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Review

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Author for correspondence:

Giovanni Buccino

e-mail: buccino@unicz.it

Action observation treatment: a novel tool in neurorehabilitation

Giovanni Buccino^{1,2}

¹Dipartimento di Scienze Mediche e Chirurgiche, Università Magna Graecia, 88100 Catanzaro, Italy

²IRCCS Neuromed, 86077 Pozzilli, Italy

This review focuses on a novel rehabilitation approach known as action observation treatment (AOT). It is now a well-accepted notion in neurophysiology that the observation of actions performed by others activates in the perceiver the same neural structures responsible for the actual execution of those same actions. Areas endowed with this action observation–action execution matching mechanism are defined as the mirror neuron system. AOT exploits this neurophysiological mechanism for the recovery of motor impairment. During one typical session, patients observe a daily action and afterwards execute it in context. So far, this approach has been successfully applied in the rehabilitation of upper limb motor functions in chronic stroke patients, in motor recovery of Parkinson's disease patients, including those presenting with freezing of gait, and in children with cerebral palsy. Interestingly, this approach also improved lower limb motor functions in post-surgical orthopaedic patients. AOT is well grounded in basic neuroscience, thus representing a valid model of translational medicine in the field of neurorehabilitation. Moreover, the results concerning its effectiveness have been collected in randomized controlled studies, thus being an example of evidence-based clinical practice.

1. Towards translational, evidence-based approaches in neurorehabilitation

Basic research has prompted the development of several therapeutic interventions that have radically changed our capacity to face problems in clinical practice. For example, consider the impact of using L-DOPA as a therapeutic agent in Parkinson's disease (PD) following the discovery of dopamine as a neurotransmitter of some circuits involving the basal ganglia. At odds with this general claim, basic research in neuroscience has had a poor impact on neurorehabilitation (for a deeper discussion on this issue, see [1,2]). Even when considering motor recovery, most approaches in this field do not take into account the enormous advancement of knowledge concerning, for example, the organization of the motor system. There are, of course, some exceptions. For example, constraint-induced movement therapy (CIMT) has a well-established neurophysiological basis grounded on the experimental evidence that monkeys can be induced to use a deafferented limb by restricting movements of the unaffected limb over a period of days. CIMT comprises two components: on the one side, the use of the unaffected upper extremity is restrained during 90% of the waking hours, on the other side, the more affected upper extremity receives intensive training for 6 h or more a day. In this way, the use of the more affected arm may be increased, and learned non-use may be overwhelmed (for review, see reference [3]). CIMT has been widely applied in patients with acute and chronic stroke and in children with cerebral palsy. CIMT has been shown to lead to brain plastic changes and contribute to a functional reorganization of sensorimotor representations in the monkey [4]. Another example is the so-called mirror therapy. In this treatment, a mirror is placed in the patient's midsagittal plane, so that he/she can see her unaffected arm/hand as if it were the affected one. This strategy has been proved to be effective to relieve phantom pain in arm amputees as well as in the recovery of upper limbs in

chronic stroke patients [5]. Despite the emphasis given in the mirror therapy to visual and proprioceptive feedback, rather than action observation, it is most likely that this approach has the mirror neuron system (MNS) as its neurophysiological basis similar to the action observation treatment (AOT), the approach we focus on in this review. Motor imagery has been applied for years as a tool in neurorehabilitation. During motor imagery, an individual imagines himself executing a particular action, almost perceiving the kinaesthetic experience of the movement. Early studies showed an improvement of balance in elderly people through motor imagery [6]. More recently, positive effects have been obtained in the recovery of stroke patients [7,8]. Motor imagery has also revealed a promising approach in PD [9]. It has been forwarded that to some extent during motor imagery, the same motor representations are recalled as during action execution and action observation [10].

Despite these examples, however, there is an urgent need in neurorehabilitation for approaches that take into account the development of our knowledge in basic neuroscience and aim at transferring ideas and facts from basic neuroscience to clinical practice, with the final goal to build up tools well grounded in neurophysiology and to provide a cure for several neurological (and non-neurological) diseases [2]. This is what is often referred to as translational medicine.

Models of translational medicine may also help to overcome a general attitude in neurorehabilitation to focus on ways to circumvent functional deficits, thus leading to a compensation or a re-education of functions rather than a cure for them through remediation. As a matter of fact, the prevalent aim of therapists is teaching lost skills and sometimes suggesting alternative strategies in order to allow their patients to face daily activities, the logic being that if you cannot paint with your hands, you can try with your mouth. Although these approaches sometimes work and help patients to recover in daily activities, the sad thing is that they do not aim at repairing the neural circuits underlying specific functions through a direct or indirect restoration. Moving to a translational model in neurorehabilitation would imply planning specific rehabilitative tools aimed at restoring the neural structures whose damage caused the impaired functions, or activating supplementary or related pathways which may perform the original functions. Last but not least, rehabilitation tools well grounded in neurophysiology allow researchers to plan well-designed, randomized controlled trials with the possibility to measure outcomes not only in terms of functional, behavioural gains (as currently happens by means of functional scales), but also in terms of changes in biological parameters, which can be tested using neurophysiological and brain imaging techniques.

2. What is action observation treatment?

It is now a well-accepted notion in neurophysiology that the observation of actions performed by others activates in the perceiver the same neural structures responsible for the actual execution of those same actions [11]. Thus, while observing other people performing everyday actions, neural structures involved in the actual execution of those actions are recruited in the observer's brain as if he/she actually performed the observed action. Several studies have consistently shown that action observation is an effective way to learn or enhance

Table 1. List of actions presented through video clips and seen by children in the case group during action observation treatment.

1.	Grasping and moving an object in the horizontal plane
2.	Grasping and moving an object in the vertical plane
3.	Using a pencil
4.	Eating a candy
5.	Eating an ice cream
6.	Manipulating a cube with both hands
7.	Playing with two small cars
8.	Reading a book
9.	Using an hourglass
10.	Opening and closing a jar
11.	Opening a house (game) with a key
12.	Drawing with a pencil, after sharpening it
13.	Playing with Lego
14.	Playing a piano with both hands
15.	Writing with a pen

the performance of that specific motor skill (for review, see [12]). In a study, participants who were required to perform a reaching task in a novel environment performed better after observing a video depicting a person learning to reach in the same novel environment, when compared with participants who observed the same movements in a different environment [13]. Action observation has been shown to facilitate motor learning and the building of a motor memory trace in normal adults as well as in stroke patients [14,15]. Moreover, during both the actual execution and observation of a simple movement (abduction of the right and middle fingers), an increase of force in performing this same movement was found in both hands when compared with a control condition [16]. The results of a very recent study [17] have shown that in healthy adults action observation is better than motor imagery as a strategy for learning a novel complex motor task, at least in the fast early phase of motor learning. In the same vein, it has been shown that action observation, but not motor imagery, may prevent the corticomotor depression induced by immobilization [18].

AOT is a novel rehabilitation approach exploiting this mirror mechanism and its potential role in motor learning for motor recovery. Typically, 20 daily actions (but this is not a rule) are practiced chosen on the basis of their ecological value (e.g. drinking coffee, reading the newspaper, cleaning the table) during a rehabilitation treatment that lasts four weeks (5 days a week). For example, table 1 lists the actions trained during AOT treatment in children with cerebral palsy (see [19]). During each rehabilitation session, patients are required to observe a specific object-directed daily action presented through a video clip on a computer screen, and afterwards to execute what they have observed. Only one action is practiced during each rehabilitation session. The presented action is divided into three to four motor acts. For example, the action of drinking coffee can be decomposed into the following motor acts: (i) pouring coffee into the cup, (ii) adding sugar, (iii) turning the spoon and finally (iv) bringing the coffee to the mouth. Each motor act is typically seen for 3 min, so that the whole duration of a video clip depicting a specific daily action is 12 min. In the video, each motor act is performed by both

an actor and an actress and is seen from different perspectives (frontal or lateral view, in foreground and background). The effectiveness of showing actions from different perspectives is supported by a very recent monkey study [20] in which the visual responses of monkey mirror neurons were recorded during the presentation of movies showing grasping actions from different visual perspectives. The authors have found that the majority of the tested mirror neurons exhibited view-dependent activity with responses tuned to specific points of view. A minority of the tested mirror neurons exhibited view-independent responses. The authors propose that view-independent mirror neurons encode action goals, irrespective of the details of the observed motor acts, whereas the view-dependent ones might contribute to a modulation of view-dependent representations in higher-level visual areas, potentially linking the goals of observed motor acts with their pictorial aspects.

During the presentation of a video clip, patients sit relaxed in front of the computer screen while observing it. After observing a motor act for 3 min (observation phase), patients are required to imitate what they observed for 2 min (execution phase). During this phase, objects used in the video clip are provided at hand in order to make the execution as close as possible to everyday life situations. Objects are known to recruit automatically the most useful motor programmes to act upon them, thus further contributing to the recruitment of the motor system [21–23]. Moreover, the modulation of the motor system is fine-tuned with the motorically relevant features of the objects to act upon them, as shown in Buccino *et al.* [24], where motor-evoked potentials (MEPs) recorded from the right hand during observation of graspable objects (e.g. a mug) with a broken handle (oriented to the right) were significantly modulated relative to MEPs evoked for observation of the complete object (handle oriented to the right).

As a whole, a typical AOT rehabilitation session takes half an hour. A few minutes are needed by the physiotherapist to explain the task to the patient (carefully looking at the movie, paying attention also to the details of presented actions) and to motivate him to the task, then 12 min of observation (3 min for each of the motor acts into which the action is divided) and finally 8 min of execution (2 min for each motor act). The patient, during the execution phase, has to perform the observed motor act at the best of his/her ability. However, he/she is informed that the focus of the treatment is on the observation of the action, not its execution.

This approach has the potentiality to train actions related to all biological effectors (mouth, upper limbs, lower limbs and trunk), although so far the focus has been on the recovery of upper limb motor functions. A further advantage deriving from AOT is the fact that the treatment can be easily tailored to specific needs of patients: in the near future, one could think of applying this approach to practice only those actions whose performance is mostly impaired in the single patient. Moreover, the whole procedure could be performed in the patient's home and repeated over time, when needed, with the involvement of carers. Finally, it is worth stressing that AOT possibly recruits the same neural structures in the brain as motor imagery. This mental practice has been successfully used both as a rehabilitative tool and in sports training [25]. As a rehabilitative tool, however, motor imagery has some intrinsic limits. On the one hand, it is more demanding than action observation, because it is related to the capacity of individuals to imagine themselves doing specific actions and to the

imageability of certain actions. On the other hand, therapists are unable to verify how correct 'the mental training' is or to influence it. Despite the fact that it may target the same neural structures, AOT is simpler, and at least in some patients can be more easily applied.

What remains to be defined is the total time of AOT training: it is not clear whether a more intensive practice, for example 1 h per session, is better than half an hour; moreover, further studies should assess whether it is better to present a video or ask the therapist to show actions on line and, again, whether it is better to present actions in front of patients (as it is currently done) or in a first-person perspective asking the therapist to sit to the right (or to the left) of the patient. It could be also interesting to present actions partially hidden, like for example in the occluder paradigm, because it seems that this recruits more deeply the related motor representations and may favour action simulation [26].

3. When does action observation treatment work?

Thus far, AOT has been used in the rehabilitation of patients suffering from chronic ischemic stroke (more than six months after the acute event), in PD patients, in children with cerebral palsy, and in non-neurologic patients such as those undergoing orthopaedic surgery of the hip or knee. In a pivotal randomized controlled study in patients with chronic ischemic stroke in the territory of the middle cerebral artery [27], AOT was applied to treat upper limb motor functions. Patients in the control group were asked to observe video clips related to historical, scientific or geographical issues, but with no specific motor content. In this study, the stroke impact scale, the Wolf motor function test and the Frenchay arm test were used as functional scales to quantify changes in motor abilities. In patients undergoing AOT, there was a significant improvement of motor functions in the course of a four-week treatment, compared with the stable pre-treatment baseline, and compared with the control group. The improvement lasted for at least eight weeks after the end of the intervention. Functional magnetic resonance imaging (fMRI) during an independent motor task, namely free object manipulation, carried out before and after therapy showed a significant increase in activity in the bilateral ventral premotor cortex, bilateral superior temporal gyrus, the supplementary motor area and the contralateral supramarginal gyrus. On the basis of these findings, the authors concluded that action observation has a positive impact on recovery of motor functions after stroke by reactivation of motor areas within the action observation–action execution matching system, the putative human correlate of the monkey MNS.

In a randomized controlled study, the effectiveness of AOT in patients with PD has been investigated to complement pharmacology in the treatment of these patients [28]. For this trial, participants in the case group observed videos depicting everyday life actions, including postural actions and walking, whereas those in the control group observed movies devoid of specific motor content. The results showed that the case group improved significantly more than patients in the control group on two functional scales, the unified Parkinson's disease rating scale and the functional independence measure (FIM). AOT has also been successfully applied in remediation of freezing of gait in PD patients [29]. The basal ganglia are heavily connected with regions of the

MNS and play a role in motor planning and motor learning [30]. Taking into account these facts from neurophysiology, it is likely that AOT may reorganize and sustain the normal loop circuits connecting the motor cortex with basal ganglia and these to motor cortex via thalamus [31]. It has been shown that action observation in PD patients is accompanied by changes in beta oscillatory activity of the subthalamic nucleus, similar to alpha and beta electroencephalography (EEG) desynchronization over the motor cortex, thus suggesting that basal ganglia may be engaged by the activity of the MNS [32]. Additionally, it is well known that PD patients improve their motor performances when externally cued [33]. AOT, while showing daily actions in context, could provide patients with convenient cues to start and execute a number of daily actions. In an fMRI study aimed at assessing the neural basis of attention to action, it has been shown that PD patients show a context-specific functional disconnection between the prefrontal cortex and the supplementary and premotor cortex, when compared with controls [34]. It might be the case, therefore, that AOT, cueing actions, also reinforces the normal connections in the brain between prefrontal and premotor cortex, thus allowing patients to better perform actions in context. Finally, a very recent study [35] has shown that action observation may improve movement rate at spontaneous pace in PD patients, but this result is still present 45 min later only in on conditions, thus suggesting that the dopaminergic state plays a role in the effects of action observation.

In a further randomized controlled study, AOT was used in the treatment of upper limb motor functions in children with cerebral palsy aged from 6 to 11 years [19]. One group of children observed daily actions appropriate for their age, whereas another observed documentaries with no specific motor content. Functional evaluation with the Melbourne assessment scale of upper limb motor functions showed that children undergoing AOT performed significantly better than controls after treatment. These results potentially provide insights into the ontogenesis of the MNS. Experimental evidence on the ontogeny of the MNS is rather poor. It is not clear whether it is innate or develops in parallel to motor experience and if so at what age this system is fully operating [36]. Classical studies do suggest that human newborns, only a few days old, are able to resonate with other adult individuals' gestures [37] and infants less than 2 years old can predict other people's action goals [38] and infer adults' intentions [39]. Moreover, the acquisition of motor skills seems to parallel or even precede the acquisition of higher cognitive functions [36,40]. If AOT targeted the central motor representations of actions in these children, then this suggests that the MNS is fully working at this age. Further, these findings raise the question whether this treatment impacted an already developed motor representation in these children or rather contributed to the development of new motor representations of the trained everyday life actions.

Interestingly, in non-neurological patients, AOT may also improve motor recovery. In a randomized controlled trial, this novel approach was used in post-surgical orthopaedic patients for hip fracture or elective hip or knee replacement [41]. Whereas all participants underwent conventional physiotherapy, patients in the experimental group also observed video clips showing daily actions related to lower limbs and subsequently imitated them. Patients in the control group were asked to observe video clips with no motor content, and then were asked to execute the same actions as the AOT

patients. Participants were scored on functional scales (FIM and Tinetti scale) at baseline and after treatment by a physician blind to group assignment. At baseline, the groups did not differ on clinical or functional measures. After treatment, patients in the AOT group scored better than patients in the control group. It should also be noted that, although patients in the case group were more frequently prescribed a walker on baseline assessment when compared with the control group, at discharge they were prescribed a single crutch for all but one individual. This measure of change was significantly different between groups. These findings suggest that AOT is an effective adjunct to conventional therapy in the rehabilitation of post-surgical orthopaedic patients. In more general terms, the findings of this study suggest a top-down effect in neurorehabilitation, showing that the reorganization of motor representations at central level, most likely occurring during AOT, may affect performance, even when the skeletal structures to implement actions are impaired.

Finally, it is worth underlining that AOT has been recently tested as a tool in speech rehabilitation. Though this was not a randomized controlled trial, but a case report, preliminary data show that the observation and execution of actions improves the retrieval of action words in patients with a selective deficit for verb retrieval [42].

In conclusion, the results of the studies reviewed thus far support the use of AOT as a rehabilitation tool in several neurological and non-neurological diseases. However, it must be underlined that the studies carried out so far involved only a few patients. Larger, polycentric trials are needed to draw any definitive conclusion on the efficacy of this treatment. Moreover, despite the fact that AOT may appear an easy approach and very simple to apply, it is worth stressing that it is rather demanding in terms of the attention to be paid to the task. Patients must be cooperative and an adequate compliance with the approach is a necessary prerequisite for its effectiveness. Finally, evidence that AOT may effectively contribute to restoring the neural structures whose damage caused the impaired functions or activating supplementary or related pathways, is still poor. Future studies should aim at defining neural plasticity owing to this treatment.

4. The neurophysiological basis of the action observation treatment

AOT recognizes its neurophysiological basis in the discovery of mirror neurons in various regions of the macaque cerebral cortex. Mirror neurons discharge both during the execution of goal-directed actions performed with different biological effectors (e.g. mouth, hand) and during the observation of another individual performing the same or a similar action [43–45]. Areas containing mirror neurons are often referred to as the MNS. There is increasing evidence that an MNS similar to the one described in the monkey is also present in the human brain and that it may play a role in a number of cognitive functions ranging from action recognition to social interactions [11,46,47]. Among the huge literature concerning the MNS, for the aim of this review the focus will be on those papers that more strictly support the use of AOT in clinical practice. In the observation phase of AOT, patients are requested to carefully observe daily actions with the aim to restore the neural structures normally recruited during the execution of those actions, as if the patients themselves

performed the daily activities. The observed actions belong to the motor repertoire of the observers. By means of non-invasive techniques, it has been possible to collect experimental evidence in humans confirming the existence of an action observation–action execution matching mechanism in specific regions of the frontal and parietal lobes. In a pivotal study [48], by means of transcranial magnetic stimulation applied over hand motor cortex, it has been assessed that the excitability of this region is enhanced when subjects observe hand actions with respect to a control condition. Later, evidence in favour of a recruitment of the motor system during action observation has been collected using different techniques spanning from EEG to brain imaging. Using magnetoencephalography (MEG), a suppression of 15–25 Hz activity has been found, known to originate from the pre-central motor cortex, during the execution and, to a less extent, during the observation of object manipulation [49]. In keeping with this, clear similarities between observation and execution of actions have been demonstrated by means of quantified EEG [50]. Brain imaging experiments have demonstrated that during the observation of actions normally performed with different effectors (mouth, hand, foot) there is a signal increase in the brain regions also active during the execution of those observed actions [51,52]. These and other studies have shown that the mere observation of several actions recruits different sectors of the premotor and parietal cortex according to a rough somatotopic organization similar to that classically described within the primary motor cortex for action execution [53]. It is worth underlining that several studies have clearly shown that the recruitment of frontoparietal areas during action observation depends on how familiar are the observed actions to perceivers and whether or not they are part of the perceivers' motor repertoire. This further supports the choice of displaying daily actions in AOT. In an fMRI study [54], it has been investigated whether the human putative MNS is activated by the observation of actions performed by different species. Participants were presented with mouth actions related either to food ingestion (biting) or to communication. These actions were performed by a human being, a monkey and a dog. The results showed that the observation of biting activates the premotor cortex and the inferior parietal lobule, regardless of the observed species, whereas the observation of communicative actions was effective in recruiting the premotor cortex and the inferior frontal gyrus (Broca's region) only when participants observed a conspecific (human being moving the lips as during speaking), but not when they observed a communicative gesture performed by a monkey or a dog. These findings have been interpreted as proof that the human putative MNS can match an observed action on the neural structures involved in its execution only if the observed action belongs to the observer's motor repertoire. Similarly, the motor expertise of the observer affects the recruitment of human putative MNS. In an elegant fMRI study, it has been shown that expert dancers (classical ballet dancers or capoeira dancers) resonate more strongly when they observe another dancer performing exactly the same kind of dance they practice compared to the condition in which they have to look at a different type of dance [55], thus confirming that the observer's motor expertise may modulate his/her ability to mirror others' actions.

In the execution phase of AOT, patients are requested to execute the observed motor act by imitation. Motor imitation

is sometimes regarded as a relatively undemanding cognitive task, but evidence increasingly suggests that this is not the case and that imitation is particularly developed in humans, intrinsically linked to social interactions, language and culture [56,57]. Imitation of movement inherently implies motor observation, motor imagery and actual execution of the movements.

The involvement of the human putative MNS in imitation has been demonstrated in several studies. In order to test if imitation may be based on a mechanism directly matching the observed action onto an internal motor representation of that action, in an fMRI study, participants were asked to observe and imitate a finger movement and to perform the same movement after spatial or symbolic cues [58]. If the direct matching hypothesis is correct, then there should be areas active during a finger movement that are also recruited by the observation of an identical movement made by another individual. Two areas with these properties were found in the left inferior frontal cortex (pars opercularis, a part of Broca's region) and the rostral-most region of the posterior parietal lobe, both belonging to the MNS. The involvement of Broca's region in imitation, especially of goal-directed actions, has been confirmed also by other studies [59,60]. The involvement of areas within the MNS in the imitation of oral actions has been assessed in a MEG study [61]. During the imitation of lip forms, cortical activation progressed from the occipital cortex to the superior temporal region, the inferior parietal lobule and the inferior frontal lobe (Broca's region), and finally, to the primary motor cortex. Indeed, the signals of Broca's region and motor cortex were significantly stronger during imitation than control conditions. Interestingly, a very recent fMRI study [62] has found an involvement of the inferior parietal lobule and Broca's region also during observation and execution by imitation of speech.

In the experiments mentioned thus far, imitation consisted of matching observed movements or actions to pre-existing motor schemata, i.e. to motor actions already part of the motor repertoire of the observer. This observation–execution matching system, involving the parietal lobe and the premotor cortex, suggests a mechanism for action understanding but does not help to explain motor learning (or re-learning, as it may happen in patients). This issue was investigated in an fMRI study [63] in which musically naive participants were scanned during four events: (i) observation of guitar chords played by a guitarist (model), (ii) a pause following model observation, (iii) execution of the observed chords and (iv) rest. The results showed that the basic circuit underlying imitation learning consists of the inferior parietal lobule and the inferior frontal gyrus plus the adjacent premotor cortex. This circuit starts to be active during the observation of the guitar chords and remains active till the actual execution by the observer. During pause and actual execution, the middle frontal gyrus (area 46) plus structures involved in motor preparation and execution (dorsal premotor cortex, superior parietal lobule, rostral mesial areas, primary motor cortex) also come into play.

These data show that the neural substrates responsible for the building up of new motor patterns include the key centres of the MNS. It has been forwarded that during learning of new motor patterns by imitation, observed actions are decomposed into elementary motor acts that activate, by a mirror mechanism, the corresponding motor representations in the inferior parietal lobule, in premotor cortex and in the

pars opercularis of the inferior frontal gyrus. Once these motor representations are activated, they are recombined, to fit the observed model. This recombination appears to occur within areas of the putative human MNS, possibly with area 46 playing an additional orchestrating role. This notion has been confirmed in a further fMRI study, where activation within area 46 was compared in expert musicians and naive participants. The results indeed showed a stronger recruitment of area 46 in naive people when compared with expert musicians as expected assuming a role of area 46 in the acquisition of novel motor capabilities [64].

In AOT, patients are asked to observe and imitate actions to restore the neural structures normally involved in the actual execution of actions. While doing this, the claim is that they also recover their ability to code the intentions of individuals performing the observed actions and eventually the capacity to interact with the environment and socially. For instance, the observation of a hand grasping an object allows the observer to realize that the agent aims at taking possession of that object. In addition to this ability to 'grasp' the immediate scope of an observed action, recent data suggest that the MNS is involved also in more refined, cognitive aspects of action understanding, which are also trained in AOT. Classically, the ability to understand the intentions underlying actions is a task that is assumed to be achieved by means of logical-deductive reasoning. The ensemble of mental processing devoted to this purpose is called theory of mind [65,66]. The MNS offers an alternative although non-exclusive explanation about how one individual can capture the intentions of other people's actions. The same mirror mechanism to comprehend the immediate scope of an action may also serve the decoding of deeper aspects of intention.

In an fMRI study [67], participants were presented with the same action embedded in two different contexts. In one case, they observed an actor grasping a cup lying on a table set for breakfast, whereas, in the other case, they observed the grasping of a cup lying on the same table at the end of breakfast. One group of participants had to just observe the actions, whereas another group was required to explicitly state the different intentions underlying the same action of grasping performed by the actor in the two different contexts. Results showed

that there was no differential activation of brain areas between the two groups of participants, suggesting that the brain automatically extracts the intentions of observed actions together with the processing of motor aspects of those same actions and of the context in which the actions take place. Indeed, the activated brain regions in the two groups were those typically belonging to the MNS.

To investigate the neural basis of the capacity of understanding when actions done by others do or do not reflect their intentions, in another fMRI study [68] volunteers were presented with video clips showing actions that did reflect the intention of the agent (intended actions) and actions that did not (non-intended actions). Observation of both types of actions activated a common set of areas including the inferior parietal lobule and the premotor cortex. When directly comparing brain areas activated for non-intended and those activated for intended actions three regions specifically emerged: the right temporoparietal junction, left supramarginal gyrus and mesial prefrontal cortex. The converse comparison did not show any activation. The authors concluded that our capacity to understand non-intended actions is based on the activation of areas signalling unexpected events in spatial and temporal domains, in addition to the activity of the MNS. The concomitant activation of mesial prefrontal areas, known to be involved in self-referential processing [69], might reflect how deeply participants are involved in the observed scenes.

In conclusion, AOT is a novel approach in neurorehabilitation well grounded in neurophysiology, thus representing a valid model of translational medicine in the field of neurorehabilitation. The results concerning its effectiveness have been collected in randomized controlled studies: in this respect, it is an example of evidence-based clinical practice. So far, it has been applied in the motor recovery of patients with neurological and non-neurological diseases. Preliminary results have also been collected in speech recovery. Larger randomized controlled studies should be planned to define the best way to apply AOT in clinical practice, the groups of patients who may most benefit from it, how biological parameters change following AOT and, finally, how to combine this approach with other well-assessed tools in neurorehabilitation.

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