Functions of the Mirror Neuron System: Implications for Neurorehabilitation

Giovanni Buccino, MD, PhD,* Ana Solodkin, PhD,† and Steven L. Small, MD, PhD†

Abstract: Mirror neurons discharge during the execution of hand object-directed actions and during the observation of the same actions performed by other individuals. These neurons were first identified in the ventral premotor cortex (area F5) and later on in the inferior parietal lobule of monkey brain, thus constituting the mirror neuron system. More recently, mirror neurons for mouth object-directed actions have also been found in the monkey. Several pieces of experimental data demonstrate that a mirror neuron system devoted to hand, mouth, and foot actions is also present in humans. In the present paper we review the experimental evidence on the role of the mirror neuron system in action understanding, imitation learning of novel complex actions, and internal rehearsal (motor imagery) of actions. On the basis of features of the mirror neuron system and its role in action understanding and imitation, we discuss the possible use of action observation and imitation as an approach for systematic training in the rehabilitation of patients with motor impairment of the upper limb after stroke.

Key Words: mirror neuron, neurophysiology, neurorehabilitation, stroke, hemiparesis, treatment, frontal lobe, parietal lobe, motor cortex, premotor cortex, neuroplasticity, motor imitation, motor observation

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H and use in humans plays a critical role for the vast majority of social and cognitive functions of the species, including most types of communication and most activities of the workplace. Hand motor skill, or "the ability to solve a motor problem correctly, quickly, rationally, and resourcefully,"[1,2] has influenced the survival of the species, as demonstrated both phylogenetically and ontogenetically, and this skill has reached maximum expression in humans. To support this increase in the complexity of hand skill, there has been a parallel increase in the size of the neuropil, reaching a maximum in the human.[3] This suggests that the central nervous system has evolved to reach very complex patterns of connectivity among areas. Such connectivity is the basis of the complex neural circuits that support skilled hand motor functions.

These integrative circuits incorporate a variety of cerebral cortical regions, which participate to varying degrees in supporting hand motor tasks. The neural context[4,5] underlying regional involvement depends on task variables, such as complexity, bimanuality, sensory trigger, and planning requirements, and on individual variables, such as handedness, experience, health, and even emotional state and affect. These circuits must integrate information from visual, auditory, somatosensory, and limbic sources, and are, as recent experimental evidence demonstrates (see below), not only involved in the execution of actions, but also in higher cognitive processes such as action understanding, action imagining (internally generated), or action imitation (externally generated). Motor imitation represents a hand motor task in which there is specific visual and proprioceptive information that may facilitate movement, possibly by way of a specialized premotor circuit.[6] Motor imagery can harness visual circuits and/or motor circuits,[7–9] depending on the type of imagery performed, and has particular interest because it plays an important role in development of motor skill and can be used in neurologic patients with complete paralysis.

A principal tenet of medicine is that an organism must constantly adapt to changes in its external and internal environments.[10] Cerebrovascular insults (strokes) lead to important changes to the internal and external environments that can affect the functioning of the human brain with respect to hand motor skill. In this article, we review the neurophysiologic and neuroanatomic basis of action understanding, imitation, and imagery, and propose that it is possible to affect the physiology of the hand motor circuits through interventions aimed at internal and external influences on the generation of skilled hand movements, with a consequent profound effect on hand motor recovery after stroke.

MIRROR NEURON SYSTEM

Mirror Neuron System in the Monkey

The modern notion of the motor system in both humans and nonhuman primates has evolved dramatically over the past several decades, and is now thought to encompass a large number of regions and subregions. The premotor cortex of the macaque brain now encompasses almost a dozen such areas, defined by a combination of anatomic, chemical, and physiologic methods. A particularly interesting area in the rostral part of monkey ventral premotor cortex (Pmv) is area F5 according to the classification of Matelli et al,[11] which is considered the monkey homolog of Broca's region in humans.[12–14]

Area F5 contains a motor representation of mouth and hand goal-directed actions.[15] Interestingly, a proportion of these neurons that discharge during the execution of both hand and mouth goal-directed actions also respond when the monkey observes another monkey or an experimenter performing the same or a similar action.[16,17] These neurons are called mirror neurons because the observed action seems to be "reflected," as in a mirror, in the motor representation for the same action of the observer. The visual properties of mirror neurons resemble those of neurons found by Perrett et al[18] in the superior temporal sulcus (STS) region. These neurons, like mirror neurons, respond to the visual presentation of goal-directed hand actions, of walking, turning the head, moving the hand, and bending the torso (for a review, see Ref. 19). However, as opposed to mirror neurons described in area F5, neurons described in the STS region do not have a motor counterpart.

The congruence between the motor action coded by the neuron and that triggering the same neuron visually may be very strict, in that only the observation of an action identical to that coded motorically by the neuron can activate it. More often, this congruence is broader, in that the observed and the executed action coded by the neuron match relative to the goal of the action, rather than to the specific movements needed to execute it.

Certain important features of mirror neurons should be highlighted: during action observation, mirror neurons discharge only when a biologic effector (a hand, for example) interacts with an object; if the action is performed with a tool, the neuron does not discharge. Furthermore, mirror neurons are not active when the observed action is simply mimicked, that is, executed in the absence of the object. Finally, mirror neurons do not discharge during the mere visual presentation of an object. Although mirror neurons were first described in the context of hand actions, recent work has demonstrated that area F5 also contains mirror neurons that discharge during the execution and observation of mouth actions. Most mouth mirror neurons become active during the execution and observation of mouth ingestive actions such as grasping, sucking, or breaking food. Some of them, however, respond during the execution and observation of oral communicative actions such as lip-smacking.[20]

Since their discovery, it has been hypothesized that mirror neurons play an important role both in action recognition and in motor learning.[21,22] If mirror neurons are responsible for action recognition, then they should discharge also when the whole sequence of the action is not completely seen by the monkey, provided that the goal of the observed action can be clearly inferred. A recent electrophysiologic study[23] supports the claim that mirror neurons may infer the goal of an action. In the experiment, 2 conditions were presented: in the first (vision condition) the animal could see the entire sequence of a hand action, whereas in the second (hidden condition), the final part of the action was hidden from the monkey by a screen. In this condition, however, the animal was shown that an object, for example a piece of food, was placed behind the screen, which prevented the observation of the final part of the performed action. The results showed that mirror neurons discharge not only during the observation of action, but also when the final part of it is hidden. As a control, a mimicked action was presented in the same conditions and, as predicted, the neuron did not discharge in either of the 2 conditions.

Actions may also be recognized from their typical sound, when presented acoustically. Besides visual properties, a recent experiment has demonstrated that about 15% of mirror neurons also respond to the specific sound of an action. These neurons are called audio-visual mirror neurons.[24] Audio-visual mirror neurons could be used to recognize actions performed by other individuals even if only heard. It has been argued that these neurons code the action content, which may be triggered either visually or acoustically, thus representing a possible step for the acquisition of language.

Mirror Neuron System in Humans

There is increasing evidence that a mirror neuron system also exists in humans. Converging data supporting this notion come from experiments carried out with neurophysiologic, behavioral, and brain imaging techniques.

Neurophysiologic Studies

The first evidence of the existence of a mirror neuron system in humans was provided by Fadiga et al.[25] In this experiment, single-pulse transcranial magnetic stimulation (TMS) was delivered while subjects were observing an experimenter grasping 3-dimensional (3D) objects. As control conditions, single-pulse TMS was delivered during observation of the same 3D objects, observation of an experimenter tracing geometric figures in the air with his arm, and detection of the dimming of a light. Motor evoked potentials (MEPs) were recorded from extrinsic and intrinsic hand muscles. Results showed that hand action observation, but not the other conditions, led to an increase in MEP amplitude recorded from precisely those hand muscles normally recruited when the observed action is actually performed by the observer. These results were recently fully confirmed by Strafella and Paus.[26] Using the same technique, Gangitano et al[27]

found that during the observation of hand actions there is not only an increase of MEP amplitude in the muscles involved in the actual execution of the observed action, but that the MEPs are modulated in a fashion strictly resembling the time course of the observed action. Taken together, these TMS data support the notion of a mirror neuron system coupling action execution and action observation both in terms of the muscles involved and in terms of the temporal sequence of the action.

The involvement of the mirror neuron system during action observation was also demonstrated by Hari et al,[28] using magnetoencephalography. With this technique, a suppression of the 15 to 25 Hz activity during both the execution and observation of goal-directed hand actions was found. Similar results were obtained in a quantified electroencephalography study, showing a block of "mu" activity in the same conditions.[29] More recently, by means of chronically implanted subdural electrodes, it has been demonstrated that there is a decrease of α band absolute power over the primary motor cortex (M1) and Broca's region during the execution and observation of finger movements.[30]

All of these studies not only provide evidence that observation and execution of action share common neural substrates in the human, but also demonstrate that action observation produces an increase in the excitability of the corticospinal pathway.

Behavioral Studies

Evidence in favor of the existence of a mirror neuron system also comes from neuropsychologic studies. Brass et al[31] investigated how movement observation could affect movement execution in a stimulus-response compatibility paradigm. Using a reaction time paradigm, they contrasted the role of symbolic cues compared with the observed finger movements in the execution of finger movements. Subjects were faster to respond to the observation cue. Moreover, the degree of similarity between the observed and the executed movement led to further advantage in the execution of the observed movement. These results provide strong evidence for an influence of the observed movement on the execution of that movement.

Craighero et al[32] found similar results in a study in which subjects were required to prepare to grasp as fast as possible a bar oriented either clockwise or counter-clockwise, after presentation of a picture showing the right hand. Two experiments were carried out. In the first experiment the picture represented a mirror image of the final position of the hand required to grasp the bar. The second experiment included the same stimuli as in the first, plus 2 additional pictures, 90-degree rotations of the hand in both leftward and rightward directions. In both experiments, responses of the subjects were faster when the hand orientation of the picture corresponded to that achieved by the hand at the end of action, when actually executed. Moreover, the responses were globally faster when the stimuli were not rotated.

Briefly, these behavioral studies not only reinforce the notion of a mirror neuron system in humans, but also suggest facilitation of execution when preceded by motor observation.

Brain Imaging Studies

The neurophysiologic and behavioral studies do not provide insight on the localization of the mirror neuron system in humans. This issue has been addressed by a number of brain imaging studies.

In an early positron emission tomography experiment aimed at identifying the brain areas active during action observation, Rizzolatti et al[33] compared hand action observation with observation of an object, and found activation in Broca's area of the left inferior frontal gyrus (IFG), the middle temporal gyrus, and the STS. Although Broca's area is classically considered an area devoted to speech production, it has recently been demonstrated that this area also contains a motor representation of hand actions.[14,34–36] Given the homology between Broca's area and area F5 in the monkey, where mirror neurons were originally discovered, this study provided the first evidence on the anatomic localization of the mirror neuron system for hand actions in humans.

A recent functional magnetic resonance imaging (fMRI) study showed that the mirror neuron system in humans is complex and related to body actions performed not only with the hand but also with the foot and the mouth. Buccino et al[37] asked subjects to observe video sequences showing different actions performed with the mouth, hand, or foot. The observed actions could be either transitive (the mouth/hand/foot acted on an appropriate object, physically present in the scene) or mimicked (the mouth/hand/foot action was performed in the absence of the object). The following actions were presented: biting an apple, grasping a cup, grasping a ball, kicking a ball, and pushing a brake. As a control, subjects were asked to observe a static image of each action.

The observation of both transitive and mimicked actions, compared with the observation of a static image of the same action, led to the activation of different regions in the premotor cortex and Broca's region, depending on the effector involved in the observed action. The different regions largely overlapped those where classical studies[38] had shown a somatotopically organized motor representation of the different effectors. Moreover, during the observation of transitive actions, distinct sectors in the inferior parietal lobule were active, including areas inside and around the intraparietal sulcus, with localization that depended on the effector involved in the observed action.

On the whole, this study strongly supports the claim that, as in the actual execution of actions, action observation recruits different, somatotopically organized fronto-parietal circuits.[39,40] In this context, it is worth noting that mirror neurons, similar to those described in area F5, have recently been reported in the inferior parietal lobule of the monkey (area PF).[41,42]

MIRROR NEURON SYSTEM IN IMITATION

Motor Imitation

Motor imitation is often regarded as an elementary, undemanding cognitive task. Recent research, coming from different fields, is demonstrating that this assumption is not true. There is clear evidence that imitation is a faculty particularly developed in humans, intrinsically linked to language and culture.[13,43,44] Motor (movement) imitation inherently implies motor observation, motor imagery, and actual execution of the movements.

The involvement of the mirror neuron system in imitation was recently demonstrated by a series of brain imaging studies. Using fMRI, Iacoboni et al[45] scanned normal human volunteers while they were lifting a finger in response to (a) visual presentation of the target action on a screen ("imitation"), (b) a symbolic cue, or (c) a spatial cue. The results showed that the activation was stronger during imitation than during the other motor conditions in the pars opercularis of the left IFG, the right anterior parietal region, the right parietal operculum, and the right STS region (see also Ref. 46). Experiments by Koski et al[47] and Grèzes et al[48] confirmed the importance of Broca's area in imitation tasks, particularly when the action to be imitated was goal directed. Nishitani and Hari[49,50] performed 2 magnetoencephalography studies in which they investigated imitation of grasping actions and facial movements. The first study confirmed the importance of the left IFG (largely corresponding to Broca's region) in imitation. In the second study,[50] volunteers observed still pictures of verbal and nonverbal (grimaces) lip forms, and either imitated them immediately after seeing them or made similar lip forms spontaneously. During lip form observation, cortical activation moved from the occipital cortex to the superior temporal region, the inferior parietal lobule, Broca's area, and finally to M1. The activation sequence during imitation of both verbal and nonverbal lip forms was the same as during observation.

Despite some minor discrepancies, these data clearly show that the basic circuit underlying imitation coincides with that active during action observation. They also indicate that a direct mapping of the observed action and its motor representation takes place in the posterior part of IFG.

The importance of the "pars opercularis" of IFG in imitation was further demonstrated using repetitive TMS by Heiser et al.[51] The task used in the study was essentially the same as that of the fMRI study by Iacoboni et al.[45] The results showed that after stimulation of both Broca's area and its right homolog, there was significant impairment in imitation of finger movements. The effect was absent when finger movements were performed in response to spatial cues.

In the experiments reviewed above individuals were asked to imitate "on line" highly practiced, simple movements made by another individual. Such on line imitation was also studied by Tanaka and Inui,[52] who asked volunteers to imitate relatively complex hand or arm postures. This study also found only that a finger condition showed significant activation in Broca's area, whereas a hand condition did not.

Many years ago, the Russian neuropsychologist Aleksandr R. Luria designed a number of tasks to investigate disturbances of complex voluntary movement that he believed required intact premotor cortices and their interaction with the parietal lobe (PL).[53] Bhimani et al[54,55] (see page X of this issue of Cognitive and Behavioral Neurology) have used functional brain imaging to reevaluate Luria's postulates. With the high spatial resolution of fMRI, it was possible to elaborate the neural circuitry underlying his observations that were based on investigations of persons with brain injury. In this study, participants performed 3 tasks, including imitation of hand shape and 2 other complex sequential hand movement tasks, based on Luria's fist-edge-palm and piano key tasks. Activation of both premotor and parietal cortices was seen during the performance of all 3 tasks. However, whereas the main portion of the supplementary motor area (SMA proper) was preferentially activated in the sequential motor tasks, the ventral portion of the lateral premotor cortex and PL were preferentially activated in hand shape imitation.

Action Observation and Motor Learning

In the experiments mentioned thus far, imitation has consisted of matching observed movements or actions to preexisting motor schemata, that is, to motor actions previously produced and remembered. This observation/execution matching system, thought to involve the PL and the premotor areas, leads to action production without motor learning. By contrast, a recent study investigated motor learning of a novel motor pattern by action observation.[56] The basic task during event-related fMRI was imitation by naive participants of guitar chords played by an expert guitarist. The 4 event types that comprised the imitation condition were performed in order—observation of guitar chords, pause, execution of the observed chords, and baseline. The 3 control conditions were observation of the chords (with no subsequent motor activity), observation of the chords followed by execution of unrelated motor actions (eg, grasp-release of the guitar neck), and free execution of guitar chords.

The results showed that the observation condition was associated with activation of a cortical network formed by the inferior parietal lobule and the Pmv plus the pars opercularis of IFG. This circuit was also active during the 2 control conditions involving observation. The strength of activation related to action observation was much stronger during imitation than during the control conditions, and was associated with additional activation in anterior mesial areas, superior parietal lobule, and the prefrontal cortex.

The pause event during action imitation was aimed at uncovering activation related to novel motor pattern formation and consolidation. Activation during this event involved the same basic circuit as in action observation,

but with some important differences, including an increase of superior parietal lobule activation, activation of dorsal premotor cortex (Pmd), and most interestingly a dramatic increase in extension and strength of prefrontal cortex activation (possibly BA 46) and of areas of the anterior mesial wall. Finally, during the execution event, activation involved the sensorimotor cortex contralateral to the hand executing the observed chords.

These data show that the neural substrates responsible for the elaboration of new motor patterns largely coincide with the key centers of the mirror neuron system. Although these fMRI experiments do not provide information on the mechanism underlying imitation, it is plausible (see the neurophysiologic sections) that during learning of new motor patterns by imitation, the observed actions are decomposed into elementary motor acts that activate, by a mirror mechanism, the corresponding motor representations in the inferior parietal lobule, and in Pmv and in the pars opercularis of IFG. Once these motor representations are activated, they are recombined, to fit the observed model. This recombination seems to occur inside the mirror-neuron circuit, with area 46 playing a fundamental orchestrating role.

Imitation and Motor Imagery

As noted, motor imitation implies motor imagery. In the most general sense, motor imagery refers to the "mental rehearsal of simple or complex motor acts that is not accompanied by overt body movements."[9,57,58] It represents the voluntary effort of an individual to imagine himself/herself executing a specific action.

There is evidence that motor imagery, and motor execution, may improve performance in different categories of people, including athletes, musicians, and people with motor system strokes.[59–62]

Although the definition seems simple, people asked to perform motor imagery do not unambiguously perform a single type of mental rehearsal. In particular, a person can use 1 of 2 very different strategies: (a) producing a visual representation of the moving limb, in which case he or she is a (third-person) spectator of the movement (visual imagery, VI) or (b) mentally simulating the movement, associated with a kinesthetic feeling of the movement, in which case the person is a (first-person) performer of the movement (kinetic imagery, KI).

Because KI shares more physiologic characteristics with movement execution than VI, it has been associated more closely with motor functions per se such as motor preparation, imitation, and anticipation, and the refining of motor abilities.[8,39,63–66]

With respect to imaging studies, several accounts of areas activated during KI or VI have been reported using positron emission tomography or fMRI. Even though some of the studies do not differentiate between KI and VI, there are several features common to most of them.[63,65,67–74] In general, studies have shown that several areas, including those belonging to the mirror neuron system, are activated during motor imagery tasks. Included in these active regions are the following: SMA,

superior and inferior parietal lobules, dorsal and ventral premotor cortices, prefrontal areas, IFG, superior temporal gyrus, M1, primary sensory cortex, secondary sensory area, insular cortex, anterior cingulate cortex, superior temporal gyrus, basal ganglia, and cerebellum. This extensive activation suggests a complex distributed circuit that shares several cortical regions fundamentally involved in action execution, observation, and imitation.[66]

MIRROR NEURON SYSTEM AND MOTOR REHABILITATION

Role of Experience in Motor Stroke Recovery

There is growing evidence that many forms of experience, from the stimulation of everyday interactions to intensive practice, can lead existing neurons to change their synaptic connectivity, forming entirely new receptive field organizations. This has been observed in the somatosensory system with peripheral nerve stimulation,[75,76] and in the visual system after striate cortex infarction with normal visual experience.[77] In experimental stroke in a cat model, thalamo-cortical and intracortical plasticity has been described with conditioning of a motor response to a sensory stimulus.[78,79] For purposes of developing treatment approaches, it has been demonstrated that the extent and direction of stroke recovery depends on the nature of both the environment and the particular training stimuli used.[80–82]

The timing of intervention may also be important. There have been questions raised about the role of experience at different time points in recovery.[83] Early after stroke, the homeostatic environment around an area of infarction is enriched in growth factors, altered transmitter receptors, and other trophic processes.[84,85] This could support the formation of synapses or enhancement of dendritic arborization,[86] and it is possible that these processes occurring early may play a disproportionate role in recovery.[87–89]

Although most interventions to aid upper extremity motor recovery emphasize proximal function,[90–93] one recent approach focuses on functional use of the extremity by undoing "nonuse."[94,95] Forced use of a paretic extremity, sometimes via constraint of the unimpaired extremity,[95] has been shown to improve function of the paretic limb[82] and to alter the neural networks involved in movement.[96] These changes seem to involve large circuits, but premotor regions ipsilateral to the lesion seem to play a prominent role.[96,97] Recent interest in the neurobiologic substrates of functional recovery has led to systems-level research in neural remodeling, including work carried out by our group.[98–101]

Action Observation and Imitation as a New Tool for Neurorehabilitation

So far, we have described a number of features of motor imitation and introduced the notions of hand motor learning and hand motor rehabilitation after

stroke. These included both behavioral and neurobiologic observations. Motor imitation is a complex cognitive function that incorporates several stages, including motor observation (ie, visual perception of ecologically valid movements), motor imagery, and motor execution. When tested individually, both action observation and motor imagery increase the excitability of the corticospinal pathway. Owing to the complexity of motor imitation itself, its neural encoding incorporates a widespread network with participation by a large number of brain regions. These networks integrate sensory inputs with stored motor patterns to generate the requisite movements.

Although it has been suggested (but certainly not proven) that motor imagery might be beneficial to the recovery of motor functions after stroke[8,61,62] (also see the paper by Lotze and Cohen in this issue), there are no formal suggestions thus far on the possible benefits of action observation and imitation in the rehabilitation of these hand movements. Treatment of the hand itself is problematic for many rehabilitation centers, which frequently do not have the time or money to address recovery of hand motor skill, because it would come at the expense of gait training, proximal arm function, and compensatory skills.

It is important, however, to consider the nature of the motor recovery process, and the relative roles for remediative and compensatory treatment in this recovery. Rather than to cure motor deficits (remediation), current practice in rehabilitation typically focuses on ways to circumvent them (compensation), because this is the most efficient way to achieve "functional outcome."[102] In compensatory recovery, different behaviors are used to meet environmental needs, and functional restoration is bypassed. In recovery through remediation, the lost behavior is actually restored, rather than circumvented. In the case of the hand, for example, a compensation approach would help a patient learn to use the nondominant hand to write, whereas a remediation approach would help him relearn to use the dysfunctional dominant hand to write.

Our focus on neural circuit reorganization represents endorsement of a biologic model of remediation, rather than an educational model. In the prevalent educational perspective for rehabilitation, therapy is understood as "reeducation," with a goal of teaching lost knowledge or skills. Patients and families are typically given low expectations, because the relearning of lost skills can be quite meager and can take tremendous effort over a long time, limiting the patience of both the patient and the insurance company. In the biologic model, the assumption is that a damaged brain is producing the impairment, and that neural circuit repair or reorganization can produce a cure for the disease.

The biologic model emphasizes both behavioral and biologic interventions to effect the necessary neural changes. Biologic remediation can take 2 different forms neurobiologically, although the outcome, that is, restoring function, remains the same. Whereas in direct restoration the original (damaged) neural circuits are reinstated, in indirect restoration adjacent or related neural circuits perform the original functions.[103] In both cases, a combination of behavioral training and biologic intervention can be used to effect the desired (direct or indirect) circuit changes. Action observation and imitation represent one type of behavioral intervention that can affect neural circuit reorganization, employing both direct and indirect mechanisms. Ultimately, behavioral interventions might be augmented with pharmacologic (eg, dextro-amphetamine) or tissue transplant (eg, stem cell) interventions.[104–108]

The role of motor learning in hand motor recovery presents certain questions, because the goal is to reestablish previously learned motor skills rather than new skills. A person with stroke may have lost a significant portion of the brain tissue supporting the neural circuits associated with the execution of movements. On the other hand, this situation might be ideally suited for the use of observation/execution matching and motor imitation, which could potentially provide a reassembly of the incomplete (but not totally lost) networks.

What are the features of motor imitation that could promote plasticity in the appropriate networks for hand motor skill? First, the distributed networks for motor imitation involve multiple sensory inputs (visual, auditory, and proprioceptive), making it possible to activate the system using different inputs. Furthermore, the widespread distributed nature of the network suggests many anatomic and physiologic options for obtaining proper activation. Second, activation of the network for observation/execution matching produces an increase in the excitability of the corticospinal path even in the absence of overt movements. Third, the network is strongly associated with learned, ecologically valid movements. Motor imitation is well known to the majority of patients who have generally used it (eg, in learning a new skill) at some point in their lives. Motor imitation also avoids the fragmentation of the movements into smaller components, as is typically performed in current rehabilitative practice, but instead emphasizes execution of the movement as a whole. Fourth, empirical data on motor recovery from stroke already suggest a possible role for motor imagery in therapy. Because motor imitation incorporates motor imagery, the additional motor components in imitation (observation and execution) might reinforce the therapeutic value.

The role of motor imagery deserves additional mention, because it seems to aid recovery from corticospinal tract stroke[59,61,62] and forms a fundamental part of motor imitation. One postulated mechanism for the benefit of imagery is the potentiation of synaptic transmission that occurs during both motor imagery and actual execution. This mechanism leads to some speculation about the role of imitation in therapy, based on 2 previously noted facts. First, action observation recruits the motor system as does motor execution. Second, during the imitation of a novel motor pattern,

the mirror neuron system is active from the observation phase until the execution of the new action. These lines of evidence raise the possibility of improving motor performance through systematic exercise based on careful observation and imitation of everyday actions.

In an ongoing, multicenter trial, action observation and imitation are being used systematically as mental practice aimed at improving motor performance in patients with ischemic stroke in the territory of middle cerebral artery. This therapy does not replace, but augments, conventional neurorehabilitation on the basis of passive or active execution of movements. Patients up to 70 years of age with a first-ever stroke are included. We excluded patients with mental deterioration, apraxia, fluent aphasia, neglect, or depression of mood.

During the treatment, patients are asked to carefully observe short movies, each lasting about 15 minutes. In each of these video-sequences a different daily action (ie, having a coffee, eating an apple) is presented. In the entirety of the study, 20 daily actions are practiced. In the visual stimuli, actions are segmented into their principal motor acts: for example the action "having a coffee" consists of the following components: grasping the cup, putting sugar in it, stirring, bringing to the mouth. During the training session, the patient is assisted by a physiotherapist who helps the subject maintain attention and motivation. After each single act, patients are required to execute the observed action with their impaired upper limb. Before, during, and after the treatment patients undergo a functional evaluation by means of functional scales (Barthel Index, Functional Independence Measure, Frenchay Arm Test, Fugl-Meyer) to evaluate the impairment of the upper limb in everyday activities.

Preliminary results have been reported in abstract form.[109] The results showed that patients undergoing the treatment experienced subjective improvement. Further they showed better motor performance as revealed by functional scales. These preliminary results need confirmation from the larger ongoing study. However, if the preliminary results are confirmed, action observation and imitation could be regarded as a new tool in rehabilitation, simple to administer, and with a well-founded neurophysiologic basis.

CONCLUSIONS

In this paper, we discuss the possibility that a systematic activation of the observation-execution matching "mirror" system of the premotor and parietal cortices can be used to affect functional changes in hand motor function in patients with ischemic stroke. Hand motor skill is heavily represented in these regions, and there is significant reason to believe that development of these motor skills played an important evolutionary role, that this phylogenesis depended on observation-execution matching, that development of such skill in children also depends on imitation, and that good recovery from stroke

might also depend on use of this system. We postulate that functional outcome of patients with hand motor dysfunction can be influenced by tasks involving observation-execution matching and that degree of recovery will depend on changes to the Pmv, the Pmd, and the pars opercularis ipsilateral to a cerebral infarction. The first step involves an ongoing preliminary trial of this concept.

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