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The Mirror Neuron System

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Mirror neurons are a class of neurons, originally discovered in the premotor cortex of monkeys, that discharge both when individuals perform a given motor act and when they observe others perform that same motor act. Ample evidence demonstrates the existence of a cortical network with the properties of mirror neurons (mirror system) in humans. The human mirror system is involved in understanding others' actions and their intentions behind them, and it underlies mechanisms of observational learning. Herein, we will discuss the clinical implications of the mirror system.

Mirror neurons were first described in the F5 sector of the macaque ventral premotor cortex.[1,2] These neurons, like most neurons in F5, discharge in association with movements that have a specific goal (motor acts). They do not fire when a monkey executes simple movements, that is, during active displacement of a body part devoid of a specific goal.

Neurons with the same characteristics as those in area F5 were also found in the inferior parietal lobule (IPL) of monkeys. These 2 areas form a network that is embedded in the system of parietofrontal circuits that organize actions.[3] Visual information on biological motor acts reaches F5 through connections with the superior temporal sulcus, where actions performed by biological agents are coded.[4] In the superior temporal sulcus, neurons do not appear to discharge in association with motor behavior.

It is generally assumed that the main functional role of parietofrontal mirror neurons is to understand motor acts performed by others in an automatic way, ie, by matching them to the monkey's own motor repertoire.[5] Evidence in favor of this hypothesis came from experiments that showed that F5 mirror neurons also fire when monkeys cannot see the triggering feature of a motor act but have sufficient clues to understand its goal[6] or when monkeys recognize an action from its sound only.[7] These data indicate that premotor mirror neurons discharge whenever the monkey builds up an internal representation of a motor act made by another agent, even if the monkey does not see it.

Recent data on the motor organization of the IPL show that mirror neurons are involved in more complex functions than motor act understanding. It was found that most hand-related neurons in the IPL differently encode the same motor act when it is embedded in different actions (eg, grasp to eat and grasp to place). These have been named action-constrained neurons.[8] Most interestingly, many of these neurons have mirror properties that are congruent with the action-constrained pattern. Their behavior is illustrated in **Figure 1**. These findings indicate that action-constrained parietal mirror neurons do not only encode the observed motor act (eg, grasping), but also the aim of the observed action. It has been hypothesized that this organization provides a neural substrate for understanding the goal of the entire observed action before it is concluded.

THE MIRROR SYSTEM IN HUMANS

Evidence of the existence of a mirror system in humans comes from neuroimaging

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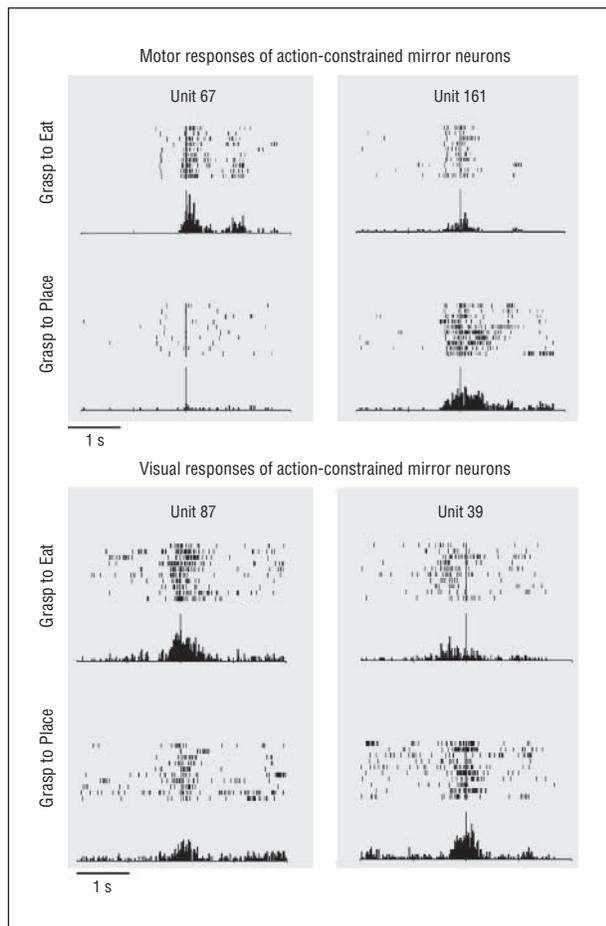
Figure 1. Peristimulus histograms of 4 action-constrained neurons recorded from the monkey inferior parietal lobule. The 2 neurons on the left (units 67 and 87) discharged when grasping was embedded in a grasp-to-eat action but would not fire when grasping was the first step of a grasp-to-place action, though these 2 actions are identical. The opposite behavior was observed in the 2 neurons on the right side (units 161 and 39).[8]

studies and noninvasive neurophysiological investigations (electroencephalography, magnetoencephalography, and transcranial magnetic stimulation [TMS]).[9] Neuroimaging demonstrated the existence of 2 main networks with mirror properties: one residing in the parietal lobe and the premotor cortex plus the caudal part of the inferior frontal gyrus (parietofrontal mirror system) (Figure 1), and the other formed by the insula and the anterior mesial frontal cortex (limbic mirror system). The parietofrontal mirror system is involved in recognition of voluntary behavior, while the limbic mirror system is devoted to the recognition of affective behavior. In the present review, we will describe only the first system.

REPRESENTATION OF OBSERVED MOTOR ACTS IN THE PREMOTOR AND PARIETAL CORTICES

A series of experiments have addressed the issue of the anatomical and functional organization of the parietofrontal mirror system. Most of them investigated transitive (goal-directed), distal motor acts. These studies showed that these acts are coded in the ventral premotor cortex according to a rough somatotopic organization,[10,11] with motor acts in the legs being located dorsally, oral acts located ventrally, and manual acts in an intermediate position.[10] The localization of proximal motor acts, ie, the transport phase of the hand to a particular location, was found in a recent functional magnetic resonance imaging (fMRI) study to be represented more dorsally than grasping acts, in the dorsal premotor cortex.[12]

These studies and other works have also explored the representation of observed motor acts in the parietal cortex. Transitive motor acts were found to be represented in the intraparietal sulcus and on the IPL convexity immediately adjacent to it.[10,11] Additional studies have investigated the organization of the parietal lobe during the observation of actions different from distal goal-directed acts. Reaching movements were shown to be located in the superior parietal lobule, extending ventrally into the intraparietal sulcus. Intransitive (non–object directed) manual actions have been shown to have their own specific parietal representation located—regardless of the act being symbolic, mimed, or meaningless—in the posterior part of the supramarginal gyrus, extending into the angular gyrus.[13] Finally, the observation of actions made with tools, besides activating the hand-manipulating region, specifically activates the most rostral part of the supramarginal gyrus, ventral to the area of representation of hand grasping.[14]

CONGRUENCE BETWEEN OBSERVED MOVEMENTS AND MOTOR ACTIVATION IN THE OBSERVER

In healthy adults, observation of others' motor behavior does not induce overt motor activity in the observer. However, several studies have discovered a subliminal motor activation that is associated with action observation by applying TMS over the primary motor cortex,[15] which also showed a strong congruence between the observed motor behavior and the evoked motor output.[16] An increase in the observer's motor evoked potentials is found when recording from the same muscles that are recruited in movement execution and with the same activation timing. This phenomenon occurs mostly at the cortical level as shown by TMS paired-pulse paradigms.[17]

Transcranial magnetic stimulation experiments have provided strong evidence that the human mirror system also codes simple movements. However, in agreement with fMRI and monkey data, TMS can also reveal mirror activation related to the goal of the observed motor act. A TMS study showed that while observing a reaching and grasping act that is suddenly modified by an unpredictable movement, motor evoked potential facilitation mirrors the time course of the predicted motor act rather than adjusting to its incongruent variant in real time.[18]

MOTOR EXPERIENCE AND MOTOR LEARNING

There is evidence that only motor acts that are present in the motor repertoire of the observer are effective in activating the mirror system. This was shown in an fMRI experiment in which oral actions made by humans, monkeys, and dogs were presented to normal human volunteers. The data demonstrated that the left hemisphere IPL and inferior frontal gyrus responded to actions made by a human and a nonhuman performer, as long as the ac-

tion was part of the motor repertoire of the human observer (eg, biting for eating). The mirror system failed to be activated when the action belonged to another species (eg, barking).[19]

Activation of the mirror system is also related to the observer's motor experience of a given action. This has been clearly demonstrated in experiments that use dance steps as observed stimuli. First, it was shown that, in the observer, the amount of mirror activation correlated with the degree of his or her motor skill for that action.[20] Another experiment ruled out the possibility that this effect could be due to mere visual familiarity with the stimuli. Observing steps particular to male dancers produced a stronger mirror activation in professional male dancers than those performed by female dancers and vice versa.[21] An additional prospective study showed that dancers who were initially naive to certain steps showed an increase in mirror activation over time if they underwent a period of motor training in which they became skilful in performing the same steps.[22]

The mechanism involved in learning by imitation has been investigated in an fMRI study in which naive participants were asked to imitate guitar chords played by an expert player. Cortical activations were mapped during chord observation, a subsequent pause, and execution of the chord. The results showed that during new motor pattern formation, ie, in the pause between observation and execution, there was a strong activation of the mirror system, namely the IPL, the ventral premotor, and the pars opercularis of the inferior frontal gyrus plus Brodmann area 46 and the anterior mesial cortex.[23]

Direct evidence that convergence of observation and execution strongly facilitates the building of motor memories comes from TMS studies. These studies have shown that after a training period in which participants simultaneously performed and observed congruent movements, there was a potentiation of the learning effect with respect to motor training alone, as shown by the kinematics of the movement evoked by TMS.[24,25] This finding indicates that coupling observation and execution significantly increases plasticity in the motor cortex. Another TMS experiment showed that the muscle recruitment typically congruent with observed movements can be modified in the short-term by experience. Participants were trained to perform one movement while observing another. After training, the typical mirror effect was reversed. Increase in motor evoked potentials was now present in the muscle that controlled the practiced movement rather than in the muscle that controlled the observed movement.[26]

INTENTION CODING IN THE MIRROR SYSTEM

Recent evidence suggests that organization of a chained motor act similar to that underlying intention understanding in monkeys[8] is also present in humans. In an electromyogram experiment, typically developing children were asked to observe the experimenter who grasped a piece of food and brought it to his mouth or grasped an object and placed it into a container. An activation of the mouth-opening muscles was recorded during observation of the reaching and grasping phases when they preceded eating but not when the same acts preceded plac-
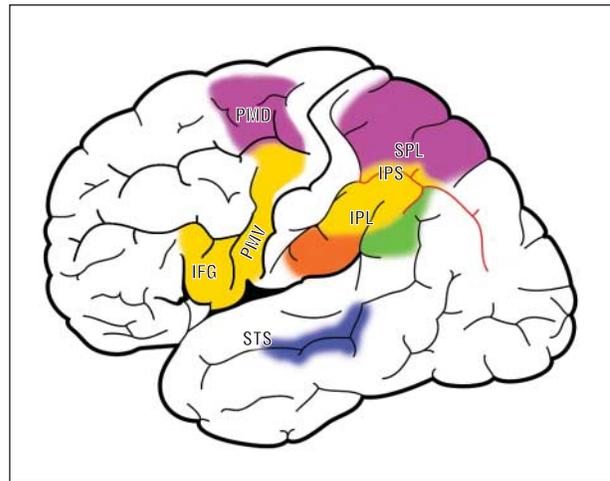
Figure 2. Cortical areas related to the parietofrontal mirror system responding to different types of motor acts.[10-14] Yellow indicates transitive distal movements; purple, reaching movements; orange, tool use; green, intransitive movements; blue, portion of the superior temporal sulcus (STS) responding to observation of upper-limb movements.[4] IFG indicates inferior frontal gyrus; IPL, inferior parietal lobule; IPS, intraparietal sulcus; PMD, dorsal premotor cortex; PMV, ventral premotor cortex; and SPL, superior parietal lobule.

ing. This activation showed a capacity of the child's motor system to predict the experimenter's intention.[27]

In line with this conclusion, 2 fMRI studies demonstrated an involvement of the mirror system of the right hemisphere in understanding intentions. In the first, contextual features were used to clarify the intention behind a hand-object interaction.[28] In the process of inferring intentions, the frontal node of the mirror system in the right hemisphere was recruited. In a second study, the right mirror system was found to be sensitive to the outcome of an action, such as opening or closing a box, independent of the means to achieve this outcome.[29] Taken together, these 2 studies indicate an important role of the right mirror system in ascribing intentions to others.

THE MIRROR SYSTEM IN DISEASE

From the point of view of the neurologist, it is important to conceive the mirror system not as a separated, self-standing neuronal system, but rather as a mechanism intrinsic to most motor-related cortical areas. In fact, it is increasingly clear that most cortical areas that organize movements also respond to movement observation (**Figure 2**). This conceptualization of the mirror system allows one to understand the lack of a selective impairment in functions that are attributed to the mirror system following focal lesions. A possible example of this is ideomotor apraxia. In this syndrome, some behavioral aspects, such as imitation deficits, may indicate mirror neuron system failure, but others, eg, the dissociation between spontaneous and on-command behavior, do not appear to be directly related to this mechanism.[30] Similarly, the dissociation between deficits in the imitation of transitive, intransitive, or tool-use acts may be interpreted as being due to lesions of specific sectors of the mirror network.[31] However, the mirror mechanism as such does not explain the motor deficits that may be associated with them.

It is more likely that syndromes of mirror system dysfunction are clinically evident in developmental disorders of the nervous system. Indeed, a role of mirror system dysfunction has recently been hypothesized for autism spectrum disorder.[32,33] Autism spectrum disorder is most likely a polygenetic disorder that is expressed as impairment of gray matter architecture and of corticocortical intrahemispheric connections.[34] Clinically, some functional deficits typical of autism spectrum disorder, such as deficits in imitation, emotional empathy, and attributing intentions to others, have a clear counterpart in the functions of the mirror system. Evidence of an involvement of the mirror system in autism has been repeatedly reported in recent years.[27,35-38]

Another aspect of possible clinical relevance of the mirror system is rehabilitation of the upper limbs after stroke. Recently, several approaches to stroke rehabilitation have been devised using techniques that induce long-term cortical plasticity.[39,40] The data on plasticity induced by motor observation provide a conceptual basis for application of action-observation protocols in stroke rehabilitation. Preliminary data indicate that this approach may produce significant clinical results.[41]

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