Journal Club

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Visuomotor Representations within the Human Primary Motor Cortex: The Elusive Markers of Visuomotor Associative Learning

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Review of Eisenberg et al.

What is the nature of representations within the human primary motor cortex (M1)? Early primate studies proposed that M1 is mainly involved in encoding muscle force, i.e., intrinsic aspects of movement (Evarts, 1968). Later studies involving single-cell recordings in primates suggested that neuronal activity within M1 also encodes extrinsic parameters of movement, such as the position of a visual target that guides movement (Alexander and Crutcher, 1990). Moreover, many primate M1 neurons become sensitive to visual cues after brief associative learning sessions that pair, for instance, a colored cue with a motor command (Zach et al., 2008). Such findings indicate that M1 might be involved in sensorimotor transformations that translate muscle-extrinsic parameters into an intrinsic coordinate framework to guide movement, as well as in sensorimotor learning that creates new associations between a cue and a motor command.

Until recently, it has been difficult to test these hypotheses in humans, because noninvasive neuroimaging tools such as functional magnetic resonance imaging (fMRI) have lower spatial resolution than the single-cell recordings performed in monkeys. In particular, it remained unclear whether human M1 is sensitive to visual information such as the position of a movement's target. Eisenberg et al. (2011) addressed this question in a recent study published in *The Journal of Neuroscience*.

Eisenberg et al. (2011) used multi-voxel pattern analysis to dissociate, within M1, visual and motor aspects of a visually guided motor task. In multi-voxel pattern analysis, spatial patterns of blood-oxygen level-dependent (BOLD) signals within a specific region are computed separately under two conditions, and then the patterns are correlated to determine how much of an overlap occurs under the two conditions. In their experiment, Eisenberg et al. (2011) recorded fMRI data while participants used a joystick to move a cursor on a computer screen toward a target that appeared at five predetermined positions, In the baseline condition, the cursor moved in the same direction as the joystick. In the subsequent rotation condition, participants performed a similar task, but this time a 45° rotation was introduced between the direction of joystick movement and that of the cursor movement. Importantly, in the rotation condition, the direction of the hand movement did not correspond to the position of the target on the screen.

The authors compared patterns of activity recorded from M1 across trials in which hand movement directions were the same, but target positions differed, and across trials in which the target positions were the same, but hand movement directions differed. These comparisons allowed the authors to assess the activity induced by the motor condition (hand movement direction) alone or by the visual condition (target location and cursor displacement) alone. The analysis indicated that patterns of activity were correlated across both motor and visual conditions, strongly suggesting that in addition to the expected motor representation, specific visual aspects associated with motor commands were also represented within M1.

As discussed above, primate studies have shown that visual cues can become associated with a specific movement. It is therefore possible that in the Eisenberg et al. (2011) study, subjects may have learned to associate the position of a visual target with the need to execute a specific motor command. This would mean that activity in M1 did not reflect the visual aspects of the task, but rather, aspects of the motor commands the visual cues were paired with. To address this question, Eisenberg et al. (2011) had subjects per-

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form a classical visuomotor associative learning task. Participants were first asked to passively watch previously recorded trials showing a cursor move toward a target (observation condition). Afterward, participants were asked to perform the visuomotor task used in the baseline condition in the previous experiment (execution condition). Finally, subjects performed a second passive observation run (second observation condition). Again, correlation coefficients were calculated for M1 activity between these conditions for identical and different directions of hand and cursor movements. Under the associative learning hypothesis, each target location/cursor displacement would have been paired to a specific motor command in M1 during the visuomotor task. Therefore, for each direction, a significant correlation would be expected between the patterns of M1 activity during the execution condition and the second observation condition. On the contrary, results showed that correlation coefficients between these conditions were not significantly different from zero. The authors thus concluded that the results from the first experiment could not be explained by visuomotor associative learning.

The visuomotor associative learning task used by Eisenberg et al. (2011) is very similar to ones used in action observation research. Interestingly, recent results in this field suggested that visuomotor associative learning might originate in the premotor region and influence M1 excitability via strong corticocortical connections (Catmur et al., 2008, 2011). Catmur et al. (2007) proposed that the cerebral response to action observation (motor-like activity in the observer's brain during the observation of someone else's movement) might be the result of visual representations of action becoming linked to motor representations through Hebbian-like learning. The results of several transcranial magnetic stimulation (TMS) studies using an associative learning task in which observed movements were paired with executed movements have supported this hypothesis (Catmur et al., 2008). Moreover, Petroni et al. (2010) demonstrated by measuring motor facilitation (i.e., increase in M1 excitability) with TMS that other visual stimuli can modulate the excitability of M1 in a similar way. In this experiment, participants were asked to associate abstract visual cues (a blue or red cross) with the execution of a specific finger movement (index or little finger abduction). The results showed that after the visuomotor associative task, the mere presentation of the visual cue was sufficient to induce a motor facilitation specific to the finger muscle to which it was paired during learning. Together, these results indicate that pairing a visual stimulus with movement execution induces a specific modulation of M1 excitability during the subsequent presentation of this cue and that this pairing mechanism may originate in the premotor cortex (Catmur et al., 2008, 2011).

In light of these results, one might be surprised that using a similar paradigm, Eisenberg et al. (2011) found no evidence for visuomotor associative learning in M1. Interestingly, this could relate to a long-lasting paradox in action observation research. Indeed, while studies using TMS have persistently found that observing a movement can produce motor priming in M1, fMRI studies have very seldom found significant BOLD increases in M1 during action observation. As mentioned by Eisenberg et al. (2011), it is possible that the modulation of M1 excitability by visual cues alone may be too subtle to be observed with fMRI when no action is performed. In fact, the authors mentioned that because the primary motor cortex was substantially less activated in the observation conditions, it resulted in poor signal-to-noise ratio in the fMRI data. Importantly, the authors stressed that this could have masked possible correlation between the conditions. Taking this into account, results from the control experiment cannot completely rule out the possibility that visuomotor association learning has taken place during Eisenberg et al.'s experiments.

The results presented by Eisenberg et al. (2011) are an important contribution to the study of visuomotor representations. Using multi-voxel pattern analysis, they showed that visual and motor aspects of a visually guided motor task may trigger different neural populations within M1, thus producing independent patterns of activity. Still, the possible role of visuomotor associative learning in the tasks presented here remains to be confirmed or refuted. Because visuomotor associative learning is heavily involved not only in action execution, but also in action observation, it is important to identify techniques that would optimize its study.

The data related to the visuomotor associative learning task presented by Eisenberg et al. (2011) stress a weakness of the multi-voxel pattern analysis technique: it heavily relies on good signal-to-noise ratio, and thus strong activation in the studied region. To compensate for this limitation, future research could take advantage of multimodal imaging approaches such as fMRI with TMS (Bestmann et al., 2008) because TMS has been shown to detect subtle changes in M1 activity stemming from visuomotor associative learning. Indeed, such multimodal approaches will likely expand our understanding of visuomotor representations and help bridge part of the huge gap between single-cell recording in monkeys and noninvasive neuroimaging in humans.

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