Vision to action: new insights from a flip of the wrist

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Interactions between the ventral premotor area (PMv) and primary motor cortex may contribute to a sensorimotor transformation between intrinsic and extrinsic coordinates.

We regularly use vision to guide our motor actions, whether we are reaching to grab a cup of coffee to start the day, hitting a nail with a hammer, or delicately grasping and picking a flower in the garden. How does the central nervous system convert visual information, initially defined by sensory receptors in retinas, into muscle activation patterns to smoothly and accurately move our limbs in space? This formidable task has generally been addressed as a problem of sensorimotor transformations, where visual information is converted through several intermediary representations. These representations include some higher-level representation related to the global goal of the task (that is, moving to a spatial target) and finally, motor commands for muscles[1,2]. However, there remains considerable debate (confusion?) as to what intermediary 'coordinate frames' are represented and how they are mapped onto the brain. A key experimental approach has been to develop motor tasks that dissociate different putative coordinate frames to identify whether neural activity relates to one variable better than another.

In this issue, Kakei and colleagues[3] used a novel protocol in which a monkey made wrist movements of similar magnitude to eight spatial targets uniformly distributed around an initial wrist position. The monkey was trained to make these movements in three different forearm orientations: pronated, neutral or supinated (**Fig. 1**). A key feature of this experimental protocol was that forearm rotation (from supination to pronation) was orthogonal to the plane of the task that involved wrist flexion/extension and radial–ulnar deviation[4]. For a given target, these wrist movements dissociated three coordinate frames when performed in pronated and supinated positions: first, a coordinate system based on hand orientation (the direction the palm of the hand moves), which varied by 180 degrees, second, muscle coordinates, which varied by approximately 90 degrees and by the magnitude of muscle activity (which often changed between arm orientations)[4], and third, spatial coordinates of hand direction, which remained constant.

There are several parietal and frontal regions related to visually guided wrist movements, including ventral premotor cortex (PMv), a premotor region that receives vision-related information from various parietal regions[5] and projects to the wrist region of primary motor cortex[6]. Whereas PMv certainly is key in vision-guided motor tasks, it is not clear which 'coordinate frame' best describes neuronal activity in this region during movement.

The first point demonstrated by Kakei and colleagues was that virtually all cells in PMv show no differences in their activity for movements performed in the different wrist orientations, either in their directional tuning (direction in which a cell is maximally active) or in the magnitude of discharge for each movement direction. This provides convincing proof that neural activity in this cortical region has little to do with the underlying patterns of muscle activation, nor the orientation of the hand in space. Rather, it seems to be related in some way to the spatial direction of hand motion.

These results are even more interesting when they are compared to the response of neurons in primary motor cortex, which show a far more complex representation of movement: some cells appeared to be spatial-like, others, muscle-like, and still others, hybrids in which changes in wrist orientation had little effect on directional tuning, but produced significant changes in the overall level of activity[4]. These results suggested a shift from a spatial representation of action in PMv to a more muscle-like representation in MI, a sensorimotor transformation.

The current article is a refreshing change for those interested in the general problem of sensorimotor transformations related to visually guided limb movements. Most previous studies on this issue, including my own, examine neural correlates of whole-limb reaching movements in primary motor cortex and dorsal premotor cortex (PMd), a region often associated with proximal-limb movements, located just medial to PMv[7–9]. Whereas these earlier reaching studies tended to show a difference in neural representations between primary motor and premotor cortices, the present results show a much stronger separation. This may reflect differences in neural representations between PMv and PMd, or the fact that the wrist protocol used by Kakei and colleagues provides a more clear dissociation between spatial and motor variables[7,8] and a more natural relationship between spatial and movement direction[9]. Although this wrist-based protocol still used computer-generated visual feedback (instead of actual spatial targets located about the wrist), the results provide a clear association between PMv activity and spatial movement direction, and a clear dissociation in the behavior of neurons in the different cortical regions.

An important feature of many PMv neurons is that they have both tactile and visual peripersonal receptive fields defined in some 'arm-centered' frame[10,11]. For example, when the forearm is pronated and the hand is palm-down, a cell may respond to tactile input on the back of the hand and visual input directly above this body surface. An interesting question is if the forearm is now supinated and the hand is palm-up, does the cell still respond to tactile input on the back of the hand and possess a visual field directly below the hand, or will the tactile response flip to the palm of the hand and the visual field remain above the hand? The spatial-like cells observed by Kakei and colleagues[3] suggest that cells may behave in the latter manner.

A point that may remain controversial in the study by Kakei and colleagues relates not to the behavior of PMv cells, but to the response of neurons in MI during this task. On the one hand, the observation that spatial-like and muscle-like neurons are almost equally represented in MI should satisfy most individuals debating the neural representation of movement in MI. On the other hand, the cortical map

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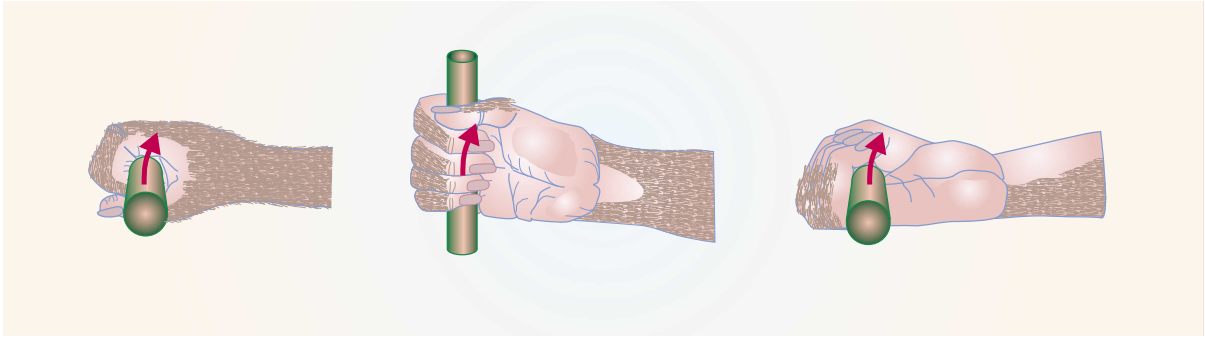

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Fig. 1. An upward movement of the hand is produced by wrist extension when the forearm is pronated (left), by radial deviation when the forearm is held in a neutral position (middle) and by wrist flexion when the forearm is supinated (right). Kakei and colleagues use this influence of forearm position on wrist motion to show that the activity of neurons in ventral premotor cortex during movement only reflects the spatial direction of movement and not the underlying muscle activity or joint motion.

where neurons were recorded shows an intriguing anatomical organization, with most muscle-like (intrinsic) neurons clustered in a central region surrounded by more spatial-like (extrinsic) neurons, reminiscent of previous suggestions of a center-surround organization of the forelimb representation in MI[12]. Does this segregation highlight a fundamental separation of wrist-related neurons in MI based on spatial and motor representations? Alternatively, the surrounding spatial-like cells may be involved not just for wrist motor tasks, but also tasks that involve other joints, such as the elbow. It should not be surprising that MI neurons may respond to motor patterns at more than one joint. As most muscles span multiple joints, neurons often respond to passive motion at multiple joints[13]; even corticomotoneurons often synapse on motoneurons of muscles at several joints[14]. It would be interesting to know whether this apparent anatomical segregation of muscle- and spatial-like cells is simply an anomaly of this single animal or a more general observation on the organization of MI.

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The short p75 neurotrophin receptor is long on function

The once-neglected p75 neurotrophin receptor ($p75^{NTR}$) has been getting a lot of attention lately – and rightly so, given its diverse signaling roles and its function as the cell death counterpart to the well studied Trk neurotrophin receptors, which promote cell survival. Dechant and colleagues from the Max Planck Institute of Neurobiology in Martinsried continue this trend on page 977 of this issue by showing that a recently identified, short splice variant of $p75^{NTR}$ is critical to development not only of the nervous system but also of the vascular system. The authors made a transgenic mouse that lacks both the full length $p75^{NTR}$ receptor and the short variant (which was still expressed in the initial knockout of this receptor). This new mutant has a number of phenotypic characteristics presumably specific to the loss of the short splice variant. In addition to more severe defects in motility and peripheral nerve morphology than the long splice variant knockout, the newly characterized mutants are smaller than their wild-type counterparts (pictured). The mutants also have increased lethality at birth, most likely due to the vascular defects. The short $p75^{NTR}$ protein has an intact intracellular signaling domain, but lacks an extracellular neurotrophin binding domain. Because the mechanism of the short isoform's signaling is not well understood, clues to its function from the knockout may be particularly important.

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