Chapter 1

The Study of Action Observation Therapy in Neurological Diseases: A Few Technical Considerations

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Abstract

Action observation therapy (AOT) is a developing neurorehabilitative tool, which is based on the existence of the mirror neuron system (MNS). This neural network involves motor regions, and its main feature is that it is activated not only during the execution of an action, but also during the observation of the same action. Bearing in mind this "dual" activation, the AOT proposes that motor symptoms of different neurological disorders can improve with the observation and imitation of different actions. While several studies have shown the benefits of this therapy, others have been less favorable indicating a lack of clarity in the field. The present study focuses on previously undiscussed aspects regarding this therapy: from the kind of actions used in the therapy to the scales that should be used to measure the results of AOT. Differences and similarities between virtual reality-based therapies and AOT are also discussed. The considerations made here about all such aspects may be useful for future studies and possible applications of AOT.

Keywords: mirror neurons, neurological rehabilitation, rehabilitation interventions, action observation, motor recovery

1. Introduction

Action observation therapy (AOT) is based on the well-known "mirror mechanism." AOT alludes to the activation of motor-related areas not only when an action is performed, but also when the action is observed [1]. This mechanism was first described in the premotor cortex of the macaque [2], and over the last two decades, several studies have focused on the identification, description and characterization of the human brain regions that present this mechanism [3–5]. Nowadays, there is much agreement about the existence of a neural network formed by regions that present the "mirror mechanism." The most consistent regions are located in the frontal lobe [mainly in the inferior frontal gyrus (IFG)] and in the posterior parietal lobe [mainly in the inferior parietal lobule (IPL)] [1, 4], though there are other regions that may also be involved [6, 7]. This brain network is the so-called mirror neuron system (MNS) (**Figure 1**).

The dual activation of the MNS has been associated with the ability to understand the actions performed by others [3, 8]. Bearing this in mind, it is easy to deduce that the MNS is essential for imitation and, eventually, for action learning [9–11]. Several experiments have provided some evidence in this respect and have led to the suggestion of the possible role of action observation (i.e., MNS activation) in motor rehabilitation. Effectively, the activation of motor regions during the simple observation of an action may result in an improvement of motor impairment; this is the AOT hypothesis. However, the MNS is associated not only with motor functions, but also with social cognition. Many authors agree in considering the involvement of the MNS in social interaction and in the relationship between people and the environment [4, 12]. This consideration makes the AOT not only a motor rehabilitation program, but also a functional recovery program.

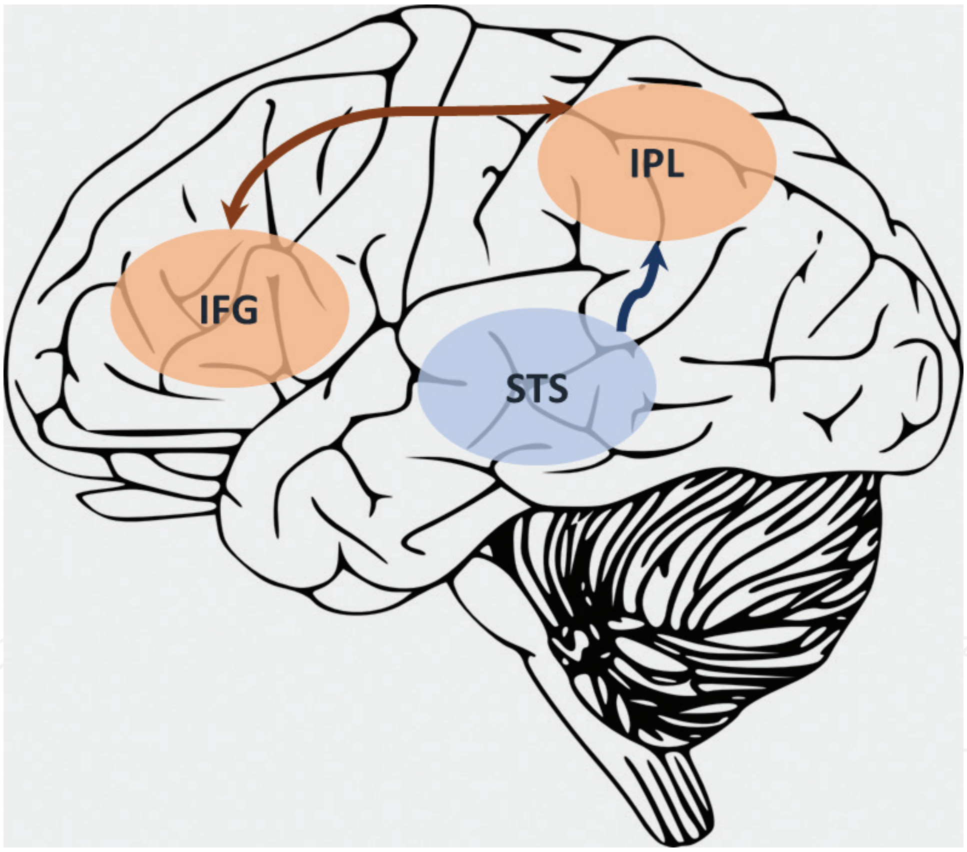

Figure 1. The MNS in humans. Many functional studies have shown that many brain regions present mirror properties. Apart from premotor cortex (PMC), parietal and temporal regions are also activated when an action is executed or observed and this is clearly related with the important role that mirror neurons seem to play in many aspects of social cognition (language, empathy, learning process, etc.). Because of this, it has been suggested that developmental MNS dysfunction leads to disordered social cognition in humans, including autism spectrum disorders. Anyway, the most studied areas that present mirror properties in humans are the inferior frontal gyrus (IFG) corresponding to BA 44 and inferior parietal lobule (IPL), corresponding to BA 40. Both form the core of the known parietal-frontal mirror neuron system (MNS). The superior temporal sulcus (STS) is consistently activated during the observation of human movements and seems to play a prominent role in the flux of information to the MNS.

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Bearing in mind only neurological diseases, stroke is, unmistakably, the most common neurological disease where AOT has been tested. Motor impairment and aphasia were the most common features of the stroke patients included in trials and prospective observational studies [13–20]. For both clinical conditions, the majority of the studies reported a clear benefit of AOT, with a maintained improvement in the motor condition and the functional status. In fact, the benefit of this therapy has been remarked on in a recent evidenced-based review of the literature concerning the effect of AOT in upper limb dysfunction after stroke [21].

AOT has also been used in other movement disorders such as Parkinson's disease and cerebral palsy, though the number of studies that have focused on these diseases is much lower than those focused on stroke. In any case, the application of AOT leads to an improvement in gait and bradykinesia in Parkinsonian patients [22–24] and in the functional status in cerebral palsy's infants [25]. Finally, cognitive benefits have been reported after the application of AOT in Alzheimer's disease [26].

New and different studies about AOT need to be performed in order to properly identify the role of this therapy in the rehabilitation of neurological disorders. Some weaknesses in the current literature about AOT can be identified. For example, most of the previously cited studies included patients with a chronic evolution of their diseases (more than 6 months after the onset) and not in the acute or subacute phase of the disease, where the therapy might also show efficacy (or even more). Furthermore, the number of patients is highly variable between the different studies and the differences in the period where patients were exposed between the different studies are large. However, these methodological aspects are not the only ones that must be considered when AOT is going to be applied. In the present work, we stress the importance of adequately selecting the actions to be used during therapy as well as the correct scale for evaluating the results of AOT. The consideration of these aspects in future studies may help to provide a better understanding of the MNS and to know the real impact of the therapy in patient's recovery. This study also discusses the differences and similarities that exist between virtual reality-based therapies, an innovative approach that is being increasingly applied in rehabilitation centers. Finally, future perspectives about AOT research are proposed.

2. Which actions should be used in AOT?

One major issue about AOT is the kind of action that should be used in order to get the maximum benefit. Most of the actions that have been employed in AOT studies consist of upper limb transitive actions (i.e., actions with object interaction, e.g., using a pencil). These are usually daily actions that have been selected on the basis of their ecological value [27]. This kind of action has been shown to have increased MNS activity in neuroimaging studies [15, 28] and corticospinal facilitation in transcranial magnetic stimulation (TMS) [29, 30].

Although the benefits of AOT have been demonstrated with the use of transitive actions, the use of intransitive ones (i.e., actions without object interaction, e.g., the opposition of the index finger and the thumb as the pantomime of a precision grasping) may also be considered for use in this therapy. Intransitive actions lead to an activation of the human MNS (there is new evidence of this activation in primates too) in a more restrictive way than transitive actions do [31, 32]. In fact, the activity of the MNS when intransitive actions are observed tends to predominantly activate posterior parietal regions more than premotor areas [31, 33]. Minor activation of the MNS does not have to mean that an AOT based on these actions had less benefit than using transitive ones. It is known that part of the brain activity obtained with the use of transitive actions is due to the presence of an object and a more complex scenario where the action takes part [34]. In this respect, many patients with neurological disorders may have attention deficits or less capacity to follow the action continuously, because there are many factors that catch the observer's attention (e.g., the object features) and they may become cognitively overloaded. Furthermore, when patients are asked to imitate the motor actions, the imitation of simple and intransitive actions would be effortless than the performance of complex and transitive ones. Consequently, future studies should incorporate intransitive actions to those which patients must observe to evaluate the efficacy of the AOT using these actions. Although they will lead to less brain activity, the patient can be more focused on the effector as well as on the kinematics of the action, and neither on the object which the effector interacts with nor on the context where the action takes place.

On the other hand, another factor that must be considered in AOT is the visual perspective from which the motor acts of others are observed. It has been demonstrated that the majority of mirror neurons in the monkey premotor cortex are view-dependent (i.e., they are only activated when the action is presented in a specific visual perspective) [35, 36] and, depending on the point of view, action observation leads to different activations of the MNS [37]. In this sense, certain evidence exists that an egocentric view (i.e., first-person perspective) of an action leads to higher brain activity than a third-person view [30] (**Figure 2**). Moreover, studies in monkeys have revealed the existence of some subcategories of mirror neurons that are selective for specific space positions, right or left hand, and for specific directions [2, 38]. Although these

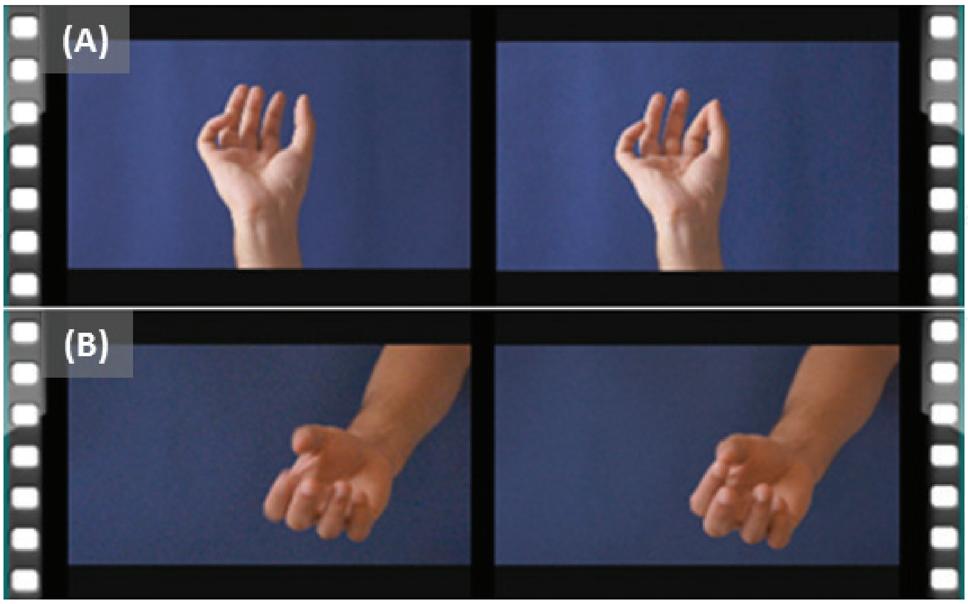

Figure 2. Different visual perspectives. First-person perspective (A) and third-person perspective (B) of an intransitive motor action (index to thumb opposition task). First-person perspective seems to conduct to higher MNS activity than a third-person view.

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properties have been less studied in the human MNS, its presence in non-human primates makes it easy to assume the existence of this diversity among the mirror neurons of human beings. Thus, the MNS is important for visuospatial and visuoperceptive abilities. Bearing this in mind, patients who are candidates for AOT should be previously tested in these functions with proper neuropsychological assessment. This evaluation may allow the adaption of the kind of actions that are shown to the patient in order to achieve better and faster results.

3. Measuring AOT results: what matters?

One of the most important aspects when considering AOT is to adequately evaluate the results. The use of an appropriate scale or index is a basic requisite to analyze the efficacy of any rehabilitative therapy. Previous studies have reported the efficacy of the AOT in terms of changes in scales that measured specific clinical aspects of each neurological disease. For instance, some stroke-based studies expressed the efficacy of AOT with changes in Upper Extremity Fugl-Meyer Motor Assessment (FMA) and Functional Test of the Hemiparetic Upper Extremity (FTHUE) [20]; similarly, the application of AOT in Parkinson's disease patients was measured with a 39-item Parkinson Disease Questionnaire (PDQ-39) [24]. Although the specific scales are vital for understanding the effect of MNS therapy in the clinical symptoms of each neurological disease, the broad implications of AOT (considering its effect on the MNS with motor and cognitive implications) mean that these scales are restricted. Moreover, these scales should also be versatile enough to be applied to the majority of the spectrum of neurological diseases where AOT may be applied. Thus, it seems reasonable to propose a more general scale or index to evaluate the results of AOT in terms of functional recovery.

Functioning is a generic term defined by the World Health Organization (WHO), which includes the positive aspects of the interaction between an individual (with a certain health condition) and the contextual factors (personal and environmental factors). This leads to a definition of disability as the restriction of a person's functioning. Neurorehabilitative approaches must converge in a recovery in the functioning that may have been lost as a result of the disease. Therefore, the efficacy of this kind of therapy has to be measured by functional scales.

There are several functional scales described in the literature. Bearing in mind its extensive applicability in neurological diseases, broad extended use and adaptability, the Barthel Index (BI) can be considered as a trustworthy scale for evaluating AOT results. The BI was designed in 1965 by Mohoney and Barthel [39] and has been subsequently modified by many others. The modification made by Granger et al. [40] should be mentioned as it is probably the most used version of the BI nowadays. The BI modified (BIm) consists of the evaluation of the independency degree when a patient performs 15 basic daily life activities (BDLA). Granger et al. grouped the activities into two subscales: one measuring the capacity to take care of themselves and the other determining the degree of mobility (**Table 1**). The BIm is a highly sensitive, valid and feasible, which is able to detect progress or impairment during the evolution of a rehabilitation program [41]. Furthermore, it is an inexpensive tool, which does not take up much of the examiner's time.

	Independent	Assistance	Dependent
Personal care			
Drinking using a glass	4	0	0
Eating	6	0	0
Dressing the upper part of the body	5	3	0
Dressing the lower part of the body	7	4	0
Putting on prosthesis	0	−2	0
Tidying up	5	0	0
Bathing	6	0	0
Urine control	10	5	0
Fecal control	10	5	0
Mobility			
Sitting/getting up from a chair/bed	15	7	0
Use of the toilet	6	3	0
Getting in/out to the shower1	1	0	0
Walking 50 m	15	10	0
Going down/upstairs	10	5	0
Propelling a wheelchair	5	0	0
Score			
0–20	Complete disabled		
21–60	Severe disabled		
61–90	Moderate disabled		
91–99	Slight disabled		
100	Independent		

Table 1. Barthel Index modified by Granger et al. Adapted from Granger et al. [40].

However, the evaluation of the capacity to perform the BDLA may not be enough to appropriately measure the impact of the AOT. "Instrumental daily life activities" (IDLA) and "advanced daily life activities" (ADLA) have been defined as activities that allow a person to be independent in the community (IDLA) (e.g., going to the supermarket, cooking) and to develop a social role (ADLA) (e.g., working, practicing sports, religion). The measurement of the capacity to develop these activities would provide a more holistic picture of the patient's situation before and after the application of AOT. It would be interesting to evaluate the results of AOT using specific scales for IDLA and ADLA, because the MNS is clearly involved in the normal development of these activities.

One of the scales for IDLA assessment is the Lawton and Brody scale, which consists of eight items related to daily activities (e.g., use of transport) which are asked directly to the patient or the caregiver [42]. It is a highly sensitive scale and has a high inter- and intra-observer correlation coefficient. However, the main disadvantage of this scale is that it was conceived for the elderly population, and thus, its application might be restricted.

Furthermore, it should be recognized that the evaluation of IDLA and ADLA is more complex than other evaluations and such activities are influenced by the culture and the geographical environment of the patient. Therefore, some effort needs to be made for testing new scales to approach the evaluation of IDLA and ADLA and apply them (with BDLA scales) to the measurement of AOT impact.

4. AOT and virtual reality: two heads of the same coin

AOT is not the only rehabilitative tool that has been investigated in the last decade to improve the functional status of patients with neurological disorders. The application of virtual reality (VR) approaches in the field of rehabilitation is extensively reported, and it has been shown to have certain benefits, not only in the recovery of motor dysfunctions [43], but also in improving cognitive impairment [44, 45]. VR therapies are based on the generation of a real-time three-dimensional environment that makes the patients feels as if they are in a real situation [46]. Normally, the patient is situated in front of a monitor and is required to perform actions with the impaired limb (or with the non-impaired limb when the deficit is notable). These actions are recognized by a movement sensor, and the patient receives the feedback by means of the monitor, observing different movements or consequences of the performed actions. The feedback will depend on which VR program has been initiated. For instance, a VR program may consist of a box moving from one side to the other; the patient performs an action and observes the displacement of the boxes on the screen). These VR approaches have demonstrated their usefulness in several neurological disorders [43, 47–49], with stroke being the subject of the largest number of studies. In fact, a recent Cochrane meta-analysis concluded that VR leads to an improvement in upper limb function and recommended its use as a complementary therapy to the usual therapy for improving the activity of daily living function [50].

VR therapy has some aspects in common with AOT. The feedback in both therapies consists of an observation task (although the feedback of VR is usually over dimensioned); moreover, patients can be requested to interact with the elements they observe, with an imitation (AOT) or by trying to modify a condition in the virtual environment. Thus, VR and AOT modulate the MNS to achieve an improvement in the functional condition of patients. In this respect, some studies have shown the presence of an intense MNS activity during VR tasks [51, 52].

However, although these therapies share common features in the conditions they use, as well as the neural substrates they take advantage of, there are important feasibility and applicability differences. On the one hand, VR therapy requires a more sophisticated informatics structure than AOT; thus, it may be less efficient and makes this therapy less practical for use at home. On the other hand, the instructions and the tasks of VR therapies are more complex than those applied in AOT (i.e., simply observing or imitating a movement). Therefore, although VR and AOT may be complementary rehabilitation tools, AOT may be more widely used than VR in different socioeconomic environments.

5. Future perspectives

The road that AOT has to travel until it can be considered a standard therapy in neurorehabilitation is still long. Although some randomized trials have been published reporting the efficacy of this therapy in stroke, Parkinson's disease and cerebral palsy patients, new studies are necessary (considering the heterogeneity in the scales used for measuring the efficacy and in the period of treatment). Furthermore, other neuropathological conditions should be considered in such trials. For example, multiple sclerosis or traumatic brain injury patients could also benefit from AOT, but no randomized trials with this kind of patients have been performed to date.

On the other hand, apart from the aspects that have been discussed above, it would also be interesting if new studies reported the results of neurofunctional studies (i.e., neuroimaging and/or other functional tests). It would provide much information about the functioning of the MNS in different pathological conditions as well as the plastic changes in the brain that may be associated with the use of AOT.

Further study of AOT may generate a new weapon in the armory against the functional and social limitations produced by neurological disorders. The decrease of such limitations is clearly associated with an improvement in the quality of life and survival periods of the patients, thanks to the reduction of complication rates (associated with the aforementioned limitations). Therefore, new and appropriate research is needed to convert the AOT in a standard therapy in our hospitals and rehabilitative centers.

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