Reaching for Answers

The exact function of motor cortex continues to be an enigma. In this issue of *Neuron*, Graziano et al. (2002) present provocative data showing that microstimulation of the precentral cortex evokes complex movements, and conclude that the motor and premotor cortex together may form a single map of complex postures.

It has long been known that the cortex of the precentral gyrus composes a motor map of the body, but the role of this area in motor control remains controversial. This is largely because the motor cortex exhibits different properties under different experimental conditions. Early studies of wrist-only movements showed that neuronal activity was correlated with muscle force (Evarts, 1968). In contrast, studies of reaching movements in space found activity related primarily to the direction (Georgopoulos et al., 1982) and speed (Moran and Schwartz, 1999) of the arm movement. Many neurons in motor cortex also exhibit directional preferences for forces applied under isometric conditions, when the arm does not move (Sergio and Kalaska, 1998). This diversity of results has led to spirited debates about whether the output of the motor cortex is primarily involved in the low-level control of muscles or in the high-order control of movement direction and trajectory.

In this issue of *Neuron*, Graziano et al. (2002) present data that are certain to add fuel to this debate. They show that microstimulation of the motor and premotor cortex elicit movements that are far more complex than would be expected if the output of the motor cortex controlled either groups of muscles or directions of movement. Unlike most previous studies, they applied microstimulation for relatively long intervals (500–1000 ms) chosen to approximate the timescale of normal reaching and grasping movements. Also, rather than training monkeys to perform tasks with special manipulanda, they achieved a range of different starting postures simply by having monkeys reach for pieces of fruit placed at various locations. The movements evoked under these conditions converged onto stereotyped and seemingly purposeful postures, typically involving many joints and muscle groups. The details of the evoked postures depended on the sites of microstimulation, and varied systematically across both the motor and premotor cortex on the precentral gyrus. For example, microstimulation at sites within the arm representation of primary motor cortex moved the hand to particular positions in space, regardless of the starting posture of the arm and hand when the microstimulation was applied. Microstimulation at some sites located within the hand and mouth representation of premotor cortex resulted in a posture that mimicked holding food at the mouth: the contralateral hand closed into a grip posture with the thumb and forefinger placed near the mouth, and the mouth opened. At sites in the premotor cortex near neurons that respond to both tactile and visual stimuli, microstimulation evoked coordinated movements of the arm, head, and face that resulted in defensive postures seemingly aimed to guard the monkey from some impending bodily threat.

Are these complex postures simply serendipitously occurring spontaneous movements? Apparently not because they occur at short latencies with respect to the microstimulation ($<$66 ms), and they persist in full form under anesthesia, albeit less consistently. The microstimulation-evoked movements also appear to supersede the monkey's normal reaching movements, and completely fail to compensate for obstacles placed in the movement path.

Are the evoked movements indistinguishable from normal voluntary movements? The hand trajectory evoked from at least one site exhibited the same bell-shaped velocity profiles that are characteristic of normal movements, but these aspects of the results are not as thoroughly documented. Indeed, the relatively unstructured nature of the experiment, combined with the complexity of the evoked movements, makes it difficult to perform the types of quantitative analyses that would be required to fully address this issue.

Might the evoked movements be artifacts of microstimulation that are not indicative of normal motor function? Interpretation of microstimulation effects is always complicated by the artificial nature of disrupting neuronal function with externally applied current. In particular, with long periods of microstimulation such as those used in this study, it is likely that neurons in other areas were recruited by the sustained and entrained activity of the neurons at the tip of the stimulating electrode. Thus, the movements evoked by microstimulation were probably due to activation of an extended network of brain regions involved in combining multiple movements into single actions, including other motor-related areas of cortex (Rizzolatti and Luppino, 2001) and possibly the cerebellum (Thach et al., 1992). It would be interesting to know if complex postures could still be evoked from motor cortex after inactivation of these other regions.

These findings are related to other recent studies showing that motor cortex is involved in higher order aspects of motor control. For example, the sites at which hand-to-mouth postures were evoked correspond to the lateral ventral premotor area (F5), which contains neurons active not only during specific types of grasping movements but also during observation of visual stimuli associated with that grasp (Rizzolatti et al., 1988; Rizzolatti and Luppino, 2001). By providing prototypes of commonly required movements that are also visually indexed, these neurons could simplify the control of visually guided reaching and grasping; the fundamental transformation of visual information into motor coordinates required to construct these complex properties involves interactions between the premotor and parietal cortices (Wise et al., 1997; Andersen et al., 1997).

Determining when and how to put motor prototypes together as components of a fully formed action involves learning at many sites along the motor pathways, including the motor cortex (e.g., Li et al., 2001). Actions also need to be gated according to learned behavioral rules, a function associated with the presupplementary motor area and the striatum (Hikosaka et al., 1999). This context-dependent gating of actions may explain why the predominant microstimulation effects observed by Graziano et al. (2002) were postures associated with manipulating food or guarding the body—the monkeys in this experiment were presumably in a "motor set" associated with receiving food from a larger and potentially dangerous primate. Is the failure to observe these complex and seemingly natural postures in previous studies a result of training monkeys to perform simple and evidently unnatural tasks? Given that many physiological studies involve more-or-less unnatural tasks, one disquieting possibility is that some of the properties attributed to "normal" brain function are actually the products of adaptive plasticity in highly trained subjects.

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Selected Reading

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