Role of motor cortex in coordinating multi-joint movements: Is it time for a new paradigm?[1]

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Abstract: Reaching movements to spatial targets require motor patterns at the shoulder to be coordinated carefully with those at the elbow to smoothly move the hand through space. While the motor cortex is involved in this volitional task, considerable debate remains about how this cortical region participates in planning and controlling movement. This article reviews two opposing interpretations of motor cortical function during multi-joint movements. On the one hand, studies performed predominantly on single-joint movement generally support the notion that motor cortical activity is intimately involved in generating motor patterns at a given joint. In contrast, studies on reaching demonstrate correlations between motor cortical activity and features of movement related to the hand, suggesting that the motor cortex may be involved in more global features of the task. Although this latter paradigm involves a multi-joint motor task in which neural activity is correlated with features of movement related to the hand, this neural activity is also correlated to other movement variables. Therefore it is difficult to assess if and how the motor cortex contributes to the coordination of motor patterns at different joints. In particular, present paradigms cannot assess whether motor cortical activity contributes to the control of one joint or multiple joints during whole-arm tasks. The final point discussed in this article is the development of a new experimental device (KINARM) that can both monitor and manipulate the mechanics of the shoulder and elbow independently during multi-joint motor tasks. It is hoped that this new device will provide a new approach for examining how the motor cortex is involved in motor coordination.

Key words: reaching movements, biomechanics, motor coordination, proximal arm.

Résumé : Les mouvements d'atteinte de cibles spatiales requièrent une bonne coordination entre les patrons moteurs de l'épaule et du coude pour transporter aisément la main dans l'espace. Bien que le cortex moteur joue un rôle dans cette tâche volontaire, il y a encore de nombreuses discussions sur la manière dont il intervient dans la planification et le contrôle du mouvement. Le présent article révise deux interprétations opposées de la fonction corticale motrice durant des mouvements multi-articulaires. D'une part, de façon générale, les études portant principalement sur le mouvement uni-articulaire soutiennent l'idée que l'activité corticale motrice est intimement impliquée dans la production de patrons moteurs au niveau d'une articulation donnée. D'autre part, les études sur les mouvements d'atteinte démontrent des corrélations entre l'activité corticale motrice et les caractéristiques de mouvement associées à la main, suggérant que le cortex moteur peut être impliqué dans des caractéristiques plus globales de la tâche. Bien que ce paradigme suppose une tâche motrice multi-articulaire dans laquelle l'activité neurale est corrélée aux caractéristiques de mouvement liées à la main, cette activité neurale est aussi corrélée à d'autres variables de mouvement. Ainsi, il est difficile d'évaluer si et de quelle manière le cortex moteur participe à la coordination des profils moteurs aux niveaux de différentes articulations. En particulier, les paradigmes actuels ne peuvent évaluer si l'activité corticale motrice participe au contrôle d'une ou de plusieurs articulations durant les tâches nécessitant tout le bras. La dernière partie de cet article porte sur la mise au point d'un nouveau dispositif expérimental (KINARM) pouvant contrôler et manipuler la mécanique de l'épaule et du coude de façon indépendante durant des tâches motrices multi-articulaires. On espère que ce dispositif fournira une approche novatrice pour l'étude du rôle du cortex moteur dans la coordination motrice.

Mots clés : mouvements d'atteinte d'une cible, biomécanique, coordination motrice, bras proximal.

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Introduction

Visually-guided reaching requires visual information to be converted into coordinated motor patterns at the shoulder and elbow to smoothly move the hand through space. This task has become a classic sensorimotor paradigm for examining how the brain functions to plan and control movement. While many sensorimotor transformations are considered to occur within the brain during this task (Kalaska and Crammond 1992; Saltzman 1979; Soechting and Flanders 1992), a major computation that must be performed is the conversion from a kinematic (i.e., spatial target, hand

trajectory, or joint angular motion) to a kinetic (i.e., joint torques or muscular activity) representation. This computation is not trivial since motion at a given joint is dependent on torque generated at other joints, as described by the laws of Newtonian motion. Therefore, motor patterns at each joint must be carefully coordinated together to smoothly move the joints and thus the hand through space. While the exact details of the timing and magnitude of muscle activity will only be reflected in the discharge patterns of motoneurons that innervate each muscle, it is of considerable importance to understand at what level of the nervous system, cortical or spinal, the process of muscle selection begins.

It has been known for over a century that primary motor cortex participates in volitional movement control (for review, see Porter and Lemon 1993). Electrical stimulation of this cortical region elicits discrete body movements, while focal lesions result in immediate paralysis of a portion of the motor periphery. Primary motor cortex receives sensory input from the periphery and reciprocal input from several brain regions involved in movement control, such as the cerebellum and basal ganglia. Given the fact that single unit recordings in chronic behaving animals have been performed in this cortical region for over thirty years, it seems reasonable to believe that we would know if and how the primary motor cortex participates in coordinating the selection and timing of motor patterns during multi-joint movements. Surprisingly, considerable debate exists. One interpretation is that the motor cortex is intimately involved in motor coordination and descending commands from this cortical region provide important details on motor patterns at each joint. Another interpretation is that the primary motor cortex is involved in more global details of the motor task, such as specifying the direction of hand movement, and that the coordination of motor patterns is performed exclusively at the spinal level.

The purpose of this article is to review this scientific dilemma on the putative role played by the motor cortex in coordinating motor patterns during multi-joint movements. The article begins with a small review of the mechanics of multi-joint movement followed by a description of the two main experimental paradigms and corresponding alternate views on how the primary motor cortex participates in the planning and execution of movement. While both approaches involve the analysis of single unit activity in chronic behaving non-human primates, differences in the experimental paradigms result in considerable disparity in the interpretation of motor cortical function. With regards to multi-joint movements, neither paradigm can easily address how the motor cortex is involved in coordinating movements at different joints. The final point to be discussed is a brief description of a new experimental paradigm specifically designed to examine how regions of the brain such as the motor cortex are involved in motor coordination.

Mechanics of multi-joint movement

Muscle force and joint motion are tightly coupled in single-joint motor tasks. The net muscular torque equals joint angular acceleration multiplied by the moment of inertia of the limb, a term related to limb mass. A more complex rela-

tionship exists between motion and torque for multi-joint tasks. For a simple planar task involving flexion and extension at the shoulder and elbow, net muscular torque at the two joints equals

[1]
$$T_s = (I_1 + I_2 + m_1 c_1^2 + m_2 (l_1^2 + c_2^2 + 2l_1 c_2 \cos\Theta_2))\ddot{\Theta}_1 + \\ (I_2 + m_2 c_2^2 + m_2 l_1 c_2 \cos\Theta_2)\ddot{\Theta}_2 - (m_2 l_1 c_2 \sin\Theta_2)\dot{\Theta}_2^2 - \\ (2m_2 l_1 c_2 \sin\Theta_2)\dot{\Theta}_1\dot{\Theta}_2$$

[2]
$$T_e = (I_2 + m_2 c_2^2 + m_2 l_1 c_2 \cos\Theta_2)\ddot{\Theta}_1 + \\ (I_2 + m_2 c_2^2)\ddot{\Theta}_{2 + (m_2} l_1 c_2 \sin\Theta_2)\dot{\Theta}_1^2$$

As described by the laws of Newtonian mechanics, net muscular torque is dependent on the acceleration, velocity, and position of other joints (see Fig. 1A for nomenclature). This mechanical coupling of motion and torque between joints is generally referred to as intersegmental dynamics. While the exact magnitude of these interaction terms depend on the nature of the variables used to describe joint motion (i.e., relative versus absolute angles), the most common form of the equations is based on relative angles between adjacent limb segments (Hollerbach and Flash 1982; Karst and Hasan 1991). The equations described above for two-joint planar limb movement are quite simple compared with the equations of motion to describe more natural movements involving many joints with multiple degrees-of-freedom. Equations to describe whole body movement would fill this entire page.

While it seems reasonable to assume that intersegmental dynamics have minimal effects on multi-joint motion, these interaction terms can contribute substantially to joint motion (Hollerbach and Flash 1982). Figure 1 illustrates the kinematics and kinetics of limb movement generated by a monkey making a planar reaching movement from a central start position to a target located in front of itself. Hand movement involves shoulder extension motion coupled with elbow flexion motion. Note the similarity in the magnitude and temporal patterns of joint velocity at the two joints. In contrast, the underlying net muscular torques required to generate the movement are quite different. There is first an extensor shoulder torque initiating movement followed by a flexor torque to brake limb movement. The elbow muscular torque is much smaller than the muscular torque at the shoulder. Motion at the elbow for this movement is not primarily generated from muscular torque at the elbow. Rather, shoulder torque contributes to elbow motion. The lack of a one-to-one correspondence between motion and torque at each joint means that motor patterns do not simply reflect the requisite motion at that joint during movement. Rather, the central nervous system must carefully coordinate motor patterns at each joint together to make skilled and graceful body movements.

Frameworks for interpreting motor cortical activity during multi-joint movements

Visually-guided reaching requires spatial information to be converted into motor patterns at the shoulder and elbow to move the hand through space. A common framework for interpreting this motor task is as a series of sensorimotor

Fig. 1. The kinematics and kinetics of shoulder and elbow motion during a reaching task. (A) The monkey's arm was modelled as two segments, the upper arm (segment 1) and forearm–hand (segment 2), with single degree-of-freedom joints at the shoulder and elbow joints. T_s and T_e are the net muscular torques generated at the shoulder and elbow joints, respectively. Θ_1 and Θ_2 are the angles of the shoulder and elbow joints, respectively. m and l denote the mass and length of each segment, respectively. c and I are the location of the centre of mass relative to the proximal end of each segment and the moment of inertia of each segment, respectively. (B) The trajectory of the monkey's hand when it reached from a central start position to a target towards itself. (C) Shoulder and elbow velocity and net muscular torque for the reaching movement. Flexor motion and torque are defined as positive (counter-clockwise), whereas extensor terms are negative (clockwise). Note the mirror temporal and spatial pattern of joint angular velocity. In contrast, the corresponding net muscular torques are quite different reflecting the complex transformation between motion and torque for multi-joint movements.
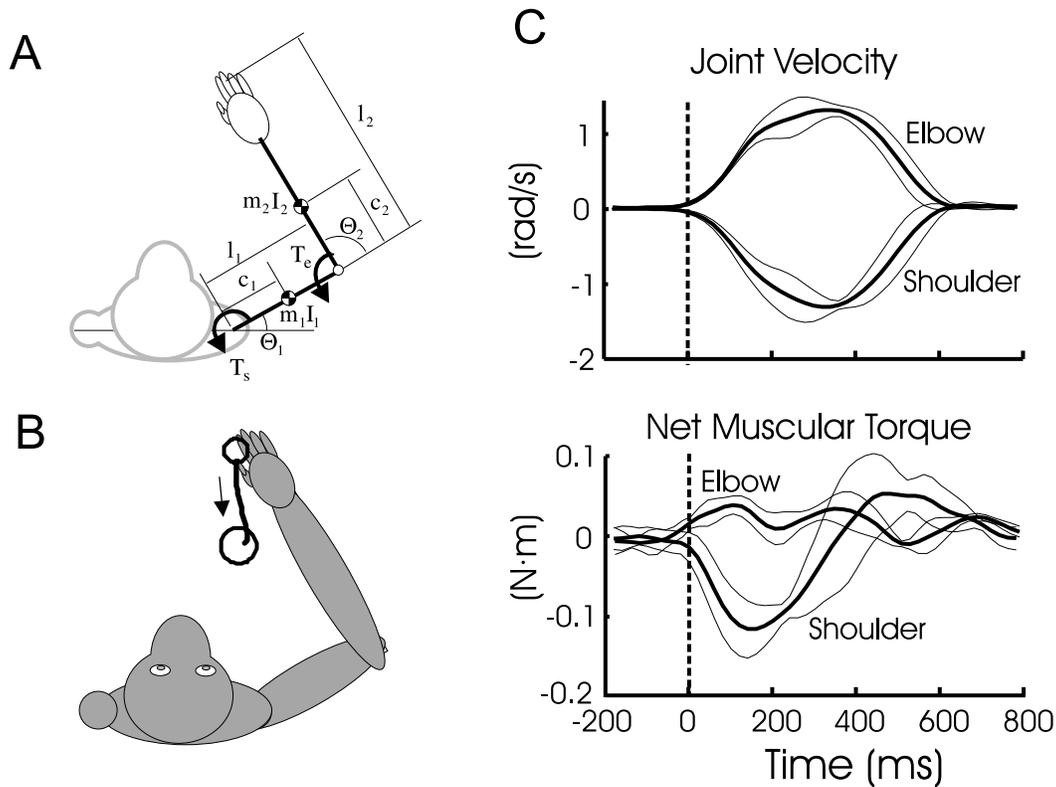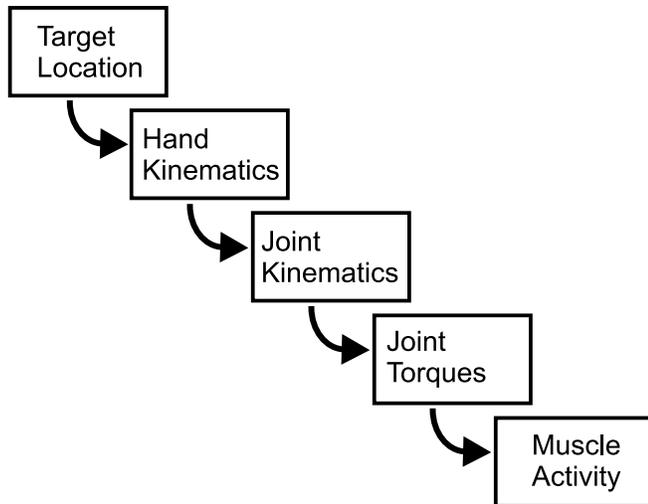

transformations creating a number of coordinate frames (Kalaska et al. 1997; Saltzman 1979; Soechting and Flanders 1992). This engineering-inspired model generally assumes sensory signals related to target location are converted into commands related to hand trajectory, which are then converted into the corresponding joint angular trajectories. Angular motion at the joints is then converted into muscular torques and then finally into the requisite patterns of activity of muscles at each joint (Fig. 2). As described below, a major focus of many studies has been to identify which of these different coordinate frames or representations are best defined in the discharge pattern of cells in the primary motor cortex.

A less frequently posed question about how the motor cortex participates in controlling arm movements is what portion of the motor periphery is related to a given motor cortical cell. For didactic purposes, I have identified three putative levels in which neural activity could be involved in a multi-joint motor task. First, neural activity could reflect motor patterns for a small portion of the motor periphery involving only a single joint (Fig. 3A). Within this single-joint

framework, neural activity could reflect any feature of movement behavior at that joint from the activation of several muscles acting as synergists or antagonists to the activity of a single muscle. Second, neural activity could be related in a more complex way to multi-joint motor behaviors such as the activation patterns of muscles spanning different joints or even differences in motor patterns at various joints (Fig. 3B). A basic difference between a single- and multi-joint framework is that in the former model neural activity reflects motor behavior at one joint and not at others during a multi-joint task. In contrast, neural activity in a multi-joint model would reflect variations in motor behavior at multiple joints, such as motor patterns at both the shoulder and elbow joints. Finally, neural activity in a given brain region could reflect more global aspects of movement performance, such as the direction of hand movement or the location of the spatial target (Fig. 3C). Unlike the former two, in this latter framework neural activity is not directly involved in controlling details of motor behavior for the peripheral motor apparatus. With regards to reaching, we will classify neural activity related to the global goals of the task

Fig. 2. The problem of reaching to a spatial target is often defined as a series of sensorimotor transformations between distinct representations or coordinate frames. Sensory information is converted into a number of intermediate frames representing the kinematics of the task and finally into the kinetic features of the task.

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┌──────────┐
│  Target  │
│ Location │
└──────────┘
      ↘ ┌──────────┐
        │   Hand   │
        │Kinematics│
        └──────────┘
              ↘ ┌──────────┐
                │  Joint   │
                │Kinematics│
                └──────────┘
                      ↘ ┌──────────┐
                        │  Joint   │
                        │ Torques  │
                        └──────────┘
                              ↘ ┌──────────┐
                                │  Muscle  │
                                │ Activity │
                                └──────────┘
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as representing a hand-based framework. Note that multi-joint and hand-based frameworks are not the same. A joint-based frame assumes that neural activity is related to the motor behavior of the joints, whereas a hand-based frame is independent of how the joints or musculature are used to create limb motion. For example, a hand-based frame would not be sensitive to changes in arm orientation when moving the limb in space (see Scott and Kalaska 1997). As described below, several studies have illustrated that motor cortical activity correlates with motor patterns at single joints or with features of movement related to the hand. In contrast, little information exists on if and how motor cortical activity is related to motor patterns at multiple joints.

Motor cortical activity related to motor patterns at single-joints

Single-unit recording techniques in chronic behaving monkeys were first used in the primary motor cortex by Ed Evarts to explore how neural activity is related to movements of the wrist (Evarts 1967). Evarts recognized the importance of dissociating different movement variables and his earliest studies examined whether neural activity was related to joint motion or to the underlying muscular torques required to generate movement. Monkeys were trained to make wrist flexion and extension movements with and without loads applied to a manipulandum grasped by the monkey. These loads biased the muscular torque at the wrist in order to dissociate joint torque and motion. Neural activity in the motor cortex was found to vary with the direction of movement and in many cases neural activity was also modulated by the mechanical load applied at the joint. Therefore, neural activity in motor cortex appeared to be related to both the motion and the underlying motor patterns at the joint. The single-joint paradigm has been used predominantly to examine wrist and elbow motion and demonstrate correla-

tions between neural activity and motor behavior at a joint (for a review see Fetz 1992).

The focus on single-joint movements as an experimental paradigm to assess neural activity could be interpreted as support that motor cortical cells are principally involved in controlling single-joints. While motor cortical activity is often tightly coupled to the onset time and magnitude of motor output at a joint, these single-joint studies cannot examine how the motor cortex coordinates motor output at different joints during multi-joint movement.

There have been a few studies that have compared motor cortical activity and motor patterns at single joints during multi-joint tasks. A series of studies by Murphy and colleagues examined how cell activity was related to each of the major joints of the upper limb. Several observations suggested that individual neurons in the primary motor cortex were principally related to individual joints. First, they found that electrical stimulation at threshold levels generated movements principally at single joints (Kwan et al. 1978). Except for the distal joints of the hand, electrical stimulation generally did not cause movement at more than one joint. Second, they examined how individual neurons responded to passive movement of each joint of the upper limb (Wong et al. 1978). They found that most cells modulated their activity for passive movement at only a single joint and only a few cells responded to movements at multiple joints. Finally, neural activity was recorded during a reach and grasp task which first required motor patterns initially at the shoulder and elbow to move the hand to the object and then required muscle activity at the distal joints to touch a button (Murphy et al. 1985). Neurons related to the shoulder and elbow were found to be recruited first, followed by neurons related to the more distal joints. Evidence that neurons were related to single joints was parsimonious with existing non-human primate studies that had principally focussed on examining neural activity during single-joint motor tasks. While these studies suggest that neurons are related to individual joints, it should be noted that cell classifications were qualitative. Cell classification was purely subjective with no measures of magnitude of relative motion at each joint induced by stimulation nor the magnitude of cell response to motion at each joint.

One approach that has been used to examine how the primary motor cortex is involved in coordinating multi-joint movements is to correlate neural activity to muscle activity at each joint. For example, Drew and colleagues have examined the relationship between gait modifications to step over obstacles and the activity of pyramidal tract cells in motor cortex in cats (Drew et al. 1996). Changes in the onset time and magnitude of cell activity was commonly associated with changes in the activity of specific muscles or muscle groups, supporting the notion that the motor cortex is involved in coordinating multi-joint movements. Motor cortical activity in non-human primates has also been found to correlate with grip force or muscle activity during prehension tasks requiring coordination between the index finger and thumb (Smith et al. 1975; Bennett and Lemon 1994).

With regards to reaching movements, correlates between neural activity in the motor cortex and activity of specific muscle groups have been found during horizontal reaching

Fig. 3. Three putative ways in which neural activity in motor cortex may be involved in multi-joint reaching movements. Neural activity could reflect motor behavior at only a single joint (A), multiple joints (B), or reflect more global features of the task related to the hand or spatial target (C).

Neural Activity Related to Reaching Movements

A   Single-joint   B   Multi-Joint   C   Hand
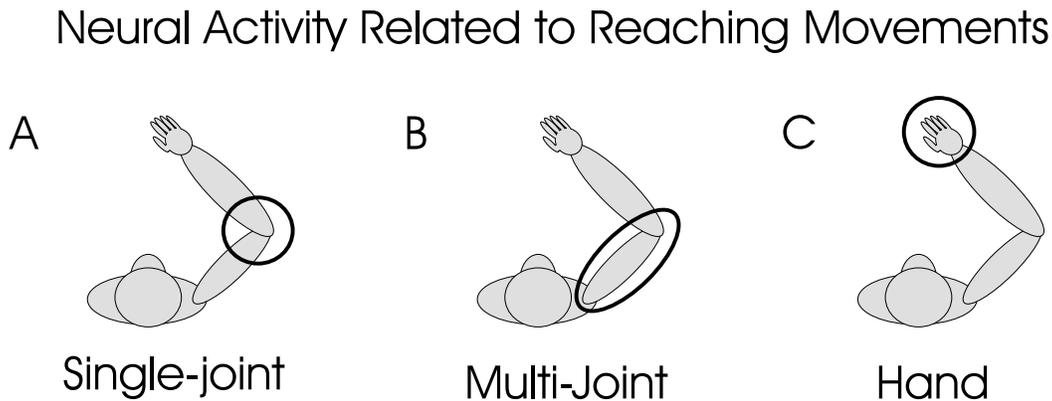
movements (Scott 1997). One of the two arm orientations examined by Scott and Kalaska (1997) required the monkey to abduct its shoulder approximately 90 degrees in order to grasp and move a handle in space; this arm posture predominantly involved movements of the whole-arm in the horizontal plane. It has been shown in a planar reaching task in humans that there are systematic changes in the timing and magnitude of muscle activity at the shoulder and elbow that are dependent on the direction of movement (Karst and Hasan 1991). I performed a similar analysis to identify whether the onset time and magnitude of motor cortical cells related to the shoulder and elbow joints co-varied with corresponding muscles at the two joints. Several similarities were observed between the muscle activity at each joint and corresponding neurons related to each of these joints. Neurons were classified based on their response to passive movement of the shoulder and elbow joints. Muscles and neurons related to a given joint showed systematic biases in the distribution of directions that they were maximally active. Both elbow muscles and elbow-related neurons were maximally active for movements towards or away from the monkey. In contrast, shoulder muscles and shoulder-related cells tended to be maximally active for movements to the left and right. Further, variations in the magnitude and onset time of muscle activity for movements in different directions were paralleled by the population of cells related to that joint. This study illustrates how neural activity in the motor cortex correlates with specific details of muscle activity, onset time, and magnitude, supporting the notion that the motor cortex participates in coordinating motor patterns at different joints.

Motor cortical activity related to hand movements

A dramatically different perspective on the role of the primary motor cortex emerged from an experimental task developed by Georgopoulos and colleagues almost twenty years ago. These researchers wanted to examine how neurons related to the shoulder in the motor cortex of monkeys responded during reaching movements made from a central target to one of eight peripheral targets located on the circumference of a circle (Georgopoulos et al. 1982). Since shoulder motion is rather complex in this task, neural activity was related to movements of the hand in space.

The most notable finding from this reaching task was that neural activity was broadly tuned to the direction of hand movement. Cell activity was maximal in a given direction, designated the cell's preferred direction (PD). The magnitude of activity diminished as the angle between movement direction and the cell's PD increased, with the least amount of activity observed for movements in the direction opposite to the cell's PD. In many cases neural activity fit relatively well with a cosine tuning function. Furthermore, the distribution of PDs of the population of cells recorded in the task spanned all possible movement directions. While the first report noted a preferential clustering of PDs in some quadrants, later studies emphasized the near random distribution of PDs throughout space.

A second key finding from these experiments was the comparison between the direction of hand movement and the direction of a population vector constructed from the discharge pattern of cells during the task (Georgopoulos et al. 1983). In the population vector method, each cell contributes an individual vector with an orientation defined by its PD and its magnitude based on the discharge rate of the cell for a given movement. The length of the individual vector is longest for movements in the cell's preferred direction and shortest for movements in the opposite direction. The population vector is simply the vector sum of the individual vectors from each cell recorded in the task. The ubiquitous finding in the literature is that this population vector tends to point in the direction of movement. While some statistically significant deviations have been found between the population vector and the direction of hand movement (Scott and Kalaska 1995), they have been generally small and ignored.

This new reaching task was a major shift from previous studies. The first major change was intentional and that was the motor requirement to control multiple degrees of freedom at a joint. In this case, reaching movements throughout space require combined flexion–extension, abduction–adduction, and internal–external rotation at the shoulder. Due to this focus, preliminary studies by Georgopoulos and colleagues examined how shoulder-related neurons behaved during these tasks. While this new task was an obvi-

ous important extension from previous studies on cerebral cortical control of single-joint movement, it included a number of other changes to previous experiments. First, movements of the hand in space required motor patterns to be coordinated at several joints, most notably the shoulder and elbow joints. Therefore, the complexity of this task was substantially greater than previous studies involving a single degree-of-freedom movement at one joint. Perhaps the most important change was in the choice of variables correlated with neural discharge. Rather than joint-based variables related to angular motion or muscular torque, this new paradigm correlated neural activity to movements of the hand in space. While it seems initially rather unusual to examine shoulder-related neurons based on hand kinematics, this simplification was necessary technically due to the difficulty in quantifying movements of the shoulder in this task. Kinesiological devices to monitor joint motion during whole-arm tasks were not readily available in the late 1970s and certainly no systems were automated enough to monitor on-line a thousand movements per day on a daily basis. The measurement of hand rather than joint movement using a modified drafting device was a logical simplification in this new task. The final major shift was the class of variables manipulated in the experiments. Whereas previous studies varied parameters related specifically to a joint, future extensions of this new paradigm manipulated parameters related to the hand, such as the magnitude and direction of hand movement or loads applied to the hand.

This reaching paradigm where neural activity in primary motor cortex was related to hand-based variables was clearly a new experimental paradigm, as initially coined by Kuhn (1970). Previous studies had focussed exclusively on variables related to the motor periphery and this new reaching task shifted attention towards neural correlates of the global goal of the task: to move the hand through space. It had already been shown that hand movements were relatively straight, suggesting that hand trajectory may be explicitly controlled by the CNS at some level (Morasso 1981). Evidence for neural activity that covaried with hand movement direction provided an obvious neurophysiological bridge with these psychophysical observations on human movement. This led to further studies to examine whether correlates of other features of hand movement were also evident in the discharge of motor cortical cells. With time, several studies have shown that neural activity in the motor cortex also correlates with hand speed, movement distance, and position (Fu et al. 1995; Schwartz 1992). Comparable studies on force modulation during isometric tasks also found that motor cortical activity was correlated to the direction of force applied by the hand (Taira et al. 1996). While the earliest studies discussed how neural correlates of hand movement were likely related to the underlying mechanics of movement at the shoulder, these discussions back to the motor periphery quickly disappeared and were no longer considered. By the early 1990s, the separation between this reaching paradigm and other experimental work on the motor cortex had been completed. Studies on reaching generally interpreted neural activity based on hand-related features of movement, whereas all other studies interpreted neural activity based on the motor patterns at the periphery.

Part of the reason for this separation between experimental paradigms was created by studies illustrating neural correlates of higher level cognitive function in the motor cortex, such as mental rotation (Georgopoulos et al. 1989). The concept of mental rotation came from human studies which showed increases in reaction time with increasing angular deviation between two objects that were to be compared (Shepard and Metzler 1971), or the angle between stimulus and movement directions (Georgopoulos and Massey 1987). Corresponding experiments in monkeys were performed to explore whether neural correlates of a mental rotation were present in the motor cortex of monkeys trained to move in a direction 90 degrees counter-clockwise to a spatial target (Georgopoulos et al. 1989). Georgopoulos and colleagues noted two key pieces of evidence to support the notion that motor cortical activity reflected a process of mental rotation. First, the population vector generated by neural activity in the motor cortex initially pointed in the stimulus direction and then rotated to the upcoming direction of movement. Second, there was a tendency for a sequential shift in the number of cells recruited during the reaction time period; stimulus direction cells tended to be active first, followed by cells intermediate between the stimulus and movement directions, and finally by cells that were aligned with the direction of movement. Both observations were consistent with the notion of a process of mental rotation to resolve this motor task. Further studies demonstrated neural correlates of higher level cognitive functions such as memory recall and sequential order (Carpenter et al. 1999; Pellizzer et al. 1995). These studies suggest the motor cortex participates in higher level cognitive tasks and is not simply involved in controlling the motor periphery. One possibility is that motor cortical cells do not provide details on motor output at different joints. Rather, neurons in the motor cortex treat the limb as a functional whole (Georgopoulos 1996) and the details of the temporal and spatial features of motor output to muscles is relegated to the spinal cord.

The hypothesis that coordinated motor patterns at different joints are principally developed at the spinal level is consistent with a number of studies on spinal cord function. Most notable are studies illustrating that a specific group of neurons located in the spinal cord at cervical levels 3 and 4 were specifically involved in coordinating reaching movements in cats (Alstermark et al. 1981). Further support for the importance of the spinal cord in whole-limb function comes from another series of studies on spinalized frogs (Bizzi et al. 1991). Electrical stimulation in the cord was found to generate coordinated motor patterns involving the musculature of the entire limb.

The reaching paradigm has created a unique perspective on how neural activity in the primary motor cortex is related to movement planning and execution. Broad directional tuning and population vectors pointing in the direction of movement provide a simple and concise framework for interpreting neural discharge during motor tasks. However, the interpretation that motor cortical activity is related to global features of movement appears to be quite different than those from other studies using different experimental paradigms that illustrate relations between motor cortical activity and the temporal and spatial features of motor output.

While the results from reaching paradigms continue to illustrate neural correlates of hand movement in motor cortical cell discharge patterns, a key question as to the significance of these correlates remains heavily debated. Several theoretical studies have noted that neural activity broadly tuned to the direction of hand movement and population vectors that tend to point in the direction of movement can be predicted if neural activity is correlated to almost any variable related to the task, such as muscle activity or length (Mussa-Ivaldi 1988; Todorov 2000). Moreover, alternate frameworks have been proposed for motor cortical activity and higher cognitive functions such as mental rotation (Cisek and Scott 1999). This ambiguity in interpreting cell discharge stems from the fact that movement variables are highly inter-correlated and thus neural discharge will co-vary with many variables, obfuscating the ability to identify the nature of neural activity during a task such as reaching. In many ways, this difficulty in dissociating movement variables is not new or unique to reaching paradigms. Evarts, in his seminal work in the 1960s, recognized this problem and dissociated movement direction from muscle force by applying bias loads to the handle grasped by the monkey.

There have also been a number of other studies developed to dissociate different movement variables during reaching. One of the first studies by Caminiti and colleagues explored neural activity in the motor cortex while monkeys made reaching movements in three different regions of space: to the left, central, and to the right of the monkey (Caminiti et al. 1990). They found that neural activity of shoulder-related cells tended to rotate with shoulder angle and did not remain invariant to the direction of hand movement in Cartesian space. However, since the spatial location of the targets in the three parts of space rotated relative to the head, these results are consistent with neural discharge being related to movement of the hand relative to the body or to movement of the shoulder itself.

Perhaps the largest series of studies developed to assess how variables of movement related to the motor periphery may influence motor cortical activity during reaching has been directed by John Kalaska over the last fifteen years. One of these studies focussed on whether neural activity in the motor cortex was sensitive to changes in arm orientation during reaching (Scott and Kalaska 1997). Monkeys were trained to make reaching movements from a central target to one of eight peripheral targets located on the circumference of a circle using two different arm orientations. The first was the monkey's preferred or natural arm orientation where the monkey grasped the handle and the elbow was positioned vertically below the hand and shoulder. The second posture required the monkey to abduct its arm approximately 80 degrees to grasp and move the handle. Most neurons significantly changed their activity when making reaching movements with different arm orientations even though the hand paths were similar. Most cells changed their directional tuning, their magnitude of activity, or both. Other studies from this laboratory have shown how mechanical loads and hand location change the activity of motor cortical activity during reaching (Kalaska et al. 1989; Sergio and Kalaska 1997). The conclusion from all of these studies is that neural activity is sensitive to changes in features of movement re-

lated to the motor periphery and this is inconsistent with the notion that neural activity in the motor cortex is simply related to features of movement related to the hand.

While the above experiments were designed to separate variables related to the hand from variables related to the motor periphery, another class of experiment has been developed to dissociate variables related to movement execution from stimulus direction (Shen and Alexander 1997; Zhang et al. 1997). One of these studies dissociated these variables by training a monkey to make movements with a joystick that moved a cursor on a computer screen using two different mappings. The first, simple mapping coupled rightward movements of the joystick with rightward movements of the screen, forward movements of the joystick with vertical movements on the screen and so forth. The second mapping shifted the above relationships by 90 degrees. For example, rightward movements of the joystick elicited upward motion of the cursor. Neural activity in the motor cortex during a delay period was often related to the stimulus. However, neural activity immediately prior to and during movement was predominantly related to the actual motion of the limb, suggesting that neural activity was principally related to the motor rather than the spatial aspects of the task.

A recent study has again explored the issue of whether neural activity is related to the global features of movement or more detailed information related to muscle activity (Kakei et al. 1999). In this case, hand movement was dissociated from muscle activity by training monkeys to make wrist movements in three different wrist postures: supinated, neutral, and pronated. The major point of this article was that some cells were closely coupled to the direction of hand movement, whereas other cells were closely coupled to the patterns of muscle activity which systematically changed with arm posture. While the emphasis of the article was to illustrate that hand-based variables were equally if not more prevalent than joint-based variables, this interpretation was almost exclusively based on the directional tuning of cells. Another important feature of neural discharge is the magnitude of cell discharge. If neural discharge was exclusively related to features of movement related to the hand, they should show no changes in cell discharge when movements are performed in different wrist orientations. However, most cells (86%) showed a change in directional tuning or in the magnitude of activity with wrist posture. Clearly, these results along with those described above illustrate that neural activity in motor cortex does not reflect one single feature of movement.

The dilemma

Reaching movements require the central nervous system to coordinate motor patterns at the shoulder and elbow to smoothly move the hand in space. The discussion above outlines two very different perspectives as to how the primary motor cortex contributes to the coordination of multi-joint movements. Correlations between motor cortical activity and motor patterns at single joints suggests that the motor cortex plays a pivotal role in motor coordination. In contrast, the results from hand-based paradigms have been interpreted as evidence that the motor cortex provides global information related to the task and that details of motor coordination be-

Fig. 4. Side and Top Views of a monkey wearing KINARM. Hinge joints are adjustable and can be aligned with the center of rotation of the monkey's shoulder and elbow joints. The linkage allows the monkey to move its hand in the horizontal plane by making combined flexion and extension movements at the shoulder and elbow. Accelerometers are located underneath the monkey's hand and torque sensors are attached to the base of the torque motors. Each motor is attached to the device using timing belts.
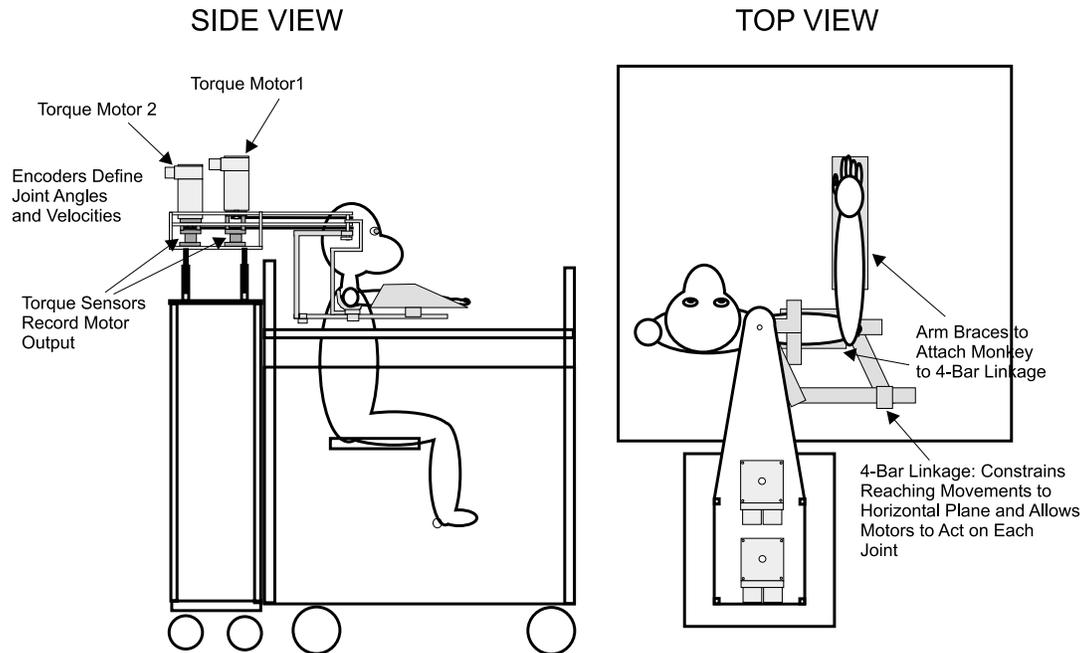

tween the joints only occurs at the spinal level. While several studies have shown that neural activity in the motor cortex is influenced by variables related to the motor periphery during reaching, such as arm posture, these studies cannot tell us the portion of the motor periphery, shoulder, and (or) elbow, that cell activity is related to.

This raises a rather surprising question, "Why can't a reaching paradigm that requires coordinated motor patterns at multiple joints tell us anything about how regions of the brain coordinate motor patterns at different joints?" The answer to this question is simply that this reaching paradigm was never developed to examine multi-joint coordination. As described above, the centre-out reaching task developed by Georgopoulos and colleagues twenty years ago was designed to examine how shoulder-related cells behaved during a task in which shoulder motion included multiple degrees-of-freedom. For technical reasons, neural activity was related to the hand rather than the shoulder. As a result, it was much easier to manipulate hand- based rather than joint-based variables and kinematics was easier to study than kinetics. While some studies illustrate that neural activity in the motor cortex is strongly influenced by features of movement related to the hand, it provides no information on how the motor cortex coordinates motor patterns at different joints.

As described in the previous section on motor cortical activity during reaching, the debate on how motor cortex participates during movement has generally focused on examining what features of the task, sensory versus motor, hand versus joint, kinematic versus kinetic, are reflected in the discharge patterns of cells. While evidence continues to

mount that neural activity in motor cortex can reflect all of these features to varying degrees, the basic question on the peripheral focus of each cell remains largely unexplored. Neural activity could reflect the involvement of only a single joint in a multi-joint task (Fig. 3A) or it could reflect the involvement of multiple joints (Fig. 3B). This issue cannot be resolved easily with existing experimental paradigms. However, there are certain observations in the literature that would suggest that the activity of at least some cells in the motor cortex is likely related to motor patterns at the shoulder and elbow during reaching. First, spike triggered averaging techniques relating limb muscle activity to motor cortical cell discharge suggest that some cells synapse directly onto motoneurons that innervate muscles spanning multiple joints, including muscles that span the shoulder and elbow (McKiernan et al. 1998). It seems reasonable to believe that the activity of these cells would reflect the motor patterns at more than one joint. Second, detailed studies on finger movements illustrate that neural activity is related in a complex way to movements of multiple digits (Schieber 1993). This activity likely reflects the distributed influence that motor cortical cells have on the motor periphery as well as the complex organization of the intrinsic and extrinsic muscles of the hand (Schieber 1995). Such distributed influence on the control of muscles at different joints is likely to exist also at the shoulder and elbow during whole-limb movements. Third, Scott and Kalaska (1997) found that many cells received proprioceptive input from both the shoulder and elbow, suggesting that neural activity in motor cortex may be related to motor patterns at multiple joints. However, exploring how these cells are related to motor pat-

Fig. 5. Comparison of the kinematics and kinetics of limb motion with (dot-dashed line) and without (solid thick) a viscous load applied to the shoulder and elbow (top and bottom rows, respectively). Thin lines denote one standard deviation for each respective signal. Movement for the unloaded condition is from Fig. 1. A viscous load is generated by the motors based on the angular velocity of the joint; the faster the motion, the larger the opposing load. Note how the joint position and velocities are quite similar for the two tasks. In contrast, there are large temporal changes in the elbow torque between viscous and unloaded conditions.
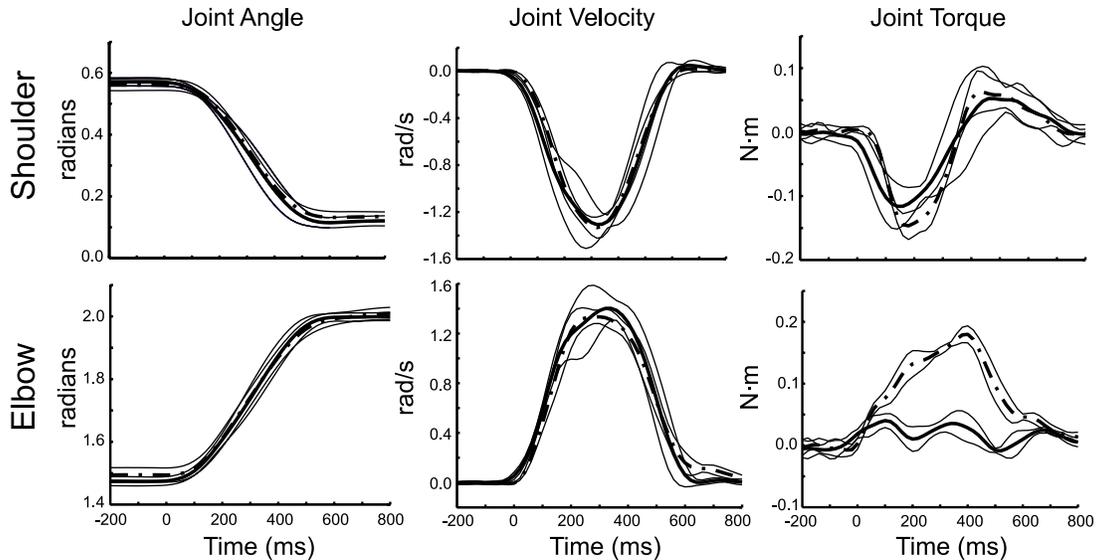
terns at the different joint is difficult with existing paradigms since they cannot systematically manipulate the motor patterns at each joint independently.

A new experimental paradigm

To explore how neural activity is related to coordinating motor patterns at different joints, it is necessary to both directly monitor and manipulate features of coordinated movement (Scott 1999). Towards this goal, we have developed a new experimental device specifically designed to examine the relationship between neural activity and motor coordination (Fig. 4). The device called KINARM (Kinesiological Instrument for Normal and Altered Reaching Movements) is an exoskeleton that is attached to the upper arm and forearm of a monkey. The mechanical linkage allows the monkey to make combined flexion and extension movements of the shoulder and elbow joints to move its hand to targets in the horizontal plane. The linkage is adjustable to align its low-friction, ball-bearing joints with the centers of rotation of the shoulder and elbow joints. Two torque motors are attached to the linkage with one motor coupled to the upper-arm and the other coupled indirectly to the forearm. The motors can be used to apply loads to the shoulder and elbow independently. KINARM measures several kinesiological variables of movement. Joint angular position is obtained from motor encoders and hand position is computed from joint angles using trigonometry. Hand acceleration is measured by two linear accelerometers (Entran, EGAXT-5) attached to the linkage just below the hand. The magnitude of torque applied to the mechanical linkage by each motor is monitored using reaction torque sensors (Transducer Techniques, TRT-50) attached to the base of the motors. Finally, the time-varying net muscular torque generated at the shoulder and elbow can be estimated during limb movements given the kinematics of the joints, and the length, mass, and inertial characteristics of KINARM and the monkey's arm.

The present device simplifies multi-joint movements so that they occur in the horizontal plane with motion at each joint restricted to a single degree-of-freedom. While the device does not allow variations in arm orientation during posture and movement, the device can be used to examine issues related to the selection of hand trajectory for movement. The ability to directly manipulate the motor patterns at each joint independently is the most important feature of the new device. Figure 5 compares the kinematics and kinetics of limb motion when the monkey performs a reaching movement with and without a viscous load applied to the elbow. A viscous load is proportional to movement velocity: the faster the joint motion, the larger the opposing torque applied by the motors. In this case, the monkey was trained so that the kinematics of the limb motion, both in the trajectory of the hand as well as the angular motion of the joints, are similar between loaded and unloaded movements. In contrast, the net muscular torque at the elbow in the loaded condition increased substantially when movements were performed with the viscous load. Net shoulder torque remained the same as observed for the unloaded conditions.

There are several important issues that this device and this type of load can address with regards to examining neural discharge in a region such as the primary motor cortex. Most obvious is the ability to dissociate kinematic and kinetic features of movement and the use of torque motors to apply transient loads during movement rather than a constant load acting during both posture and movement. However, the present device allows us to go one step further by examining whether neural activity is related to changes in motor patterns at only the shoulder or only the elbow, or at both joints. Preliminary observations on the discharge patterns of

motor cortical cells during these tasks illustrate that in some cases neural activity is modulated by loads at only the shoulder or only the elbow, whereas the activity of other cells is modulated by loads at both joints (Cabel and Scott 1999; Gribble et al. 1999).

While the facility was developed to relate neural activity to the motor periphery, it is important to recognize that hand position can be computed from joint kinematics so that neural activity can also be related to global features of the task such as the direction of hand movement. Further, simple modifications of the device can allow loads to be applied through a grasped handle rather than directly onto the limb segments and allow experimental paradigms that manipulate features of movement related to the hand.

Our ability to move our hand effortlessly and gracefully through space belies the underlying complexity of the mechanics of limb motion. It is known that the primary motor cortex plays an important role in volitional movement yet we know very little about how neural activity in this region of the brain contributes to coordinated motor patterns at different joints. The goal of this article has been to review this issue and to describe a new device developed to address this problem. It is hoped that this new experimental facility will provide an additional perspective on how regions of the central nervous system, such as the primary motor cortex, contribute to movement planning and control.

Acknowledgements

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