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Review article

Action observation and motor imagery for rehabilitation in Parkinson's disease: A systematic review and an integrative hypothesis

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ABSTRACT

This article discusses recent evidence supporting the use of action observation therapy and motor imagery practice for rehabilitation of Parkinson's disease. A main question that emerges from the review regards the different effectiveness of these approaches and the possibility of integrating them into a single method to enhance motor behaviour in subjects with Parkinson's disease. In particular, the reviewed studies suggest that action observation therapy can have a positive effect on motor facilitation of patients and that a long-term rehabilitation program based on action observation therapy or motor imagery practice can bring some benefit on their motor recovery. Moreover, the paper discusses how the research on the combined use of action observation and motor imagery for motor improvements in healthy subjects may encourage the combined use of action observation therapy and motor imagery practice for therapeutic aims in Parkinson's disease. To date, this hypothesis has never been experimented.

Contents

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1. Introduction

This article discusses the recent evidence supporting the use of Action Observation Therapy (AOT) and Motor Imagery Practice (MIP) as therapeutic means to potentially benefit Parkinson's disease (PD). We first briefly discuss data on the effects of action observation (AO) and motor imagery (MI) in healthy subjects (section 1.1), their use for rehabilitative purposes in general as AOT and MIP (section 1.2), and the brain network underlying their operation (section 1.3). This discussion will be propaedeutic for section 2 where we systematically review the findings on AOT and MIP effects when these are applied to PD. In particular, in section 2.1 we indicate the criteria used for the retrieval and inclusion of the works reviewed here. In section 2.2 we review the effects of AOT and MIP found in single session experiments. In section 2.3 we review the effects of AOT and MIP found in long-term therapeutic programs studies. Finally, in section 3 we draw the conclusions by stressing the possible joint exploitation of AOT and MIP for rehabilitation based on their synergistic effects on the brain network affected by PD.

1.1. AO and MI in healthy subjects

AO and MI have long been studied in healthy subjects but only recently they have become a major subject of debate in the clinical setting. The idea of learning by observation has its roots in the social learning theory (Bandura, 1977). From the discovery of the mirror neuron system in the monkey's brain (di Pellegrino et al., 1992; Rizzolatti et al., 1996) and in the homologous areas of the human brain (Rizzolatti and Arbib, 1998; Buccino et al., 2001; Mukamel et al., 2010; Thill et al., 2013) a new breath has been given to the idea of observation-based learning. Rizzolatti et al. (2001) postulate that during observation of a movement, the related action representation "resonates" (re-activates) in our motor system. This motor resonance can drive learning and the process of understanding the intention of the agent performing the action through a facilitatory effect on motor pathways (Buccino et al., 2001; Wheaton et al., 2004). In this line, substantial evidence indicates that observation can drive learning and the acquisition of motor skills in analogous ways as physical exercise (Porro et al., 2007; van der Helden et al., 2010; Higuchi et al., 2012).

Jeannerod (2001) and many others (Decety et al., 1989; Jeannerod and Decety, 1995; Kosslyn et al., 1995) describe MI as a type of mental simulation whereby we imagine to perform an action without actually moving any muscles of the body. There is much evidence on MI relation with motor execution and learning: time to imagining a certain action correlates with the execution time of that action (Decety and Michel, 1989; Sirigu et al., 1995); there is a change in heart rate imagining to cover a distance dragging a weight (Decety et al., 1991; Oishi et al., 1994); respiration rate increases in proportion to the imagined effort (Wuyam et al., 1995); mental training based on MI can lead to plastic changes in the brain (Butler and Page, 2006; Page et al., 2009); MI can have the same effect as physical practice on learning (Yaguez et al., 1998) and can improve athletes performance (Roure et al., 1999; Guillot et al., 2009).

What AO and MI seem to share is the internal "replica" of the behavior, which enhances learning and neural traces of motor actions. However, it is not yet clear whether the effect they have on learning can be the same or if some factors, such as knowledge of the movement, can influence them (Vogt et al., 2013). AO alone has a stronger effect on learning of new movements than MI alone (Mulder et al., 2004; Gatti et al., 2013). This is probably due to the fact that during AO the mirror neuron system is strongly activated promoting a better collection of preparatory information for a better physical performance (Gonzalez-Rosa et al., 2014). Some studies show that AO and MI can interact in a very specific way to affect motor execution (Conson et al., 2009) and that MI can modulate the effect of AO increasing the effects of motor learning (Sakamoto et al., 2009; Lawrence et al., 2013; Taube et al., 2015; Helm et al., 2015).

1.2. AOT and MIP in rehabilitation in general (outside PD)

Starting from the studies on healthy subjects, the focus of research has shifted to the clinical side, driven by an interest in the application of AO and MI as re-learning techniques to recover from motor deficits (Mulder, 2007). Action observation therapy (AOT) is based on the observation of action performed by others. In this technique, participants are typically required to carefully observe videos showing actions that then they have to execute. Many studies demonstrate that AOT has a positive effects in rehabilitation (for

a review see: Mulder, 2007; Oouchida et al., 2013; Buccino, 2014). The technique has been used in stroke patients (Ertelt et al., 2007; Franceschini et al., 2010; Bang et al., 2013); in language deficits (Marangolo et al., 2010, 2012; Lee et al., 2010); and in the rehabilitation of postsurgical orthopedic patients (Bellelli et al., 2010).

Recent approaches for motor treatments are based on mental practice by applying MI (termed "motor imagery practice (MIP)", cf. Tamir et al., 2007; Helmich et al., 2007). The difference between MI and MIP consist in the fact that while MI is a cognitive process of imagining movement only, MIP is the act of repeating the imagined movement to improve motor performance (Ravey, 1998). MIP has been successfully applied in patients with low back pain due to lordosis and kyphosis (Fairweather and Sidaway, 1993), and in stroke patients, both in the sub-acute (Page et al., 2001) and chronic stage (Page, 2000; Stevens and Stoykov, 2003; Page et al., 2009; Cho et al., 2013).

One reason why so much interest has focused on these two new therapeutic techniques lies in the fact that AO and MI recruits high-level brain processes involved in motor behaviour. More in details, traditional motor rehabilitation techniques mainly focus on the peripheral brain component of movement and the possible effects at the higher cortical levels are produced as the result of bottom-up effects (Bellelli et al., 2010). By contrast, applying AOT and/or MIP in rehabilitation programs can enhance the effects of physical therapy by reinforcing at the same time the peripheral circuits involved by traditional therapy, going from peripheral districts of the body to the motor areas of the brain, and higher-level circuits going from central movement preparatory areas to motor areas and the periphery of the body (Mulder, 2007).

1.3. Cortical-subcortical neural network underlying AO and MI

AO and MI involve a large cortical-subcortical network. A wide range of regions that contribute to action execution are also active during AO. These areas include parietal and premotor cortices (Buccino et al., 2001), inferior frontal gyrus, visual temporal (Caspers et al., 2010) and supplementaty motor areas (Hari et al., 1998), basal ganglia (Marceglia et al., 2009; Alegre et al., 2010) and cerebellum (Caligiore et al., 2014).

Similarly, MI is associated with the activation of the neural circuits involved in the early stages of motor control (i.e., during motor programming). These circuits include supplementary motor, premotor, primary motor and inferior parietal cortical areas as well as basal ganglia and cerebellum (Roth et al., 1996; Jeannerod, 2001). Recently, Guillot et al. (2009) showed that circuits mediating MI partially differ as a function of imagery ability. Specifically, strong imagers recruit parietal and ventro lateral premotor regions while weaker imagers recruit mainly the cerebellum, the orbito-frontal, and posterior cingulate cortices.

These data suggest that the neural circuitry for AO, MI and action execution appears to overlap extensively. Elements of this common circuitry involve superior temporal sulcus, supplementary motor cortex, premotor cortex, inferior frontal and inferior parietal areas, basal ganglia and cerebellum (Grèzes and Decety, 2001; Maeda et al., 2002; Buccino et al., 2004; Mulder, 2007; Taube et al., 2015). Recently, Vogt et al. (2013) suggested that the mental simulation during AO and MI differs only from the point of view of the input from which they are generated. While AO is driven by visual stimuli of external origin (others' behavior), MI is driven by internal stimuli (re-activation of a motor representation stored in memory). This view is supported by imaging data showing an overlap in the activity within dorsal premotor cortex, superior parietal lobe and intraparietal sulcus during observation, execution and imagery of reaching movement. The main differences between AO and MI were found in occipital regions (Filimon et al., 2007). Based on this neural overlapping, recent studies suggest that combining AO and MI

Table 1
Single session experiment on PD and AOT – Sociodemographic and clinical characteristics.

Author and year	Sociodemographic characteristics								Clinical characteristics of participants								Brain activity recording
	Sample size		Age (mean ± SD)		Males (no.)		Education, years (mean ± SD)		Illness duration (mean ± SD)		Diagnosis		Medication status		Inclusion criteria (test, scores)		Disease severity (test, mean scores ± SD)		
	EX	CON	EX	CON	EX	CON	EX	CON	EX	CON	EX	CON	EX	CON	EX	CON	EX	CON	
Castiello et al., 2009	16	16	53	52	8	NA	NA	NA	1.75	-	IP	HC	ON	-	Diagnosis of PD; No dementia; Normal visual acuity	Normal neurological examination; Normal visual acuity	H&Y: R: 1-2; MMSE: 29-30	-	NA
Pelosin et al., 2013	38 divided in 4 group	14	67.4 ± 7.4	65.9 ± 7.6	17	8	NA	NA	1° group: 9.1 ± 3.7; [2°] group: 8.9 ± 3.1; [3°] group: 8.0 ± 4.7; [4°] group: 8.8 ± 4.5	-	IP	HC	ON/OFF	-	No other pathological-neurological disorder; No DBS; MMSE > 24; Normal visual and auditory acuity	Normal neurological examination; No history of neurological disorders	H&Y: R: 1–3	-	NA

EX, Experimental Group; CON, Control Group; SD, Standard Deviation; PD, Parkinson's Disease; NA, Not Available; IP, Idiopathic PD according to the UK Parkinson's Disease Brain Bank clinical criteria; HC, Healthy Control; ON, On stable medication regimen; OFF, Off medication regimen; H&Y, Hoehn and Yahr scale (Hoehn & Yahr, 1967); R, Range; MMSE, Mini Mental State Examination; DBS, Deep Brain Stimulation.

Table 2
Single session experiment on PD and MIP – Sociodemographic and clinical characteristics.

Author and year	Sociodemographic characteristics								Clinical characteristics of participants								Brain activity recording
	Sample size		Age (mean years ± SD)		Males (no.)		Education, years (mean ± SD)		Illness duration (mean years ± SD)		Diagnosis		Medication status		Inclusion criteria (test, scores)		Disease severity: (test, mean scores ± SD)		
	EX	CON	EX	CON	EX	CON	EX	CON	EX	CON	EX	CON	EX	CON	EX	CON	EX	CON	
Dominey et al., 1995	7	7	56.3 ± 8.0	54 ± 11.7.0	4	5	NA	NA	R: 1-7	–	IP	HC	ON (n2) ON-OFF	–	Responsive to levodopa; Early or mid-stage (duration illness range 1–7 years)	Normal neurological examination	H&Y: R: 1.5–2.5; Right lateralized symptoms	–	NA
Cunnington et al., 1997	14	10	67.6 ± 10.5	64.0 ± 8.9	14	10	NA	NA	NA	–	IP	HC	ON	–	No other pathologic-neurological disorder; No depression; No dementia	No history of neurological disorders; No depression; No dementia	H&Y: 2.1 ± 0.9 Webster scale: 10.5 ± 4.9	–	MRPs
Yaguez et al., 1999	11	11	67.0 ± 10.3*	47.6 ± 10.0*	6	5	9.8 ± 2.1	10.4 ± 2.1	6.0 ± 4.0	R: 0.5–7.0	IP	HD	ON (n9)	ON (n3)	No dementia	No dementia	H&Y: R: 1–3	Grade of Chorea: R: 0.5–2.0	NA
Thobois et al., 2000	8	8	49.4 ± 5.3	54 ± 12.8	5	3	NA	NA	4.9 ± 2.6	–	IP	HC	OFF	–	Responsive to levodopa; Right-lateralized symptoms; Prominent akinetic-rigid signs; No tremor	Normal neurological examination	UPDRS: 18.7 ± 6.0 H&Y: 2.0 ± 0.5	–	PET
Cunnington et al., 2001	6	3	66.0 ± 7.5	60.7 ± 3.8	4	2	NA	NA	NA	–	IP	HC	OFF	–	No excessive dyskinesia or Tremor; MMSE 28-30	Normal neurological examination	H&Y: R: 3–4; modified Webster scale: 18.8 ± 2.1	–	PET
Samuel et al., 2001	6	6	62 ± 6	55 ± 4.0	NA	3	NA	NA	10 ± 8.0	–	IP	HC	OFF	–	Mild-moderate symptoms	No history of neurological or psychiatric disorder; Normal neurological examination	UPDRS: 24 ± 13; MMSE: R: 28–30; n5 right lateralized symptoms	–	PET
Filippi et al., 2001	7	7	R: 54-63	NA	3	NA	NA	NA	R: 1–3	–	IP	HC	OFF	–	No other pathologic-neurological disorder; Unilateral bradykinesia and rigidity	Normal neurological examination	UPDRS: 19.0 ± 7.7	–	MEPs; TMS
Frak et al., 2004	8	8	59 ± 4.49	58 ± 5.08	4	5	NA	NA	NA	NA	IP	HC	ON	–	Idiopathic PD	Normal neurological examination	H&Y: 3; Little or no akinesia in dominant hand after medication	–	NA
Lim et al., 2006	6	7	69.9 ± 9	71 ± 7.0	5	5	NA	NA	NA	NA	IP	HC	ON	–	NA	NA	H&Y: range 1–2	–	CNV
Helmich et al., 2007	19 (n7: main exp.; n12: contr. exp.)	1° group: n10 adults; [2°] group: n15 young. All in contr. exp.	53.2 ± 9.1	1° group: 57 ± 6.2; [2°] group: 26 ± 3.3	13	1° group: 8; [2°] group: 7	NA	NA	NA	NA	IP	HC	OFF	–	Right-lateralized symptoms; No moderate-severe tremor; MMSE > 24; No other pathologic-neurological disorder; No exclusion criteria for MRI scanning	Normal neurological examination	H&Y: 2.1 ± 0.5 UPDRS: 4.6 ± 2.8 UPDRS: 13.5 ± 5.0	–	fMRI
Heremans et al., 2011	14	14	59.1 ± 9.6	61.1 ± 6.6	9	8	NA	NA	R: 0.5-17 years	–	IP	HC	ON	–	MMSE < 24; No other pathologic-neurological disorder; No severe tremor; No motor fluctuation; No DBS	Normal neurological examination	H&Y: R: 1–3	–	NA

Table 2 (*Continued*)

Author and year	Sociodemographic characteristics								Clinical characteristics of participants								Brain activity recording
	Sample size		Age (mean years ± SD)		Males (no.)		Education, years (mean ± SD)		Illness duration (mean years ± SD)		Diagnosis		Medication status		Inclusion criteria (test, scores)		Disease severity: (test, mean scores ± SD)		
	EX	CON	EX	CON	EX	CON	EX	CON	EX	CON	EX	CON	EX	CON	EX	CON	EX	CON	
Cohen et al., 2011	n11 FOG-PD; [13n] PD no FOG	10	FOG PD: 68 ± 8; PD no FOG: 67 ± 6	67 ± 7.0	FOG PD: 9; PD non FOG: 10	10	NA	NA	FOG PD: 9.9 ± 7.8; PD no FOG: 6.3 ± 3.6	–	IP	HC	OFF	–	No dementia; No other pathologic-neurological disorder; Ability to stand and walk for 20 min	Normal neurological examination	FOG PD: H&Y: 3.0 ± 0.8, UPDRS:44.9 ± 15.1; PD no FOG: H&Y: 2.1 ± 0.5; UPDRS: 32.2 ± 7.6	–	NA
Heremans et al., 2012	14	14	59.1 ± 9.6	61.1 ± 6.6	9	8	NA	NA	R: 0.5-17 years	–	IP	HC	ON	–	MMSE < 24; No severe tremor; No other pathologic-neurological disorder; No motor fluctuation; No DBS	Normal neurological examination	H&Y: R: 1–3	–	NA
Pickett et al., 2012	28	33	71.0 ± 8.9	69.9 ± 10.7	17	17	NA	NA	NA	–	IP	HC	OFF	–	Independent ambulatory ability; MMSE ≥ 24; Normal visual and acoustic acuity; No other pathologic-neurological disorder	Independent ambulatory ability; MMSE ≥ 24; Normal neurological examination; Normal visual and acoustic acuity	NA	–	NA
Helmich et al., 2012	n18 Tremor PD; [20n] No tremor PD:	19	Tremor PD: 56.7 ± 10.0; Non tremor PD: 59.1 ± 9.4	58 ± 7.9	Tremor PD: n10; No tremor PD: n16	12	NA	NA	Tremor PD: 4.3 ± 2.1; No tremor PD: 4.5 ± 2.6	–	IP	HC	OFF	–	No other pathologic-neurological disorder; No dementia; No contraindications for MRI scanning	Normal neurological examination; No contraindi-cations for MRI scanning	Tremor: H&Y:2 ± 0.3 UPDRS: 27.2 ± 8.1; Non tremor: H&Y: 2.1 ± 0.2 UPDRS: 27.9 ± 9	–	fMRI
Avanzino et al., 2013	14	12	68.78 ± 8.71	64.15 ± 10.8	8	7	NA	NA	R: 1-13	–	IP	HC	ON	–	H&Y stages: 1–3; Stable dopaminergic medication regimen; No other pathologic-neurological disorder; MMSE < 24; No ongoing functional brain surgery treatment; Normal visual and acoustic acuity	Normal neurological examination; No history of neurological disorders	H&Y: R: 1–2.5; UPDRS: R: 5–37	–	NA
Peterson et al., 2014	19	20	64.9 ± 7.6	66.6 ± 7.6	11	5	NA	NA	6.7 ± 6.0	–	IP	HC	OFF	–	No other pathologic-neurological disorder; No contraindications for MRI; KVIQ mean ≥ 3; MMSE > 26	Normal neurological examination. No contraindi-cations for MRI KVIQ mean ≥ 3	H&Y: 2.34 ± 0.33; UPDRS-III: 31.2 ± 10.0	–	fMRI
Maillett et al., 2015	8	8	63.3 ± 6.3	62.9 ± 6.7	4	4	NA	NA	12.3 ± 3.8	–	IP	HC	ON/OFF	–	MMSE > 27; FAB > 14; Mattis dementia rating scale >130; No other pathologic-neurological disorder; No marked resting tremor; No neurosurgery; FOG improved in ON phase	MMSE<27; FAB>14;	H&Y: 3.4 ± 0.5	–	PET

EX, Experimental Group; CON, Control Group; SD, Standard Deviation; PD, Parkinson's Disease; NA, Not Available; R. Range; IP, Idiopathic PD according to the UK Parkinson's Disease Brain Bank clinical criteria; HC, Healthy Control; ON, On stable medication regimen; OFF, Off medication regimen; H&Y, Hoehn and Yahr scale; KVIQ, Kinesthetic and Visual Imagery Questionnaire; FAB, Frontal Assessment Battery; MRI, Magnetic Resonance Imaging; FOG, Freezing of gait; MMSE, Mini Mental State Examination; DBS, Deep Brain Stimulation; HD, Huntington's Disease.

* Significant difference.

could induce a stronger engagement of commonly involved areas than observation or imagery alone (Filimon et al., 2007; Macuga and Frey, 2012; Villiger et al., 2013). This in turn could produce stronger behavioural and neurophysiological effects compared to AO or MI only (Eaves et al., 2014, 2016). For example, recent data on healthy subjects show that combining AO and MI facilitates corticospinal excitability with respect to either observation or imagery alone (Wright et al., 2014; Taube et al., 2015). In the same line, it has been shown that action observation can improve motor imagery (Conson et al., 2009). In agreement with this perspective, combined AO and MI procedures have been recently recommended for neurorehabilitation (Vogt et al., 2013; Eaves et al., 2014, 2016).

2. Materials and methods

2.1. Literature search

We used the Medline literature search engine to search for scientific articles that applied the AOT and MIP to PD patients. The PubMed database was searched through August 2016 using the keywords Parkinson's Disease and any of the following terms: motor imagery; mental practice; action observation or action observation therapy. The reference list of identified studies and review papers was also hand-searched to obtain additional articles. Studies were considered for inclusion if: 1) they were published in English in a peer-reviewed journal; 2) they included participants with a primary diagnosis of idiopathic Parkinson's Disease according to the United Kingdom Parkinson's Disease Society Brain Bank criteria (Hughes et al., 1992); 3) they investigated AOT or MIP; 4) they compared an experimental group with a control group. Studies that investigated AOT together with the application of other instruments were excluded (e.g.; Esculier et al., 2014; Ajimsha et al., 2014). This because including works where AOT and MIP are applied simultaneously with other techniques may be misleading for the reader whose aim is to understand the "pure" effect of AOT and MIP. We also did not include studies that report only preliminary results in an abstract (e.g., Agosta et al., 2014), works of review (e.g., Poliakoff, 2013; Abbruzzese et al., 2015), and works where patients are involved in AO and MI tasks without performing overt movements or where movement performance is not recorded (e.g., Marceglia et al., 2009; Alegre et al., 2010). We found 25 studies that fulfilled the inclusion criteria. Of these: two investigated the effect of AOT in a single session experiment (Table 1); 18 investigated the effect of MIP in a single session experiment (Table 2); one compared the effect of AOT and MIP (Table 3); two investigated the effect of AOT as long-term treatment (Table 4); two investigated MIP as long-term therapy (Table 5). No study investigated the joint action of AOT and MIP long-term therapy. The sociodemographic and clinical features of the participants of the selected studies are briefly summarized in Tables 1–5. The tables also indicate the type (or lack thereof) of analyses of the brain activity performed on the participants. Below, we group the works on the basis of the motor behaviour performed by the patients rather than on the basis of the type of technique used to record the brain activity. We believe that this kind of categorization better highlights the links between the effects of AOT and MIP on PD features.

2.2. Single session experiment

2.2.1. AOT effects on PD

The two selected studies include a total of 54 PD patients and a total of 30 healthy controls (HC). The PD and HC participants of the two studies differ in both sociodemographic and clinical characteristics (Table 1).

Table 3
Single session experiment on PD, MIP and AOT – Sociodemographic and clinical characteristics.

Author and year	Sociodemographic characteristics								Clinical characteristics of PD patients										Brain activity recording
	Sample size		Age (mean ± SD)		Males (n)		Education, years (mean ± SD)		Illness duration (years ± SD)		Diagnosis		Medication status		Inclusion criteria (test, scores)		Disease severity (test, mean scores ± SD)		
	EX	CON	EX	CON	EX	CON	EX	CON	EX	CON	EX	CON	EX	CON	EX	CON	EX	CON	
Tremblay et al., 2008	11	11	68.6 ± 5.8	66.2 ± 4.9	6	3	NA	NA	R: 5-12	–	IP	HC	ON	–	No contraindications for TMS; MMSE > 24	No contraindications for TMS; MMSE > 24	H&Y: R: 1.5-3	–	MEP

Table 4
Long-term therapeutic AOT programs in PD – Sociodemographic and clinical characteristics.

Author and year	Sociodemographic characteristics								Clinical characteristics of PD patients								Brain activity recording
	Sample size		Age (mean ± SD)		Males (no.)		Education, years (mean ± SD)		Illness duration (mean ± SD)		Diagnosis		Medication status		Inclusion criteria (test, scores)		Disease severity: (test, mean scores ± SD)		
	EX	CON	EX	CON	EX	CON	EX	CON	EX	CON	EX	CON	EX	CON	EX	CON	EX	CON	
Pelosin et al. (2010)	9	9	68.8 ± 4.1	70.2 ± 6.8	12 men assigned condition excluded	NA	NA	NA	11.6 ± 4.9	9.5 ± 3.7	IP	IP	ON	ON	Occurrence of freezing at least once a week; MMSE≥24		UPDRS: 17.5 ± 4.6 H&Y: 2.1 ± 0.3	UPDRS: 20.6 ± 5.7 H&Y: 2.2 ± 0.3	NA
Buccino et al. (2011)	7	8	68 R: 59–80	73.5 R: 67.5–76.5	5	5	NA	NA	7 (5–19)	9 (5.5–13.5)	IP	IP	ON	ON	Age R:18–75; Normal visual and acoustic acuity; MMSE≥24; No depression		H&Y:3 (R:2.5–4)*	H&Y: 1.7 (R:1.5–2.3)*	NA

EX, Experimental Group; CON, Control Group; SD, Standard Deviation; NA, Not Available; IP, Idiopathic PD according to the UK Parkinson's Disease Brain Bank clinical criteria; ON, On stable medication regimen; UPDRS, Unified Parkinson's Disease Rating scale; H&Y, Hoehn and Yahr scale; R, Range; MMSE, Mini Mental State Examination.

Table 5
Long-term therapeutic MIP programs in PD – Sociodemographic and clinical characteristics.

Author and year	Sociodemographic characteristics								Clinical characteristics of PD patients								Brain activity recording
	Sample size		Age (mean ± SD)		Males (no., %)		Education, years (mean ± SD)		Illness duration (years ± SD)		Diagnosis		Medication status		Inclusion criteria (test, scores)		Disease severity (test, mean scores ± SD)		
	EX	CON	EX	CON	EX	CON	EX	CON	EX	CON	EX	CON	EX	CON	EX	CON	EX	CON	
Tamir et al., 2007	12	11	67.4 ± 9.7	67.4 ± 9.1	8 (66%)	7 (64%)	13.7 ± 5.8	15.7 ± 4.8	7.4 ± 3.1	7.8 ± 4.5	IP	IP	ON	ON	H&Y: R: 1.5–3; MMSE≥26		H&Y: 2.29 ± 0.4	H&Y: 2.31 ± 0.4	NA
Braun et al., 2011	25	22	70	69	17 (68%)	15 (68%)	NA	NA	5.2	6.6	IP	IP	ON	ON	Sufficient cognitive level and communication skills; No other pathological-neurological disorders		n19: H&Y < 3 n6: H&Y > 3	n17: H&Y < 3 n5: H&Y > 3	NA

EX, Experimental Group; CON, Control Group; PD, Parkinson's Disease; SD, Standard Deviation; NA, Not Available; IP, Idiopathic PD according to the UK Parkinson's Disease Brain Bank clinical criteria; ON, On stable medication regimen; H&Y, Hoehn and Yahr scale; MMSE, Mini Mental State Examination.
*Significant difference.

2.2.2. Experimental design

Experimental designs were different in the two studies. Castiello et al. (2009) used a visuomotor priming paradigm in which PD and HC participants observed a model and performed the observed action. Pelosin et al. (2013) compared the performance of sequential finger movements between PD and HC participants and within the PD group (comparing PD patients in ON and OFF medication conditions). In the Main experiment PD and HC participants had to perform the action in two conditions: observe a video showing the movement; listen only to the sound of a metronome. PD patients were tested only in the ON medication condition. In the Control experiment (only for PD groups) participants had to perform the action after experiencing either one of two conditions: observe a video of a static picture; watch the video of the action. For this last condition patients were tested twice after an interval of three weeks to compare the ON and OFF medication states. Assessment for Castiello et al. (2009) consisted in kinematics recording while for Pelosin et al. (2013) consisted in the movements rate measured at different testing times (baseline, immediately after, 45 minutes later, 2 days later).

2.2.3. Main outcomes for AOT effects on PD

In both studies PD patients were slower in performing the motor tasks with respect to HC participants. The main finding of Castiello et al. (2009) was that whereas HC participants showed a facilitation effect both when the observed model was a healthy individual and when the model was a patient with PD, the PD patients showed the motor facilitation only when the model was a PD participant. The main finding of Pelosin et al. (2013) was that video observation induced a larger increase of spontaneous movement rate than acoustic training in both groups. Moreover, the PD groups exhibited a significant difference in motor performance between the ON and OFF medication states. PD in OFF state were slower in performing finger opposition movements at baseline and after 45 min.

Overall, these studies suggest that AOT can induce an improvement in performing spontaneous movements (Pelosin et al., 2013) especially when movements used for rehabilitation have a timing that PD patients can reproduce (Castiello et al., 2009).

2.3. MIP effects on PD

The 18 selected studies include a total of 262 PD patients and a total of 204 HC participants. Table 2 below summarizes the main differences in sociodemographic and clinical characteristics between PD and HC participants.

2.3.1. Experimental design

All the selected studies used experimental designs based on motor execution of movements and the MI of the same movements. They differed in the type of motor task used to test the participants. We have finger-to-thumb opposition movements task (Dominey et al., 1995; Cunnington et al., 2001; Avanzino et al., 2013); press a button of a keyboard with fingers (Cunnington et al., 1997; Lim et al., 2006); graphomotor task (Yaguez et al., 1999; Heremans et al., 2012); mental rotation task (Dominey et al., 1995; Frak et al., 2004; Helmich et al., 2007, 2012); sequential movements with a joystick (Thobois et al., 2000; Samuel et al., 2001); task involving contraction of finger muscle (Filippi et al., 2001); test battery for assessing imagery ability (Heremans et al., 2011); gait and walking tasks (Cohen et al., 2011; Pickett et al., 2012; Peterson et al., 2014; Maillett et al., 2015).

2.4. Main outcomes for MIP effects on PD

2.4.1. Finger-to-thumb opposition movements

Dominey et al. (1995) and Avanzino et al. (2013) found that PD patients were slower than HC participants in completion times of both physical execution and MI. Using Positron Emission Tomography (PET), Cunnington et al. (2001) found that in OFF condition PD patients imagining movement showed less activation in the anterior cingulate and dorsolateral prefrontal cortex compared to HC participants. In the ON condition they did not differ from HC participants.

2.4.2. Press buttons with fingers

Lim et al. (2006) investigated whether kinesthetic and/or visual imagery could alter the contingent negative variation (CNV) for PD patients. They found that the CNV did not change after the visual imagery for both PD patients and control subjects. By contrast, kinesthetic imagery resulted in significant group differences pre-, versus post-imagery global field power of CN. Cunnington et al. (1997) compared the motor-related potentials (MRPs) associated with imagined and actual movements to examine the components related to movement preparation and execution. They found that early-stage pre-movement activity was present in both PD patients and control subjects when they imagined movement, but was reduced in amplitude compared with that for actual movement.

2.4.3. Graphomotor task

Heremans et al. (2012) found that PD patients had significantly longer reaction times than HC participants in both execution and imagery tasks. Yaguez et al. (1999) also found that PD participants did not benefit from MI training.

2.4.4. Mental rotation

Dominey et al. (1995) found that PD patients were slower than HC participants in hand rotation. Conversely, Helmich et al. (2007) found no significant differences in response time between PD patients and control subjects. Frak et al. (2004) found that PD subjects were impaired in the mental representation of a grasp orientation but were still capable of normally executing this movement. Helmich et al. (2012) divided the experimental group in PD patients with tremor (tremor PD) and without tremor (non-tremor PD). They found that only the non-tremor PD group had a higher error rate for biomechanically difficult movements. Tremor PD patients had increased imagery related activity in the somatosensory cortex, primary motor cortex, cerebellum, and ventral intermediate nucleus (VIM) of the thalamus. Tremor PD patients showed an overlap between tremor and imagery related activations in the VIM.

2.4.5. Sequential movements with a joystick

Thobois et al. (2000) and Samuel et al. (2001) found that PD patients were slower than HC participants. Through a PET scanning, Thobois et al. (2000) also found that in HC participants the prefrontal cortex, SMA, superior parietal lobe, inferior frontal gyrus, and cerebellum were activated during MI with both hands. Through a PET scanning, Samuel et al. (2001) found that in PD patients there was underactivation of dorsolateral and mesial frontal regions and underactivation of right dorsolateral prefrontal cortex and basal ganglia respectively in imagery and execution condition.

2.4.6. Contraction of finger muscle

Filippi et al. (2001) recorded motor evoked potentials (MEPs) of the abductor digiti minimi muscle during three conditions: rest; motor and visual imagery of little finger abduction; execution of contraction of target muscle. In all conditions transcranial magnetic stimulation (TMS) was applied. They found that the PD group

threshold intensities in the hemisphere contralateral to the affected hand were lower compared to the other hemisphere during MI.

2.4.7. Test Battery

Heremans et al. (2011) measured the performance of the two groups of participants in a test battery for imagery ability, consisting of four parts: the MI Questionnaire–Revised version, the Kinesthetic and Visual Imagery Questionnaire, the Chaotic MI Assessment Battery, and an adapted version of the Box and Block Test. They found that PD patients did not differ from HC participants in MI Questionnaire–Revised version, Kinesthetic and Visual Imagery Questionnaire, Chaotic MI Assessment Battery. This suggests that imagery accuracy is well preserved in the two patient groups. The only significant differences was found in the Box and Block Test in the duration of both execution and imagery task indicating that PD were slower than HC in both conditions.

2.4.8. Gait and walking tasks

Cohen et al. (2011) found that freezing of gate (FOG)-PD patients were slower with a narrow doorway than HC participants or other PD patients. FOG-PD patients imagined that they could walk more quickly than they actually could. Pickett et al. (2012) found no significant differences between groups. Peterson et al. (2014) found that imagery times were positively correlated to actual gait times and there were no significant differences between PD and HC groups. MRI analysis showed that across gait tasks PD patients exhibited reduced beta weights in left globus pallidus (GP) compared to controls. In addition, PD patients exhibited larger beta weights in SMA during imagined turning compared to forward or backward. Maillet et al. (2015) found that Kinesthetic and Visual Imagery Questionnaire (KVIQ) improved after training both in HC and PD group. Walking and MI durations differed only between HC participants and PD patients in the OFF condition. Imagined gait elicited activations within motor and frontal associative areas, thalamus, basal ganglia, and cerebellum in HC. In the OFF condition PD mainly activated premotor-parietal and pontomesencephalic regions. Levodopa increased activation in motor regions, putamen, thalamus, and cerebellum, and reduced premotor-parietal and brainstem involvement.

Taken together these studies suggest that PD patients are slower in both physical execution and mental simulation of movements compared to healthy participants (Dominey et al., 1995; Cohen et al., 2011; Heremans et al., 2012; Avanzino et al., 2013). This slowness seems enhanced when PD patients are required to move or imagine to move their affected hand (Filippi et al., 2001). Aside from this, the results of some imaging investigations in PD patients support a partially altered activity of brain areas typically related to MI in healthy subjects (Thobois et al., 2000; Filippi et al., 2001; Samuel et al., 2001; Helmich et al., 2012; Peterson et al., 2014; Maillet et al., 2015). In addition, coordination processes for execution seems to be separated from those for motor imagery (Frak et al., 2004) and the effect of motor facilitation induced by MI typically found in healthy participants seems to be missing in PD patients (Cunnington et al., 1997; Lim et al., 2006). Nevertheless, some studies found no significant differences between PD patients and HC in completion time of a physical or imaginative task (Frak et al., 2004; Helmich et al., 2007; Heremans et al., 2011; Pickett et al., 2012; Peterson et al., 2014; Maillet et al., 2015). Finally, PD patients seem to not benefit from a mental training (Yaguez et al., 1999).

2.5. Combined AOT and MIP effects on PD

The work of Tremblay et al. (2008) is the only one that studied the effects on motor behaviour of a combined AOT and MIP in a single session experiment. The work included a total of 11 PD patients and 11 HC participants which differed in sociodemographic and clinical characteristics (Table 3).

2.5.1. Experimental design

The experimental paradigm compared the effect of motor facilitation in response to TMS of the left motor cortex between healthy participants and PD patients during the observation, imagination and imitation of a hand-movement. Participants watched four video consisting of a sequence of preset instructions for four different conditions: REST: instructed to relax with eyes closed for the duration of a tone signal; OBS: instructed to observe a model performing a scissoring action; IMAG: instructed to close their eyes and to mentally simulate the scissoring action; IMIT: instructed to imitate the scissoring action. The authors monitored the changes in the amplitude of MEPs of the first dorsal interosseous and abductor digiti minimi muscles delivering TMS at a pre-determined delay in the video sequence, which corresponded with the closing phase of the scissors action, where the first dorsal interosseous muscle is most active.

2.5.2. Main outcomes for combined AOT and MIP effects on PD

The authors found a significant facilitation in the observation and imagery conditions only in healthy participants, while they did not find this effect in PD patients. MEPs of the first dorsal interosseous muscle were facilitated under the OBS, IMAG, and IMIT conditions, significantly different from REST in both groups. In the PD group, only the IMIT condition was associated with significant amplitude facilitation. MEPs of the abductor digiti minimi muscle were facilitated under the IMAG and IMIT conditions in the healthy group, whereas only IMIT was significantly different from REST in the PD group.

This study shows that the simultaneous observation and execution of a movement can produce motor facilitation in PD. In addition, the effect of motor facilitation induced by MI typically found in healthy subjects seems to be missing in PD patients.

2.6. Long-term therapeutic program studies

2.6.1. AOT effects on PD

The two selected studies include a total of 33 PD patients divided in experimental and control groups. The sociodemographic and clinical characteristics of the two groups are shown in Table 4.

2.6.2. Experimental design

In both studies, the treatment had the same structure, in particular it was divided into video observation and execution sessions. However, the two studies differed in terms of video content. In Buccino et al. (2011) the experimental group observed videos showing everyday actions and then performed these actions whereas the control group observed videos of static images (e.g., landscapes) and then perform the same actions as the experimental group. In Pelosin et al. (2010) the experimental group observed videos showing actions concerning strategies to avoid episodes of freezing and then executed such actions; the control group observed videos of static images (e.g., landscapes) and then performed the same actions of the experimental group. The total duration of treatment was the same in both studies (four weeks). However, the weekly frequency of sessions was different. In Buccino et al. (2011) both groups underwent five sessions per week (but the duration of a single session is not available). In Pelosin et al. (2010) both groups underwent three sessions per week (60 minutes per session in which two videos of action/landscapes were observed).

2.6.3. Main outcomes for AOT effects on PD

In Buccino et al. (2011) two scales were used to assess the motor recovery after treatment: UPDRS (Unified Parkinson's Disease Rating scale) and FIM (Functional Independence Measure). In Pelosin et al. (2010) the scales used to measure outcomes were: FOG diary; FOG-Q (FOG Questionnaire); TUG (Time Up and Go test); 10M-WT (10-meter walking test); BBS (Berg Balance Scale); PDQ-39 (39-item PD questionnaire). Buccino et al. (2011) found a significant effect only in the experimental group in both scales used. Pelosin et al. (2010) found that FOG-Q scores and numbers of FOG episodes (assessed by FOG diary) were reduced in both groups at the end of treatment. Moreover, they found that the improvement in the FOG-Q was also present at a four week follow-up but only in the experimental group. Thus, despite the study of Buccino et al. (2011) is a pilot study and the small sample size of the two studies, both works show positive results after the AOT. However, the positive results of Pelosin et al. (2010) seem to be confined only to the symptom of freezing, even if the follow-up assessment shows that the improvement lasts over time. The results achieved by Buccino et al. (2011) show instead that a treatment based on daily actions can be an effective therapeutic tool as it allows the generalization of motor benefit, as evidenced by the significant results of both UPDRS and FIM.

2.7. MIP effects on PD

The two selected studies include a total of 70 PD patients divided in experimental and control groups. The participants of the two studies differ in both sociodemographic and clinical characteristics (Table 5).

2.7.1. Experimental design

In Tamir et al. (2007) patients underwent to rehabilitative intervention only individually, while in the work of Braun et al. (2011) patients were treated both individually and in group. The total duration of the treatment is different. In Tamir et al. (2007) patients of both the experimental and control group underwent rehabilitation sessions with a twice-a-week frequency. In Braun et al. (2011) the duration of the rehabilitation program was six weeks in total but with different week frequency for patients treated in group or individually. In Tamir et al. (2007) the duration of a rehabilitation session was one hour of which 15–20 minutes were devoted to mental practice. In Braun et al. (2011), for patients treated in group the duration of the session was an hour of which 20 minutes were dedicated to mental practices; in patients treated individually sessions took place twice a week with a duration of 90 minutes each, of which 10 minutes were dedicated to mental practice. Moreover, the contents of the treatments were different: in Tamir and colleagues treatment focused on everyday actions while in Braun and colleagues concerned only locomotor actions.

2.7.2. Main outcomes for MIP effects on PD

Braun et al. (2011) used as outcome measures three test: VAS (visual analogue scale); TUG; 10M-WT (10-meter walking test). Tamir et al. (2007) measured the recovery of patients after treatment with tests for motor ability, autonomy in daily living, and cognitive function: TUG; standing up and lying down; turning in place; tandem stance; functional reach, shoulder TUG; UPDRS; Schwab and England's Activities of Daily Living scales; Clock drawing; Stroop Test. Braun et al. (2011) did not find significant results after treatment. Tamir et al. (2007) found that only the experimental group improved in TUG, standing and lying down, turning in place, in mental subsets of the UPDRS, and in Schwab and England's Activities of Daily Living scales.

The differences in results of the two studies are probably due to differences in experimental conditions and experimental group composition. In particular, alongside the differences in sample size, in Braun et al. (2011) treatment was administered both individually and in group with a duration of sessions devoted to mental practice different for those who were treated individually and those who were treated as a group. Moreover, there was an important difference in the disease severity of patients included in the two studies (see Table 5).

Table 6 briefly summarizes the main results of the studies reviewed above in terms of the potential benefits for motor behaviour of PD patients.

3. Conclusions

A main question that emerges from this review concerns the different effectiveness of AOT and MIP and the possibility of integrating them into a single method to enhance motor behaviour in PD. The studies reviewed here on single session experiments suggest that AOT in PD patients can facilitate the performance of spontaneous movements (Pelosin et al., 2013; Castiello et al., 2009) and that the simultaneous observation and execution of a movement can produce motor facilitation in patients (Tremblay et al., 2008). By contrast, there is less agreement among studies investigating MIP effects on PD. Several studies suggest that PD patients are slower than healthy participants in both physical execution and mental simulation (Dominey et al., 1995; Cohen et al., 2011; Helmich et al., 2007; Avanzino et al., 2013; Thobois et al., 2000; Filippi et al., 2001). Moreover, PD patients did not show the motor facilitation typically induced by MI in healthy participants (Cunnington et al., 1997; Yaguez et al., 1999; Lim et al., 2006; Tremblay et al., 2008). Tremblay et al. (2008) also found a significant facilitation in the observation and imagery conditions in healthy participants, while they did not find this effect in PD patients. On the other hand, some studies found no significant differences in completion time of a physical or imaginative task when PD patients are in ON state of medication (Frak et al., 2004; Pickett et al., 2012; Peterson et al., 2014; Maillet et al., 2015). The lack of congruence in the results obtained with these works is probably due to the diversity of the experimental conditions and the experimental groups as well as to the difference in the disease severity of patients included in the studies.

The few works found in literature and reviewed here on long-term therapeutic programs suggest that a program based on AOT or MIP can improve motor abilities of PD patients (Tamir et al., 2007; Pelosin et al., 2010; Buccino et al., 2011). This is especially true when patients are in the early stages of the disease, when the two techniques are used along with physical therapy, and when tasks are focused on activities of daily life useful to re-activate motor representations which are part of the patients' motor repertoire. However, we did not find any study that investigated the joint potential of AOT and MIP in PD patients in long-term therapeutic programs. In this respect, the results obtained by the research on healthy participants may encourage the combined use of AOT and MIP for therapeutic aims in PD. For example, data on healthy subjects suggest that combining AO and MI may facilitate corticospinal excitability (Wright et al., 2014; Mouthon et al., 2015). In PD patients, the increase of the corticospinal excitability due to a combined use of AO and MI may contribute to deal with the premovement facilitation abnormalities (Hiraoka et al., 2010). Whereas some works suggest that the two types of mental processes are effectively different at the brain level and thus have specific and separated functions as well as different effects in terms of learning (Gatti et al., 2013; Gonzalez-Rosa et al., 2014), other studies found that: (a) the effects of AO and MI may influence each other in a very specific ways (Conson et al., 2009): for example, MI can modulate the effects of AO on motor learning (Lawrence

Table 6
Main outcomes of the studies investigating the effects of AOT and MIP in PD in terms of benefits in motor behaviour of patients.

	Type of intervention	Number of studies	Effects on motor behaviour
Single session experiments	AOT	2	Improvement in performing movements (Castiello et al., 2009; Pelosin et al., 2013)
	MIP	18	Slower performance in both physical execution and mental simulation of movements (Dominey et al., 1995; Thobois et al., 2000; Filippi et al., 2001; Helmich et al., 2007; Cohen et al., 2011; Avanzino et al., 2013) Missing effects of motor facilitation (Cunnington et al., 1997; Yaguez et al., 1999; Lim et al., 2006) No significant differences in completion time of a physical or imagerye task when PD patients are in ON state of medication (Frak et al., 2004; Pickett et al., 2012; Peterson et al., 2014; Maillet et al., 2015)
	AOT + MIP	1	No significant facilitation in the observation and imagery conditions (Tremblay et al., 2008)
Long term therapeutic programs studies	AOT	2	Benefit to the motor recovery of patients (Pelosin et al., 2010; Buccino et al., 2011)
	MIP	2	No significant improvement after the treatment (Braun et al., 2011) Significant improvement after the treatment (Tamir et al., 2007)
	AOT + MIP	–	–

et al., 2013); (b) the simultaneous action of AO and MI gives the same benefits of physical training in healthy participants (Taube et al., 2014) and can enhance automatic (Eaves et al., 2014, 2016) and voluntary (Bek et al., 2016) imitation: facilitating imitation has implications for the use of imitation-based training and therapies in conditions where the ability to imitate may be compromised, such as in PD (e.g., Leiguarda et al., 1997; Bonivento et al., 2013); (c) there is a greater activation in the AO-MI overlapping cortical-subcortical network with respect to the activation measured when AO and MI act separately (Lui et al., 2008; Munzert et al., 2008; Macuga and Frey, 2012; Villiger et al., 2013; Taube et al., 2015). Concerning brain activity during AO and MI in PD, we only found evidence in the case of MI in single session experiments. This evidence shows that MI in PD involves similar brain areas with respect to healthy subjects, with some exceptions related to the kind of motor task and to the medication condition.

Taken together these findings suggest that AOT and MIP used as therapeutic programs can improve or slow the deterioration of motor capabilities in PD patients. Overall, this might be possible because they evoke a greater neural activation of the cortical-subcortical network that supervises motor control. The consequent strengthening of this network, largely not impaired in the early stages of the disease (e.g., Peterson et al., 2012; Poliakoff, 2013), might so partially compensate the damages of motor execution areas. For example, acting on the circuits that mediate the reactivation of the motor representations of the movements may be especially useful for ameliorating the impairments observed in PD patients, both in accuracy and in speed, concerning the sequencing of the multiple motor acts making up a whole action (Harrington and Haaland, 1991). Among the main advantages of AOT and MIP, we should remember that they are non-invasive, do not raise safety risks, do not require sophisticated equipment, can be administered in the patient's house, and do not require highly qualified staff for their implementation.

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