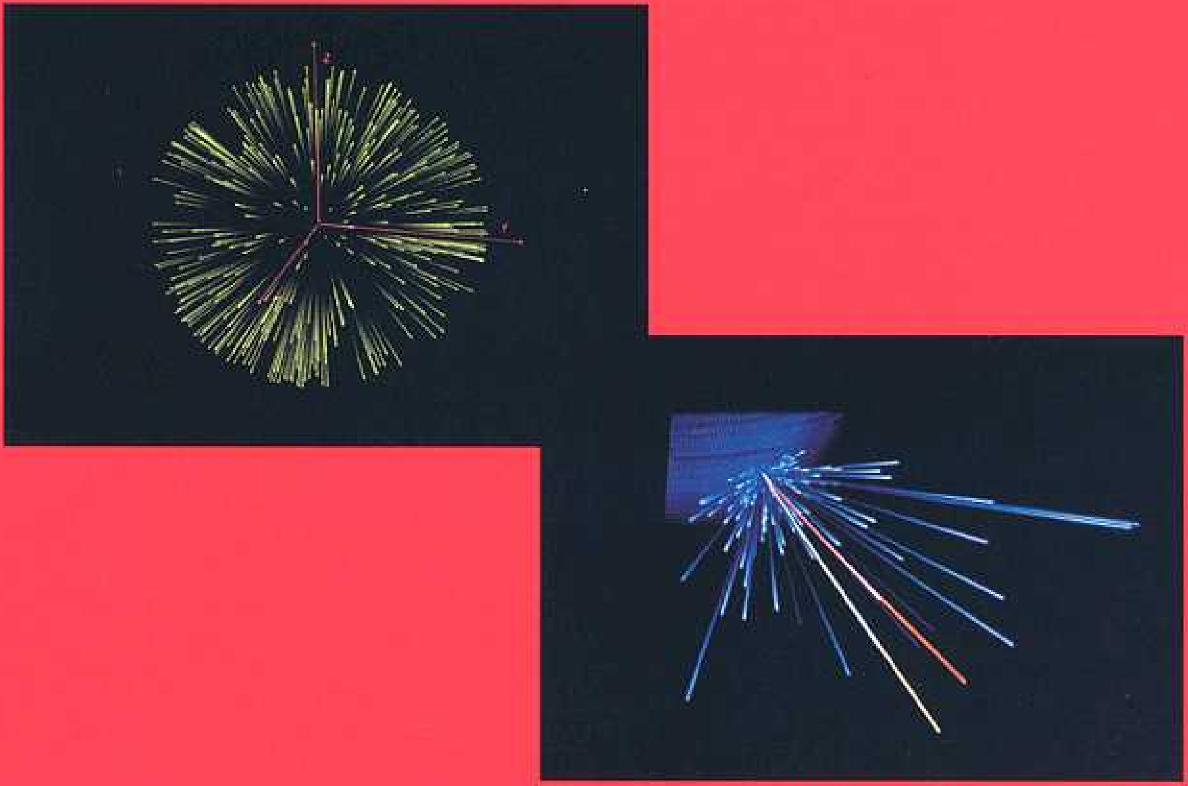
INDEX ISSUE

The Journal of LABORATORY and CLINICAL MEDICINE

The official publication of the Central Society for Clinical Research

VOLUME 124 DECEMBER 1994 NUMBER 6



The electricity of behavior (see page 862)

68th ANNUAL MEETING

Central Society for Clinical Research Sept 28-30, 1995 Drake Hotel, Chicago, Ill.

Abstract deadline June 1, 1995

Mosby
ISSN 0022-2143

REVIEW ARTICLE

Behavioral neurophysiology of the motor cortex

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The study of the motor cortex in behaving monkeys during the past 20 years has provided important information on the brain mechanisms underlying motor control. With respect to reaching movements in space, several aspects of motor cortical function concerning the specification of the direction of movement have now been elucidated and are reviewed in this article. The activity of single cells in the motor cortex is broadly tuned with respect to the direction of reaching, so that the discharge rate is highest with movements in a preferred direction and decreases progressively with movements made in directions more and more away from the preferred one. Thus the neural command for the direction of reaching can be regarded as an ensemble of cell vectors, with each vector pointing in the cell's preferred direction and having a length proportional to the change in cell activity. The outcome of this population code can be visualized as a vector that points in the direction of the upcoming movement during the reaction time, during an instructed delay period, and during a memorized delay period. Moreover, when a mental transformation is required for the generation of a reaching movement in a different direction from a reference direction, the population vector provides a direct insight into the nature of the cognitive process by which the required transformation is achieved. (J Lab Clin Med 1994;124:766-74)

Most of the brain deals with motor function. A number of areas of the cerebral cortex and a number of subcortical structures, including the cerebellum and large portions of the basal ganglia, brainstem, and spinal cord, are concerned with the specification, control, and ongoing modification of self-initiated or stimulus-elicited movements. The variety and complexity of the structures involved and the intricacy of the aspects of motor function controlled can be appreciated by considering the large variety of motor syndromes produced by disease processes affecting motor structures. The cardinal signs of these defects are well known even to the general physician. For example, cerebellar lesions result in dysmetria in reaching, usually overshooting the target; basal ganglia lesions manifest in very slow movements (as in Parkinson's disease) or in violent throwing movements (as in hemiballismus); and cortical damage can bring out a variety of signs, ranging from weakness and paralysis to optic ataxia, a fascinating disorder of visually guided reaching. Practically all of these areas cooperate to produce smooth, graceful, and apparently effortless movements such as reaching to objects of interest, drawing, and handwriting. This review deals with the workings of a particular brain area, namely the motor cortex.

On the lateral surface of the cerebral hemisphere, the motor cortex lies anterior to the central sulcus and comprises the precentral gyrus. The effects of lesions of the motor cortex can vary in severity, depending on the extent of the lesion. Total disconnection of the motor cortex from subcortical structures, as seen in a stroke at the level of the internal capsule, leads to a devastating hemiplegia, but localized destruction of the motor cortex usually leads to weakness or paresis

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Supported in part by United States Public Health Service Grant NS17413.

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0022-2143/94 $3.00 + 0 **5/1/59624**

of a specific body part, depending on the location of the lesion within the motor cortex. The production of movements by electrical stimulation of the surface of the motor cortex of dogs[1] and monkeys[2] established the motor function of the precentral gyrus and led to a series of detailed experiments by which the somatotopic organization of the motor cortex was revealed. These reached their height at the neurosurgical table at which the effects of electrical stimulation of the motor cortex of awake human subjects were observed during operations for the purpose of removing an epileptic focus.[3,4] These studies confirmed for human subjects what was known for animals, namely (1) that electrical stimulation of the motor cortex elicits movements of contralateral body parts and (2) that movements of different body parts are represented in an orderly, somatotopic fashion in the motor cortex.

The motor function of the precentral gyrus and an initial suggestion for a topographic organization were postulated by Hughlings Jackson in the nineteenth century on the basis of observations of the spread of *grand mal* or *Jacksonian* seizures.[5] Jackson speculated about the functional organization of the motor cortex (the "middle motor centre"), a subject still unresolved to a good extent. He postulated three levels of "motor centres":

> (1) The anterior spinal horns and their homologues higher up (nuclei of motor cranial nerves) are the lowest motor centres (both of the cerebral and cerebellar systems). These lowest motor centres, with the corresponding sensory centres, make up the lowest level of evolution of the central nervous system. (2) The convolutions of the Rolandic region are the middle motor centres. With the corresponding sensory centres, they make up the second or middle level of the central nervous system. (3) The prae-frontal lobes are the highest motor centres of the cerebral system With the corresponding sensory centres, they make up the third or highest level of the central nervous system, that is, the 'organ of mind' . . . .[5]

He based the distinction among these levels on the degree of combinatorial representation of muscles to form complicated motor acts. He stated that

> To speak figuratively, the central nervous system knows nothing of muscles, it only knows movements. . . . There are, we shall say, thirty muscles of the hand; these are represented in the nervous centres in thousands of different combinations—that is, as very many movements; it is just as many chords, musical expressions and tunes can be made out of a few notes. I now speak of the representation of the muscles of the hand in the three orders of motor centres just spoken of. (1) In some lowest motor centres . . . these muscles are represented in numerous different combinations, as simple and very general movements. (2) In the middle motor centres . . . the same muscles are represented (re-represented) in still more numerous different combinations, as complex and special movements. (3) In the highest motor centres . . . the same muscles are represented (re-re-represented) in innumerable different combinations, as most complex and most special movements.[5]

Therefore, for Jackson "higher" meant a larger number of degrees of freedom in combinations and recombinations of motor elements. This idea is still being actively investigated.

The findings summarized above from lesion and electrical stimulation studies, as well as from observations of motor seizures, provided a wealth of information but fell short of addressing the question of function of the motor cortex at the cellular level. For that purpose a new technique was needed, namely the possibility to record the activity of single cells during behavior. Indeed, this technique was developed in 1957 by Ricci et al.[6] and was perfected and applied later to motor cortex by Evarts.[7] In this combined behavioral-neurophysiologic experiment, animals, usually monkeys, are trained to sit on a primate chair and perform various tasks.[8] During electrophysiologic recording sessions, microelectrodes are inserted into the brain area of interest through the dura and the activity of single cells is recorded while the animal performs the task. This setup provides a direct tool, one with fine grain by which the brain mechanisms underlying performance can be studied. Most of the results discussed here come from experiments that investigated the activity of single motor cortical cells and cell populations during the generation of reaching movements.

REACHING MOVEMENTS

Reaching out toward objects of interest is very common in the behavioral repertoire of primates. Reaching serves to position the hand at desired points in immediate extrapersonal space, literally "within reach." It is accomplished by well-coordinated and tightly coupled motions at the shoulder and elbow joints[9] and is usually directed to visual targets. During reaching, the hand is preshaped according to the characteristics of the object that will be manipulated.[10] Thus, behaviorally, reaching is a complex act that involves sensory-motor integration and the concurrent preparation for handling the object of interest.

The spatial parameters of a reaching movement are its direction and amplitude. The results of several studies support the view that these two parameters reflect separate processing constraints. First, accuracy of pointing is much better for direction than for amplitude.[11] Second, when subjects are forced to make a motor response before completion of the reaction time, the direction and amplitude of the motor trajectory are affected differently.[12] And third, peripheral sensory neuropathy affects differentially the direction and amplitude of the movement.[13] An important role of proprioceptive information in the specification of the motor command for the movement vector is also suggested by the finding that the pattern of electromyographic activity that initiates a movement reflects both the posture of the arm and the direction of movement in space.[14]

Finally, it should be noted that the generation of arm movements is not a stereotypic process but seems instead to involve processing that is subject to interference by distracting sensory and cognitive loads[15]; this is in contrast to visually evoked saccades that are unaffected under such conditions. This susceptibility of the arm movement-generating process to distracting (or competing) processes underscores the complexity of the central nervous processes involved in this function. We now examine some of the neurophysiologic aspects of the movement-generating processes.

DIRECTIONAL TUNING OF SINGLE MOTOR CORTICAL CELLS

The directional selectivity of motor cortical cells was studied by training rhesus monkeys to point to visual targets in two-dimensional or three-dimensional space. In the two-dimensional experiments, monkeys moved an articulated manipulandum toward visual targets on a planar working surface[16]; in the three-dimensional studies, monkeys reached freely to target buttons.[17] The electrical activity (action potentials, neural impulses) of single cells in the forelimb area of the contralateral motor cortex were recorded extracellularly while the monkeys performed the task. The main finding from these studies was that the activity of single motor cortical cells is broadly tuned around a "preferred direction"; cell discharge is highest with movements in that direction and decreases gradually with movements made in directions farther and farther away from the preferred one. This is illustrated in Figs. 1 and 2 for the two-dimensional and three-dimensional case, respectively. The directional tuning can be described as a linear function of the cosine of the angle formed between the direction of the movement M and the cell's preferred direction C (Fig. 2, *B*). The preferred directions of individual cells differ among cells and range throughout the directional continuum[17] (Fig. 3).

CODING OF THE DIRECTION OF REACHING BY THE NEURONAL POPULATION

The results summarized above indicate that single motor cortical cells are engaged with reaching in different directions throughout two-dimensional or three-dimensional space. From this it follows that for a movement in a particular direction, a population of cells with various preferred directions will be active. How could such a neuronal population encode uniquely a particular direction of reaching? We proposed a code for that problem, first for two-dimensional reaching[18] and then for three-dimensional reaching.[19,20] In brief, the motor cortical command for movement direction can be regarded as the weighted sum of vectorial contributions of individual cells: each cell "votes" in the direction of its preferred direction, and the vote is weighted, for a particular direction or reaching, by the change in cell activity during that movement. The vector sum of these contributions (the "population vector") points in or near the direction of reaching. Fig. 4 illustrates the results obtained for three-dimensional reaching.

The vectorial representation of directional information at the motor cortical level is a distributed code in the sense that each element (i.e., a neuron) carries only part of the information, whereas the neuronal population determines uniquely the direction of reaching. It is interesting that a population size of about 150 to 200 cells can provide a good estimate of the direction of the population vector, within 10 to 15 degrees.[20] With respect to cortical location, it is noteworthy that neuronal populations in different cortical layers can provide adequate coding for movement direction; for example, the population vectors calculated from cells located in layers II and III or in layers V and VI of the motor cortex both predict well the direction of reaching.[21] Given that cells in different layers project to different brain regions,[22] this finding suggests that the same directional information may be distributed to various brain areas.

NEURAL EVENTS SIGNALING PREPARATION FOR MOVEMENT

A common case of preparing to move is when a movement is produced in response to a visual stimulus: then some time intervenes between the occurrence of the stimulus and the beginning of the movement, which is the traditional reaction time. In other cases a delay can be imposed so that the movement will be initiated after a period of waiting, while the stimulus is still present. These *instructed delay paradigms* probe a step further the representation of planned movements, in the sense that there is not an immediate motor output while the representation is being kept active. Finally, a specific case of delayed tasks involves movements that have to be produced on the basis of information kept in *memory*. The difference from the instructed delay task is that now the stimulus defining the direction of the movement is turned off after a short period of presentation and the movement is triggered after a delay by a separate "go" signal. Thus information concerning the intended move-

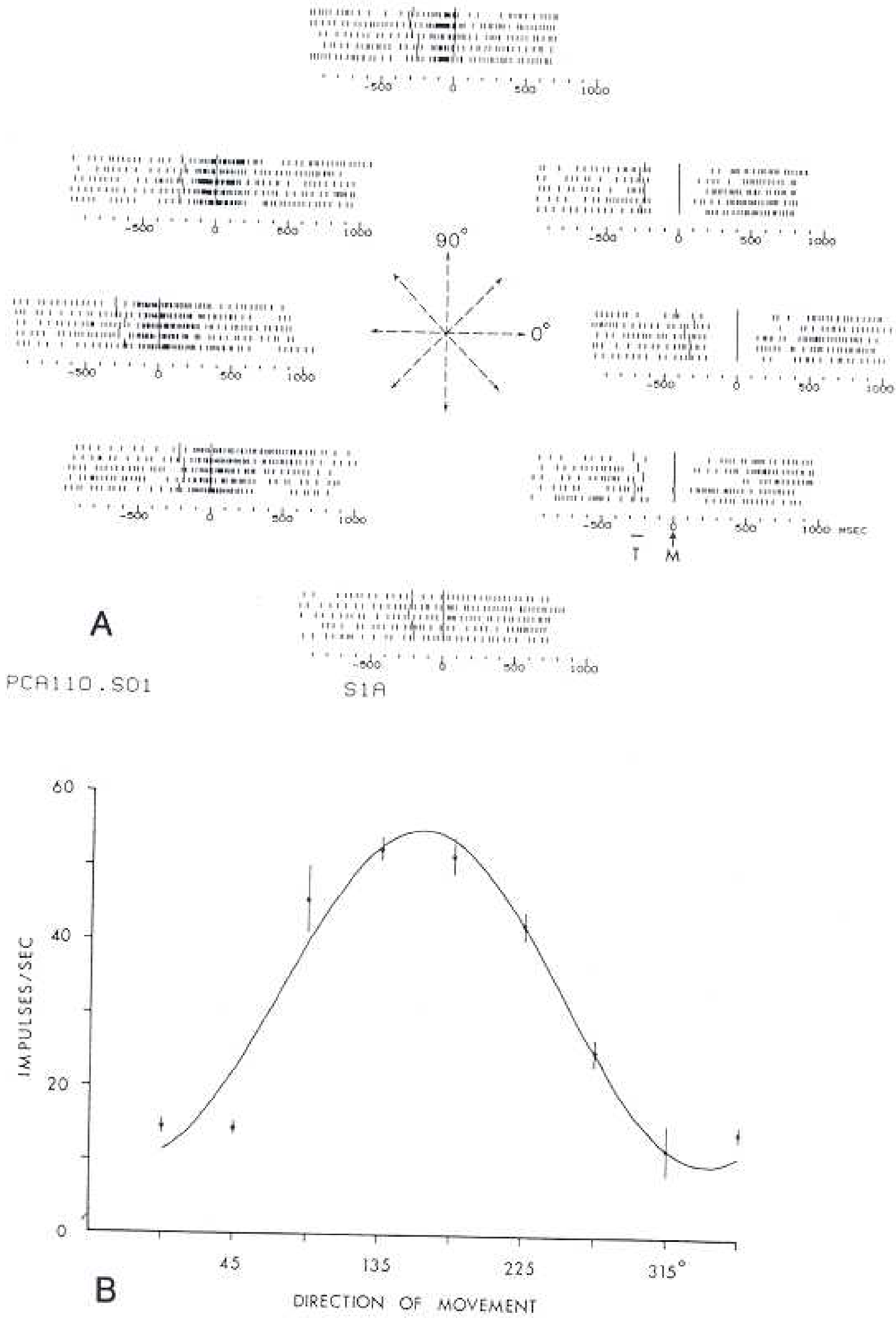

Fig. 1. Directional tuning in two-dimensional space. **A,** Impulse activity during five trials in which equal amplitude movements were made in eight directions from the center of the working surface toward peripheral targets, as indicated by the diagram in the center. The rasters are aligned to the onset of movement *(M)*. Longer vertical bars preceding movement onset denote the time of stimulus onset *(target)* onset *(T)*. **B,** The average frequency of discharge during the time interval from the onset of the target to the end of the movement is plotted against the direction of the movement. Points are means of five trials ± SEM; the curve is a fitted sinusoidal function. (From Georgopoulos et al. J Neurosci 1982;2:1527-37. By permission.)

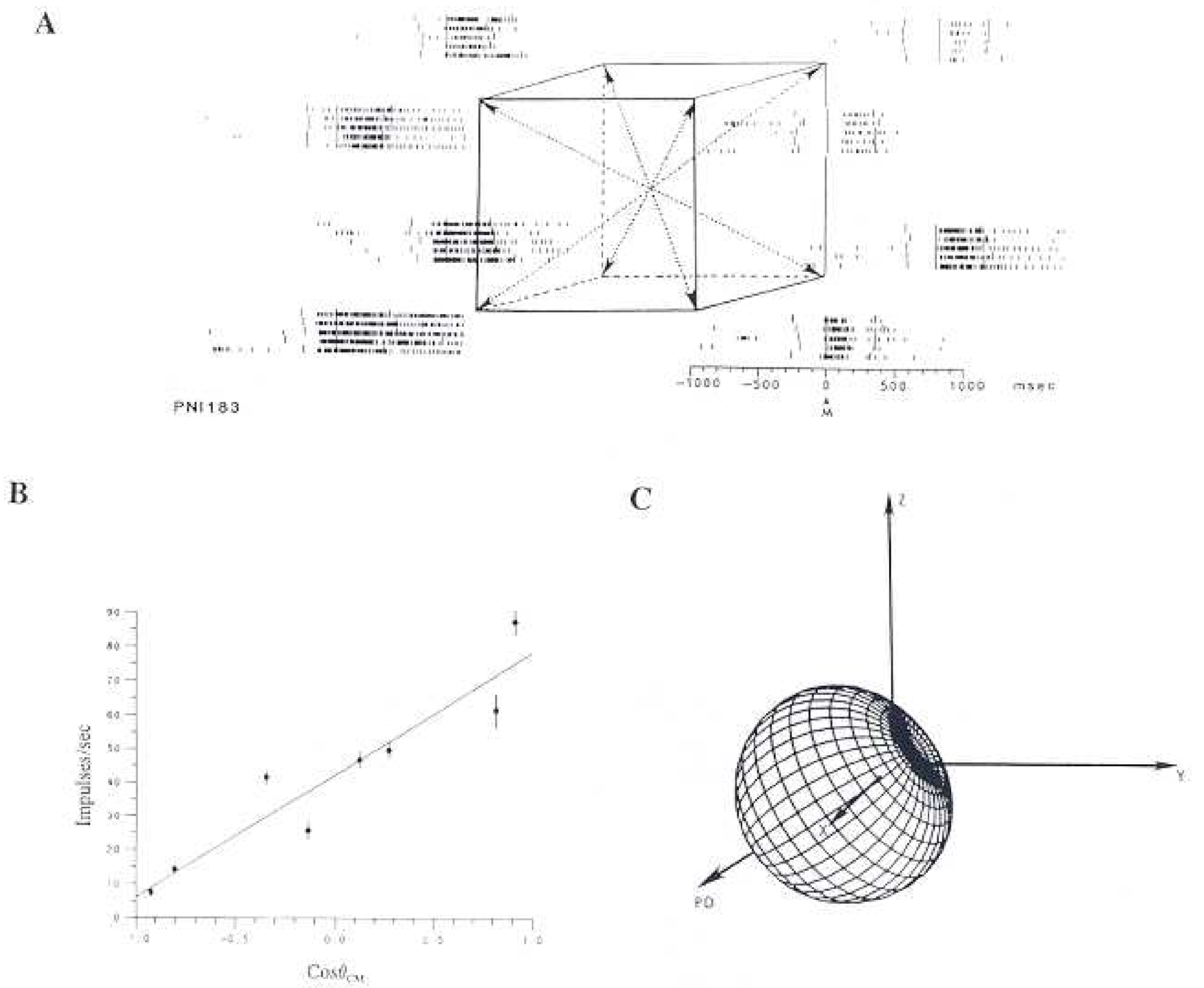

Fig. 2. Directional tuning in three-dimensional space. All data are for one motor cortical cell. **A,** Impulse activity *(short bars)* during movements in different directions *(arrows)*. Rasters of five repeated trials for every movement direction are aligned with the onset of movement *(M)*. *Longer bars* preceding and following the movement onset indicate the onset of the target and the end of the movement, respectively. **B,** Mean discharge rate (± SD) from onset of target to end of movement is plotted against the cosine of the angle θ formed between the direction of the movement and the cell's preferred direction. **C,** Predicted tuning volume based on cosine tuning function. *PD,* Preferred direction. (From Schwartz et al. J Neurosci 1988;8:2913-27. By permission.)

ment has to be retained during the memorized delay.

In all three cases above the representation of information about the intended movement can be studied under different conditions that impose different constraints on the system. It would be interesting to know whether this representation could be identified and visualized during the reaction time, the instructed delay and the memorized delay periods. Because the information assumed to be represented is about direction, the neuronal population vector could be a useful tool by which to identify this representation. For that purpose the population vector was computed every 10 or 20 msec (1) during the reaction time,[20,23] (2) during an instructed delay period,[24] and (3) during a memorized delay period.[25] The results were clear: in all these cases the population vector pointed in the direction of the planned movement during the above time periods. These findings underscore the usefulness of the population vector analysis as a tool for visualizing representations of the planned movement and show that in the presence or absence of an immediate motor output, as well as when the directional information has to be kept in memory, the direction of the intended movement is represented in a dynamic form at the ensemble level. These results also document the involvement of the motor cortex in the representation of intended movements under various behavioral conditions.

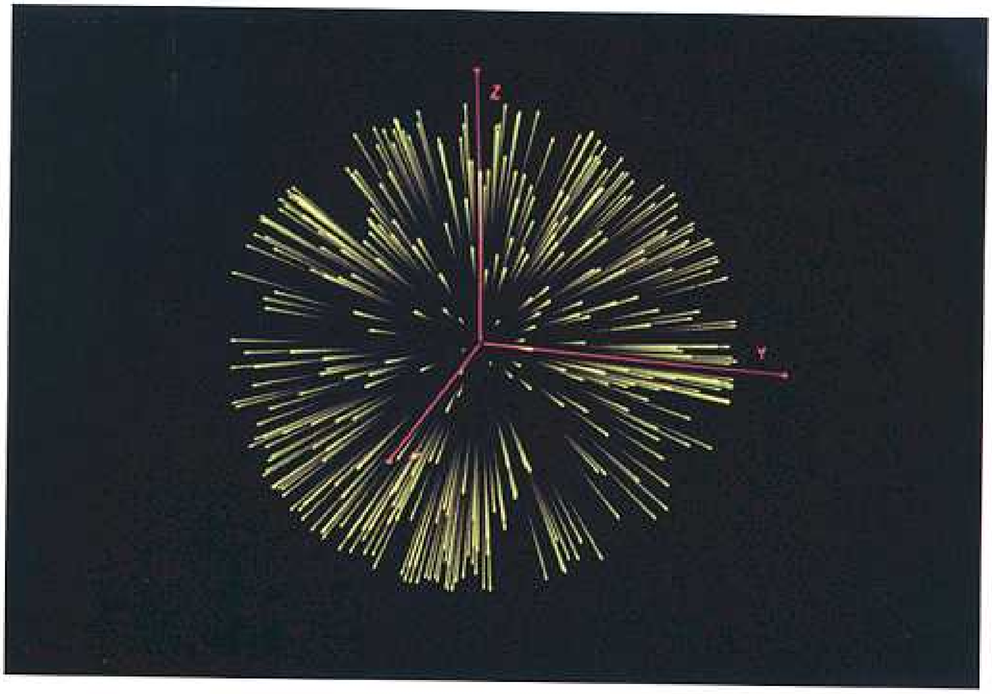

Fig. 3. Preferred directions (unit vectors) of 475 motor cortical cells in three-dimensional space. (From Schwartz et al. J Neurosci 1988;8:2913-27. By permission.)

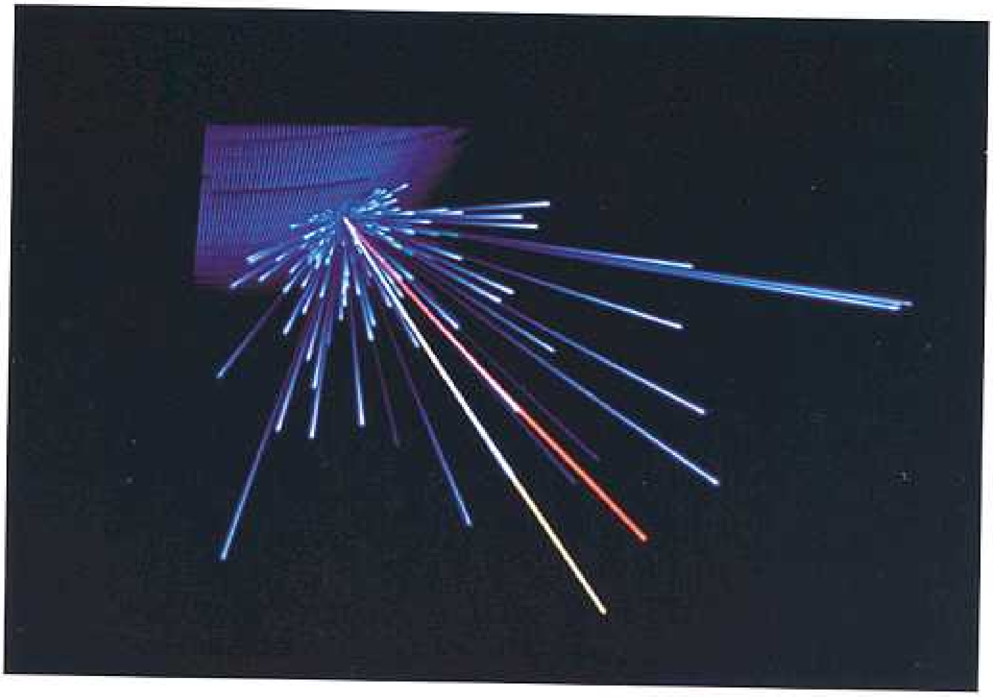

Fig. 4. Population coding of movement direction. The *blue lines* represent the vectorial contributions of individual cells in the population (n = 475). The movement direction is in *yellow*, and the direction of the population vector in *red*. (From Schwartz et al. J Neurosci 1988;8:2913-27. By permission.)

THE PROBLEM OF COGNITION: NEURAL OPERATIONS SUBSERVING MOTOR COGNITIVE TRANSFORMATIONS

In the delayed tasks described above the movement to be made was unequivocally defined in the sense that its direction was determined by the location of a stimulus relative to the starting point. In that situation the visual information concerning direction is used to generate the appropriate motor command to implement a movement in that direction; truly, this movement direction has to be generated and kept available during the delay period but it is defined from the beginning; therefore, the direction of the movement is the same throughout the various times considered above. A very different situation was created in an experiment[26] in which the direction of the movement to be made had to be determined freshly at every trial according to a certain rule, namely that the movement direction be at an angle (counterclockwise or clockwise) from the stimulus direction. This experiment takes us away from the case of a *fixed* motor intention; instead, this intention has now to be derived as the solution to the problem. In fact, there are many ways by which this problem can be solved. For example, an obvious way would be to form a look-up table that contains the movement directions that correspond to the stimulus directions. Using this strategy, one would simply memorize the corresponding directions in the table and, given a stimulus direction, one would search the table to select the movement direction corresponding to the particular stimulus direction. Of course, one would not have to use numbers, simply imagined directed radii in a unit circle.

A different strategy would be to mentally rotate the stimulus direction in the instructed departure (counterclockwise or clockwise) by an amount equal to the required angular shift. The look-up table and mental rotation hypotheses lead to different predictions concerning how the reaction time would change, and on this basis they can be distinguished. If the look-up table strategy is followed, the reaction time would increase because of the time taken for the search, but this increase should not be greater for larger angles because there is no reason to suppose that searching the table in the case of a large angle should take more time than when searching the table in the case of a small angle. In contrast, the mental rotation hypothesis predicts an increase of the reaction time with the angle because the time to be taken to rotate a radius through an angle should be proportional to the angle itself. Indeed, the results of the experiments in human subjects[26] showed an increase of the reaction time with the angle and therefore supported the mental rotation hypothesis. The average rate of the hypothesized rotation was approximately 400 degrees per second. Remarkably, this is very close to the value obtained in experiments on mental rotation of visual images.[27] Another similarity between the motor rotation[26] and visual rotation[27] studies is that there is appreciable diversity in the rotation rates obtained among different subjects. In fact, we used this feature to test the idea that motor and visual mental rotation processes may be associated: indeed, a significant correlation was found between the two rotation rates in a group of subjects who performed both tasks.[28] This suggests that the two processes might share a common processing stage, or that both processes involve constraints that result in the relation obtained.

The neural mechanisms underlying the process of mental rotation in the movement domain were investigated by training monkeys to perform a task in which they made a movement in a direction 90 degrees counterclockwise from a stimulus direction. We supposed that if a mental rotation of an imagined vector was taking place, it could be revealed by using the population vector analysis. Indeed, the population vector rotated during the reaction time from the stimulus to the movement direction through the 90-degree counterclockwise angle (Fig. 5).[29-30] It is interesting that the rotation rates (direction of population vector versus time) observed[30] were very similar to the rates (increase in reaction time versus angle) observed in the human studies.[26] Thus the dynamic processing of a directional transformation was successfully visualized by using the neuronal population vector analysis.

CONCLUDING REMARKS

The results of the experiments discussed above raise several points concerning the representation of movement in the motor cortex. The *first* point is that this representation is not obligatorily connected with the production of movement; that is, its presence does not necessarily lead to motor output. This is in accord with findings of psychophysical studies that movement planning and movement triggering are different processes.[31] It is interesting that when a delay is introduced, there seem to be at least two different subsets of cells: one that is active during the delay and becomes further active after the movement triggering signal, and another that is not active during the delay but becomes engaged after the "go" signal.[24] Therefore, it seems that both the planning and the triggering processes involve the motor cortex. It is possible that motor cortical activity could be gated at segmental and propriospinal[32,33] levels in the spinal cord, given the extensive convergence of several supraspinal inputs on these interneuronal systems. Therefore, engagement of the motor cortex is not a sufficient condition for triggering the movement. On the other hand, motor cortical activation seems to be necessary for appropriate planning of the movement, as suggested by the disturbed reaching movements produced by reversible inactivation of the motor cortex.[34] The *second* point concerns the nature of information that is represented. It may not be appropriate to assign all of this information to the upcoming movement, for it may very well reflect processes subserving the translation of visual or memorized information to motor output. The complexity of potential explanatory factors for motor cortical activity in behavioral tasks is suggested by the results of studies where such factors were dissociated[35-37] and also by the results of the directional transformation study[29,30] discussed above that showed that motor cortical activity does reflect a process involved in mental rotation. The *third* point concerns the place of motor cortex among other motor structures. In this context, it is important to realize that unlike primary sensory cortexes, motor cortex is the site of convergence from a large number of other areas, both cortical and subcortical. For example, the large extent of the convergence on the motor cortex, in contrast to that on the somatosensory cortex, can be appreciated from the results of recent studies of the thalamocortical projections to small motor cortical areas.[38] Therefore, the discharge patterns of motor cortical cells are generated through this convergence rather than being the outcome of a faithful transmission through sensory lines. On the other hand, the motor cortex is not the "final" motor path from the cerebral cortex. It has now been shown conclusively that several premotor areas possess direct and dense projections to the spinal cord.[39] It seems that the motor cortex and premotor areas might be concerned with different but overlapping aspects of motor control[36,37,40,41] in that a particular movement might be the result of this parallel processing. These findings have an important implication, among others, and that is that the spinal motor mechanisms involved in the production of voluntary movement can be properly understood only if one takes into account (1) the convergent pattern of influences from the motor and premotor cortical areas; (2) influences from subcortical structures such as the red nucleus and the reticular formation; and (3) the organization and dynamic interplay of spinal interneuronal circuits involved in the transmission of central commands,[32,33] the generation of stereotypic motor patterns,[42,43] and the control of afferent input from the moving limb.[44] There is little doubt that understanding the interactions among the various motor areas, and in particular those between the motor cortex and the spinal cord,[45] is now the biggest challenge in deciphering the "natural intelligence" of the motor system.

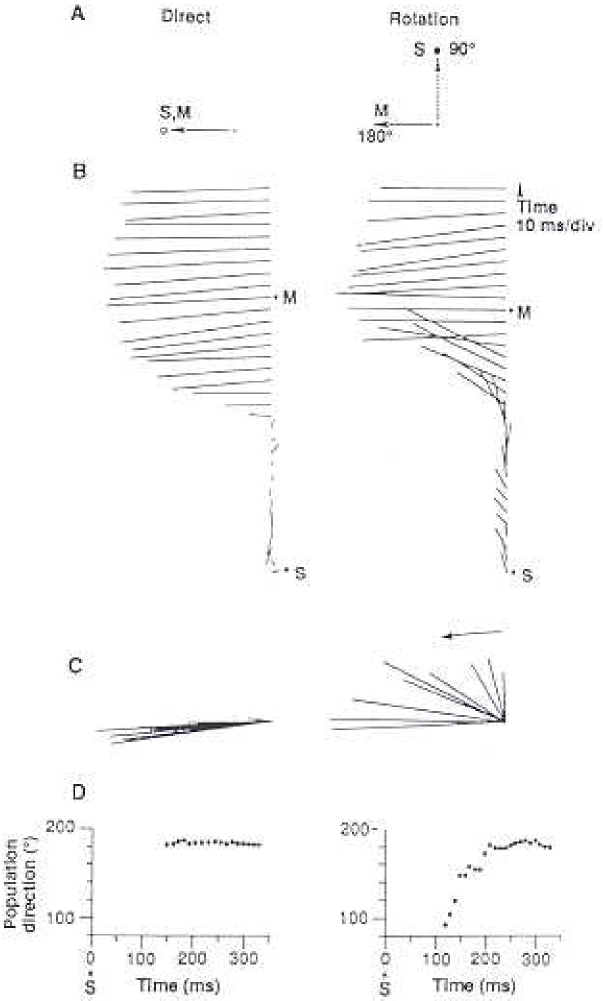

Fig. 5. Time evolution of the neuronal population vector when the movement was in the direction of a stimulus or 90 degrees counterclockwise from it. **A,** Task. Unfilled and filled circles indicate dim and bright light, respectively. Interrupted and continuous lines with arrows indicate stimulus *(S)* and movement *(M)* direction, respectively. **B,** Neuronal population vectors calculated every 10 msec from the onset of the stimulus *(S)* at positions shown at **(A)** until after the onset of the movement *(M)*. When the population vector lengthens, for the direct case *(left)* it points in the direction of the movement, whereas for the rotation case it points initially in the direction of the stimulus and then rotates counterclockwise (from 12 o'clock to 9 o'clock) and points in the direction of the movement. **C,** Ten successive population vectors from **(B)** are shown in a spatial plot, starting from the first population vector that increased significantly in length. Notice the counterclockwise rotation of the population vector *(right panel)*. **D,** Scatter plots of the direction of the population vector as a function of time, starting from the first population vector that increased significantly in length after stimulus onset *(S)*. For the direct case *(left panel)*, the direction of the population vector is in the direction of the movement (≈180 degrees); for the rotation case *(right panel)*, the direction of the population vector rotates counterclockwise from the direction of the stimulus (≈90 degrees) to the direction of the movement (≈180 degrees).

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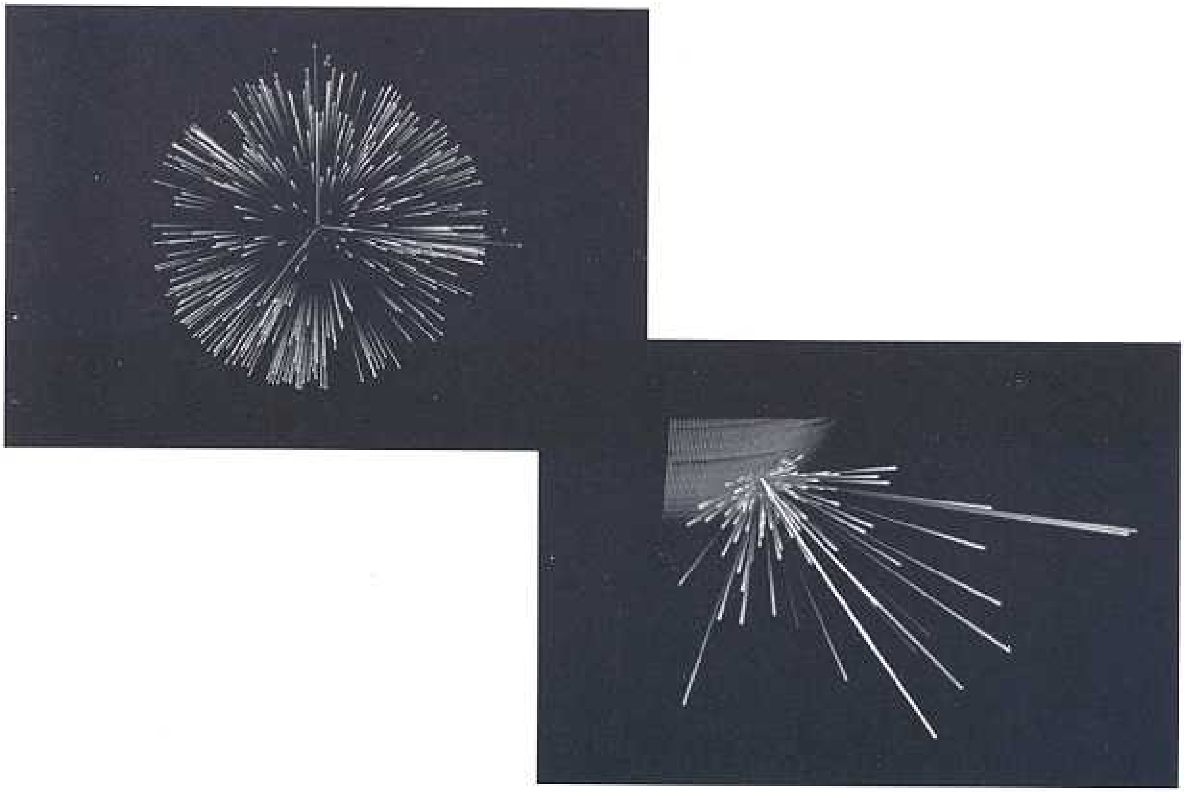
About the cover illustration



IN SEARCH OF THE ELECTRICITY OF BEHAVIOR

In this month's issue Dr. Apostolos Georgopoulos of the Minneapolis VA Medical Center reviews developments of the last decade that shed light on the electrical events involved in carrying out motor tasks.

At rest, each motor neuron has a preferred electrical orientation; the electrical unit vectors of 475 neurons are shown plotted in three-dimensional space in the *left panel*. When motion is undertaken (in fact, a bit before motion begins), the picture is quite a bit different. As shown on the *right* in blue, the individual cell vectors are now not random; rather, there is a net population vector (shown in red) that is highly directional and oriented in close agreement with the direction of the movement being made (shown in yellow).

The directionality of the population vector becomes established before the motor impulses are sent and thus may be the electrical correlate of cognitive intent to carry out the motion.

The cover reproduces Fig. 3 and Fig. 4 from Dr. Georgopoulos' review; they are reproduced with the kind permission of the Society for Neuroscience (see text of review for full citation).

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J Lab Clin Med 1994;124:862

0022-2143/94 $3.00 + 0 **5/8/60814**