Title: Combined action observation and motor imagery influences hand
movement amplitude in Parkinson's disease

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Abstract: Abstract

Background: Action observation (AO) activates the motor system,
influencing movement and increasing learning, and has been shown to
improve speed and timing of movement in people with Parkinson's disease
(PD). Importantly, however, effects on movement amplitude have not been
quantitatively demonstrated. Additionally, motor imagery (MI) can
increase behavioural and neural effects of AO, but the combined effects
of AO+MI have never previously been explored in PD.

The aim of this study was to investigate imitation of hand movement
amplitude in people with PD following (i) AO and (ii) combined AO+MI.

Methods: Twenty-four participants with mild to moderate PD and 24 healthy
older adults observed and imitated videos showing a human hand moving
between horizontal positions. Kinematics were recorded and modulation of
vertical amplitude when replicating elevated vs. direct movements
provided an index of imitation. After an initial set of AO trials,
participants were instructed to engage in MI during observation for the
remaining trials (AO+MI), emphasizing kinaesthetic (sensory) imagery.

Results: Movement amplitude was imitated (modulated) for elevated vs.
direct stimuli by both groups, and this imitation increased following MI
instructions.

Conclusions: These results demonstrate quantitatively for the first time
that people with PD are able to modulate the amplitude of their hand
movements following action observation, and that combining AO and MI
increases imitation in PD. The effects parallel findings in healthy young
participants, and indicate that combined action observation and motor
imagery could be a promising therapeutic approach for PD.

Author Declaration

Parkinsonism & Related Disorders is committed to proper scientific conduct and the protection of animal and human research subjects. Submission of this manuscript implies compliance with the following ethical requirements. Please affirm that you are representing all of the authors in stating compliance with these policies by checking the box at the end of this section.

1. Studies with human subjects must have been conducted in accordance with the Declaration of Helsinki. All persons must have provided informed consent prior to being included in the study.

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3. Protocols with animal or human subjects must have been approved by the relevant local committee(s) charged with ensuring subject protection. Studies that entail pain or distress will be assessed in terms of the balance between the distress inflicted and the likelihood of benefit.

4. The authors declare that the manuscript is original, that it is not being considered for publication elsewhere, and that it will not be submitted elsewhere while still under consideration for Parkinsonism & Related Disorders or after it has been accepted by Parkinsonism & Related Disorders.

5. All authors have seen and approved the manuscript in the form submitted to the journal. The authors declare that they have conformed to the highest standards of ethical conduct in the submission of accurate data and that they acknowledge the work of others when applicable.

6. All sources of financial support for the work have been declared in the Acknowledgements section of the manuscript. Any additional conflicts of interest must also be declared. Please include declarations of any consultancy or research funding received from relevant companies from three years prior to performance of the research until the time of manuscript submission. If the research is supported by internal funds, that should be stated as well.

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14 July 2018

Professors V Bonifati and H Fernandez
Editors-in-Chief
Parkinsonism and Related Disorders

Dear Professors Bonifati and Fernandez

My co-authors and I would like to thank you for the opportunity to resubmit our manuscript, "Combined action observation and motor imagery influences hand movement amplitude in Parkinson's disease", to Parkinsonism and Related Disorders.

We have carefully considered the reviewers' queries and suggestions and responded to the points raised in the accompanying document. We have made a number of changes to the manuscript in response to the reviews, and we have also made some further minor edits to improve clarity and readability. We believe these revisions have significantly strengthened the paper and hope that you will now consider our manuscript to be acceptable for publication.

Yours sincerely,

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Combined action observation and motor imagery influences hand movement amplitude in Parkinson's disease

Response to reviewers' comments

<u>**Reviewer 1:**</u>

This is an interesting and important study topic with implications in rehabilitation and motor learning in PD. Action observation and motor imagery techniques are in use in a variety of rehabilitation populations, including patients with stroke and chronic pain. The introduction is well written. The study of AO and MI on movement amplitude due to dysfunctional basal ganglia effect on movement amplitude and underscaling of effort in PD has potentially important clinical implications. From a motor control perspective, the experimental paradigm and theoretical foundation is strong. I have a few concerns and suggestions.

Concern: However, since patients were presumably "on" medication during testing, the results say little about the effect of AO or MI on PD, in this reviewers opinion. A strong case for the effect of AO and/or MI on scaling movements in PD is made when patients are tested on and off medication and statistical comparisons are made between the two groups ("on" versus "off" medication).

-We have now noted in the Methods section that participants were tested in the 'on' phase where applicable (p3).

We appreciate that the effects reported in this paper do not provide information on how AO and MI would affect patients off medication; however, we do not consider this to invalidate the results in any way, since the research was conducted as a precursor to developing therapeutic strategies based on action representation. Like physiotherapy or other rehabilitative programmes, this approach is intended to supplement rather than replace pharmacological treatment. We have now addressed this point in the Discussion (p11).

Previous studies have included patients either on or off their usual medication, with effects of AO found in both cases (e.g., see review by Poliakoff (2013). Additionally, vividness of motor imagery has been found not to differ between the 'on' and 'off' states (Peterson et al., 2012). Fewer studies have compared AO in patients during on vs. off states, but Pelosin et al. (2013) found evidence of more sustained effects in those on medication, indicating that AO training is best utilised in conjunction with patients' usual pharmacological treatment.

A concern is the number of ANOVA procedures conducted, the lack of transparency for how much missing data there was and how outliers were defined a -priori, and the emphasis within the results section on statistically non-significant trends for main effects, correlations (e.g., KVIQ, line 39, Section 3.1), and interactions (e.g., Results, L32-L37, L3-L11). Trends ought to be removed from the paper and the results and discussion ought to be rewritten in light of the non-statistically significant main effects, and interactions.

-We conducted two ANOVAs in order to more clearly address the two aims of the study. If reporting only an overall Group x Time x Trajectory ANOVA, paired t-tests following up the Time x Trajectory interaction demonstrate that modulation of movement amplitude is significant both before and after MI instructions, consistent with the results from the separate ANOVAs currently reported. However, we believe it is important to report the Group x Elevation ANOVA for the AO-only trials because this directly addresses the first aim of our study and highlights the finding that AO alone can influence movement amplitude.

-Data on missing trials are now included in the manuscript (p6); this detail was omitted initially to comply with article length restrictions. Outliers were defined in accordance with a widely-used procedure described by van Selst and Jolicoeur (1994) in the reference cited in this section. Outliers were calculated first within- participants and then between-participants; we have clarified this in the manuscript (p6).

-As suggested by the reviewer, we have now removed the non-significant trends suggesting effects of Group on movement amplitude and the interaction trend showing greater modulation of amplitude in controls (p7-8); these are now reported in Table 2 instead. We have also removed the trend indicating increased vividness of visual imagery in the PD group (p8).

-The discussion has also been updated accordingly (p11).

It is recommended to list the study aims in a single paragraph toward the end of the introduction, to re-articulate the rationale for the study design, and a central hypothesis.

-We thank the reviewer for this suggestion and have restructured this section of the introduction, which we feel now reads more clearly (p2).

Overall, the paper is well written

All citations are necessary and up-to-date

The figures and tables are interesting.

Minor suggestions:

1. In the methodology section, please identify the screening test used to screen for dementia and whether any patients had mild cognitive impairment.

-Dementia was screened using the Addenbrookes Cognitive Examination (ACE-III) or, in cases where participants had recently been assessed for a previous study within our lab, we used the Mini Addenbrookes Cognitive Examination (M-ACE). We have now provided this information in the manuscript (p3). Three participants in the PD group had borderline scores on the M-ACE. However, we repeated the main Group x Trajectory x Time ANOVA with these participants excluded and the results did not change; we therefore decided to retain their data in the reported analysis.

Please provide the test-retest correlation coefficient for the MI assessment measure.

-The KVIQ was only administered once, as a general indicator of MI ability, but good test-retest reliability (ICC = 0.87) has previously been reported (Randhawa et al., 2010). The MI measure used to assess imagery use and intensity during the task was devised specifically for this experiment.

How is it operationalized that patients and controls are engaged in MI during MI trials? What safeguards were taken to ensure that patients and controls attended to the task, e.g., that they were observing the action when asked to do so by the research assistant.

-Our task-specific MI questionnaire indicated greater engagement in MI in the AOMI block than the AO block in both groups (p8).

-There was a very low rate of sequencing errors when imitating the observed actions (0.7% of all trials in the PD group and none in the control group), indicating that participants attended closely to the videos. This detail is now included in the manuscript (p6).

Please also detail any co-morbidities, and non-PD medications the participants were taking at the time of testing that may have had an effect on attention, executive function, balance or visual function. Please detail the visual acuity of participants and whether they were right or left handed.

-Our inclusion criteria ruled out participants with additional neurological or psychiatric conditions. We only obtain information on medications taken to treat PD symptoms so unfortunately we are not able to provide details of non-PD medications.

-Information on visual acuity and handedness has now been added to the Methods section (p3).

2. Please identify whether the sample was a sample of convenience or a consecutive sample.

-Participants were recruited through local neurology clinics and via Parkinson's UK. We have now clarified that this was a sample of convenience (p3).

3. Please explain whether the testing took place in the "on" or "off" state?

-Participants were tested in the 'on' state where applicable (although not all participants identified as having on/off periods) - this has been added to the manuscript (p3).

4. Section 2.4: Please provide an a-priori sample-size and power analysis, the alpha used to indicate statistical significance, and the manufacturer of statistical software used by the authors.

- We did not have an estimated effect size in order to carry out an a priori power analysis. The sample size was, however, similar to or larger than that of previous studies in our lab (e.g., Bek et al., 2017) and others (e.g., Robles-Garcia et al., 2013).

-The accepted significance level was $p < .05$, which we have now added to the manuscript (p6).

-The software manufacturer information has also been added (p6).

5. Section 2.4: Please provide the amount of missing data excluded from analysis in each group (mean number of trials excluded) and how "data outliers" were operationalized.

-This information was initially omitted due to article length restrictions. We have now added further details on excluded data and outliers (p6). For the method of identifying outliers we have referred the reader to van Selst and Jolicoeur (1994).

6. The results section could benefit from headings, for example, a heading for AO and a separate heading for AO + MI. Please use these same headings in the discussion section.

-We agree that this improves readability and have now added appropriate headings throughout the Results and Discussion sections.

Results of the ANOVA procedure ought to include the number of observations used to generate the statistically significant main effects and the statistically significant interaction effects.

-We have included the degrees of freedom in all reported results (which are now presented in Table 2).

In this reviewer's opinion, results of the statistical analysis that were non-significant should not be listed in the body of the manuscript, but can, along with the F value, DF, and p values, be included in a table.

-We now present all results of the ANOVAs in a table (Table 2), and have removed the non-significant results from the manuscript. We thank the reviewer for this suggestion, which we agree improves readability of the paper.

Discussion
Line 39-44. Which result of the statistical analysis supports the statement that (at P< or equal to 0.05), (a) participants with PD can modulate the amplitude of their movement during imitation of observed hand actions, and (b) that combining AO with MI increases this effect in PD?

-Please see the following (p7-8):

(a) "…a significant effect of Trajectory ($F(1,44) = 49.16$; $p < .001$; $\eta2p = .53$), with greater amplitude for elevated trials (M = 72.82 mm) than direct trials (M = 39.96 mm), demonstrating modulation in response to the observed movements."

(b) "The difference in amplitude between elevated and direct trials was significantly larger following instructions (mean difference = 13.81 mm; $t(45) = 3.47$; $p = .001$; $d = .52$), confirming an increase in modulation."

Please kindly consider a section on study limitations. Some of the possible candidate limitations include the use of unblinded assessors, testing during "on", and use of care-partners/family members as control subjects.

-Due to article length restrictions we were unable to dedicate a section to limitations of the research. In response to the reviewer's specific suggestions: (i) since no intervention was tested in the current study, blinded assessment is not considered applicable; (ii) we have added a comment on the medication effect (p11); (iii) we consider the use of partners/family members a strength, rather than a weakness, since these individuals are likely to be more similar in factors such as education, lifestyle, etc.

<u>Reviewer 2:</u>

Overall, I found this to be a well-written manuscript and a well designed study, evaluating the utility of using action observation, combined with mental imagery, to influence the amplitude of movements of individuals impacted by PD. There are a few areas where I believe additional reporting of statistics and placing the experiment into a broader context might be helpful as outlined below.

Introduction:

The introduction is well thought out and generally understandable. However, given the readership of PDRD, which I suspect encompasses a mixture of clinical and more basic neuroscientists, it may be helpful to frame a few sections more specifically to clinical symptoms and their treatments. For example, a more logical flow to the introduction may be something along the lines of 1) difficulties with timing and amplitude of movements in PD is quite common and clinically significant 2) there's evidence that cues, like colors lasers or metronomes and the like can improve timing of movements with tasks like walking, but upper extremity movements are not as well studied 3) MI may further

facilitate the effects of external cues and imitation, but again this hasn't been studied, 4) specific aims of this paper.

I find the information on the proposed mechanism of these interventions (i.e. facilitating fronto-parietal activation) quite interesting, but as it is it seems to distract from some of the salient points of the intro and is not directly addressed in the current study. This could be combined together into a separate paragraph or omitted.

-We thank the reviewer for the helpful suggestions – we have restructured the introduction and aims, which we feel now read more clearly (p1-2). We still mention the proposed mechanism, but more briefly.

Methods:

Individuals were screened for dementia. Were they excluded if they were demented? What about if they had MCI? Given the cognitive processing of the task, knowledge of overall global cognitive characteristics (and whether it related to things like KVIQ or movement characteristics) might be helpful.

-We screened for cognitive impairment using the Addenbrookes Cognitive Examination (ACE-III), or if participants had recently been assessed for a previous study within our lab, we used the Mini Addenbrookes Cognitive Examination (M-ACE). This information has now been added to the manuscript (p3). Three participants in the PD group had borderline scores on the M-ACE, but the main Group x Trajectory x Time ANOVA results were not altered when these participants were excluded, so we decided to retain their data in the manuscript.

-We have previously found no consistent relationships between measures of cognitive performance (assessed using a range of neuropsychological tests) and action imitation in experiments similar to the present study. For this reason, we decided not to measure cognitive performance in this study.

How many outliers or missing data were excluded? Why were the two control participants excluded?

-We have re-written the Data Analysis section to clarify how missing data and outliers were defined and excluded (p6; please also see response to Reviewer 1 above). The two control participants were excluded because the amplitude of their movements fell outside of the acceptable range in terms of standard deviations of the group mean, in accordance with previous recommendations (van Selst & Jolicoeur, 1994).

Results:

Well written, and of course appreciate the inclusion of effect sizes in the results. I would consider adding in correlations on the KVIQ and movement tasks with ACE scores.

-As mentioned above, we have previously found no relationships between imitation and cognitive test performance. Based on the reviewer's suggestion, we ran correlations of the ACE/M-ACE % scores as well as a sub-test that is included in both versions (category fluency) with imitation and the KVIQ visual and kinaesthetic subscales. None of these correlations approached significance in either group (all rs < .35; p > .1). Since we did not have an a priori rationale for these analyses, we do not think it necessary to report these null findings, but could add them if required.

Discussion:
Well written and tempered.

<u>Reviewer #3:</u>

This is an interesting an well written paper describing imitation of movements in people with Parkinson's (as compared to controls) using action observation (AO) as compared to AO plus motor imagery (MI). The work could be improved by providing additional information about the nature of excluded data (e.g. the authors mention that two controls were removed from analysis but do not indicate why this was done).

-As noted above, we have now clarified how missing data and outliers were defined and excluded (p6). The two control participants were excluded because the amplitude of their movements fell outside of the acceptable range in terms of standard deviations of the group mean (van Selst & Jolicoeur, 1994).

I also think a bit more attention could be paid to the lack of randomization of the conditions such that AO was always first and AO+MI was always second.

-We appreciate the reviewer's concern about the lack of randomisation of conditions. We had considered counterbalancing the order of conditions but decided against this, since we expected that participants undertaking the AO+MI condition first might continue to apply MI during the AO-only condition, particularly as PD is associated with difficulties in cognitive set-shifting (e.g., Cools et al., 2001). We have now commented on this point in the Discussion (p10).

<u>References</u>

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Combined action observation and motor imagery influences hand movement

amplitude in Parkinson's disease

Highlights

- Action observation influences hand movement amplitude in Parkinson's disease

- Motor imagery increases the effects of action observation in people with Parkinson's disease

- People with Parkinson's disease may benefit from interventions that combine action observation with motor imagery

1. Introduction

External sensory cues can help to overcome difficulties with movement initiation and control in Parkinson's disease (PD)[1], typically targeting gait impairments (e.g., reduced stride length, 'freezing'). However, the applicability of such cues to other functional tasks (e.g., manual actions) is limited, and the longer-term effects of cueing are unclear[2]. Observation of human movement provides another external stimulus that facilitates movement and increases motor learning in healthy individuals[3], by activating a network of fronto-parietal neural structures also engaged during motor execution[4]. Action observation (AO) training has shown encouraging effects in neurorehabilitation[5] and may help to reinforce or reorganise neural connections involved in motor control[6].

AO can facilitate manual actions (reducing bradykinesia and temporal variability) in people with PD[7], and AO-based interventions have been found to increase functional independence, improve balance and mobility, and reduce freezing of gait, in PD[5,8]. However, such therapies rely on the ability to internally represent actions, which may be affected by PD[7]. Indeed, impaired imitation of gestures and facial expressions has been documented in PD[9,10], as well as an altered corticomotor response to observed actions[11]. Therefore, it is important to further investigate these processes in people with PD. In particular, quantitative effects on movement amplitude have not been demonstrated, despite the significant impact of reduced movement size (e.g., micrographia, shorter steps) on daily functioning.

Similar to AO, motor imagery (MI; the imagination of movement including associated images and sensations) also recruits neural regions overlapping with action execution[12], and facilitates movement and learning[13]. Recent studies of healthy participants have demonstrated greater effects on movement (e.g., sequential and rhythmic actions) when AO is combined with MI, compared with either AO or MI alone; moreover, combined AO+MI increases cortico-motor activity relative to either approach in isolation[14]. There is also some evidence of beneficial effects of combined AO+MI in stroke rehabilitation[15]; however, this has not previously been examined in PD[7]. People with PD are capable of engaging in MI[16], and MI can improve their performance of functional movements[17] and reduce freezing of gait[18]. Nevertheless, differences in neurophysiological responses during MI between people with PD and healthy controls suggest the use of compensatory (e.g., visual) mechanisms[19].

This study investigated the effects of (i) AO and (ii) combined AO+MI on hand movement amplitude in people with PD. Our first aim was to examine the effect of 'pure' AO, by comparing imitation of simple hand movements involving elevated (high) vs. direct (low) trajectories (based on Wild et al.[20]). Our second aim was to determine whether combining AO with MI increased the effects of the observed actions. Combined AO+MI was examined using the same imitation task, but explicitly instructing participants to use MI during action observation. Participants were encouraged to focus on the sensations associated with executing the action, since kinaesthetic MI produces greater sensorimotor activations than visual MI[21].

Based on previous evidence of AO and imitation in PD, we hypothesised that participants would imitate the amplitude of observed actions by modulating the height of their own movements. Moreover, if people with PD are able to engage in MI during AO, combined

AO+MI should increase imitation of movement amplitude, as found in healthy young adults[22]. Conversely, if MI is compromised, people with PD may fail to exhibit an effect of MI on imitation. We therefore also examined the relationship between imitation and self-reported MI.

2. Method

2.1. Participants

Participant characteristics are shown in Table 1. A convenience sample of 24 participants (9 females) with mild to moderate idiopathic PD (Hoehn & Yahr stage 1-3) were recruited through local neurology clinics and Parkinson's UK. All but one were taking dopaminergic medication. Participants remained on their usual medication during the study and were tested in the 'on' state where applicable. 24 control participants (13 females) with no history of neurological injury or illness were recruited from among relatives/friends of participants with PD and the local community. All participants except two in the PD group were right-handed. Participants had normal or corrected-to-normal vision and were screened for dementia using the Addenbrookes Cognitive Examination; ACE-III[23] or a brief version if they had been assessed recently for a previous study (M-ACE)[24]. Although three participants in the PD group scored within the borderline range on the M-ACE, the main results were not altered by removal of these participants, so their data were retained in the final analysis. The study was approved by a UK National Health Service Research Ethics Committee and participants provided written informed consent.

2.2.Stimuli and procedure

Imitation was examined using a video-based task[20]. Participants observed, and immediately replicated, movement sequences performed by a human hand with the index finger extended, shown as a mirror-image (right-handed participants viewed a left hand). Sequences consisted of two movements between three of four positions spaced 150 mm apart horizontally (Figure 1). In elevated trials, the hand moved between positions via an indirect trajectory, with a vertical amplitude of 130.9 mm. Direct trials showed a lower movement trajectory with an amplitude of 21.5 mm. In half of the trials, the four possible target positions were marked by small grey circles (see supplementary materials). The model's movements were paced using a metronome during recording of the stimulus videos (not audible during the imitation task).

Stimuli were projected at life-size onto a 1000 mm x 750 mm screen, positioned 1200 mm from the participant, who was seated at a table with their hand concealed from view by an occluding box (650 mm x 450 mm x 200 mm). A motion sensor was attached to the intermediate phalanx of the index finger of the dominant hand, and movements were tracked in X, Y and Z axes at 120 Hz, using a Polhemus Liberty motion tracking system with Motion Monitor software (Innovative Sports Training).

The trial sequence is illustrated in Figure 1. Following a fixation cross (4000 ms), a still image indicated the starting position for the sequence (4000 ms). The participant placed their index finger in the start position and the stimulus video was then displayed (4000 ms). The action execution phase was indicated by a go-signal (green cross and "beep"; 1000 ms), presented at a variable post-stimulus delay (1000 - 2000 ms). Finally, a blank screen was displayed (4000 ms) while the action was performed.

[Figure 1 here]

The task began with a short practice block (4 trials), followed by four blocks of 30 trials. For the first two blocks (AO), participants were given the following instruction: *"Copy what you have seen as closely as you can in terms of the timing and size of the movement"*.

For the final two blocks (AO+MI), the following additional instruction was given: *"Imagine what it feels like to make the movements yourself. As you watch the hand move from one place to another, imagine what your arm, hand and finger would feel like to make the movements"*.

Each block consisted of 20 test trials (10 elevated, 10 direct) containing a movement between the second and fourth positions, with 10 filler trials containing different sequences to reduce predictability. Trials were randomized within blocks. A pause halfway through each block allowed participants to take a short break.

2.3. Motor imagery

MI was assessed using a short form of the Kinaesthetic and Visual Imagery Questionnaire (KVIQ), which has been validated in people with PD[25]. Participants are asked to first perform, and then imagine performing, each of a set of simple movements, rating the clarity of images (visual subscale) and intensity of sensations (kinaesthetic subscale) using 5-point scales.

Task-specific MI was measured by asking participants to report their use and vividness of MI while watching the videos. Ratings were completed following the second block (prior to MI

instructions), and again after the final block (post MI instructions), using a 5-point scale similar to the KVIQ (see Table 2).

2.4. Data processing and statistical analysis

Kinematic data from correctly-executed movements were analysed using Matlab (Mathworks Inc.). Errors or missing data were excluded (0.7 % of trials in the PD group; none in the control group) and outliers for each trajectory condition (elevated/direct) at each time point (pre/post MI instructions) were then removed according to the procedure outlined by van Selst and Jolicoeur [26]. This resulted in the exclusion of 1.93 % individual trials in the PD group (M = 1.54 trials; range = 0-5) and 1.61 % trials in the control group (M = 1.29 trials; range = 0-3). Mean vertical amplitude was then calculated for each participant, for each trajectory and time-point. Outliers were then identified at the between-participant level using the same procedure, resulting in exclusion of data for two participants in the control group only.

To determine the effect of 'pure' AO, imitation of vertical amplitude prior to MI instructions was analysed using a Group x Trajectory ANOVA. The effect of MI instructions (AO+MI) was then analysed with a Group x Trajectory x Time ANOVA. To examine any differences in imitation of movements toward visible targets, the above analyses were repeated with Target included as an additional factor, but no main effects of Target or interactions with Trajectory or Time were found (see supplementary material).

Between-group differences in general MI (KVIQ visual and kinaesthetic subscales) and on the task-specific MI questions were analysed using Mann-Whitney U tests. Task-specific MI ratings for AO and AO+MI blocks were then compared within-group using Willcoxon signed rank tests. Finally, correlations between imitation of amplitude (elevated – direct trials) and MI measures, UPDRS motor examination, time since diagnosis and levodopa equivalent

daily dose (LEDD) were analysed using Spearman's correlation coefficient. <mark>Statistical analysis was conducted using IBM SPSS v.22, with an accepted significance level of p <.05.</mark>

3. Results

The two groups did not differ significantly in sex, but participants in the control group were significantly older (see Table 1). However, age did not correlate significantly with modulation of amplitude before or after MI instructions (all r <.4; p > .09).

[Table 1 here]

[Table 2 here]

3.1. Effects of action observation

Prior to MI instructions, there was a significant effect of Trajectory (F(1,44) = 49.16; p < .001; $\eta^2 p$ = .53), with greater amplitude for elevated trials (M = 72.82 mm) than direct trials (M = 39.96 mm), demonstrating modulation in response to the observed movements (Figure 2). <mark>The effect of Group and the interaction between Group and Trajectory were not significant (see Table 2).</mark>

3.2. Effects of AO+MI

Following MI instructions (AO+MI), a significant effect of Trajectory remained (F(1,44) = 77.90; p < .001; $\eta^2 p$ = .64), again reflecting greater amplitude for elevated (M = 79.69 mm) than direct (M = 39.80 mm) trials. There was a significant effect of Time (F(1,44) = 17.73; p

$< .001; \eta^2 p= .64$), and a Trajectory x Time interaction ($F(1,44) = 12.74; p = .001; \eta^2 p =.22$), demonstrating that amplitude increased post-instructions in elevated trials (mean difference = 13.73 mm; $t(46) = 4.44; p < .001; d = .65$) but not direct trials (mean difference = -.32 mm; $t(46) = .19; p = .85; d = .027$). The difference in amplitude between elevated and direct trials was significantly larger following instructions (mean difference = 13.81 mm; $t(45) = 3.47; p = .001; d = .52$), confirming an increase in modulation (see Figure 2). Effects of Group, Group x Trajectory, Group x Time, and Group x Trajectory x Time were non-significant (Table 2). Paired t-tests confirmed that modulation increased post-instructions in both the PD group ($t(23) = 2.39; p = .026; d = .49$) and the control group ($t(21) = 2.71; p = .013; d = .58$).

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3.3. Relationship with motor imagery

As shown in Table 1, the two groups did not differ significantly on the visual or kinaesthetic subscales of the KVIQ. Task-specific ratings of visual and kinaesthetic imagery did not differ between groups either before or after MI instructions (see Table 3). Both groups reported a significant increase in the use of kinaesthetic imagery (PD, $Z = 2.73, p = .006$; control, $Z = 3.47, p = .001$) and visual imagery (PD, $Z = 2.45, p = .014$; control, $Z = 3.15, p = .002$) following MI instructions. The control group also reported increased vividness of sensations ($Z = 2.14; p = .032$) and images ($Z = 2.35; p = .019$) after instructions, while the PD group showed no significant change in reported sensations or vividness of images.

[Table 3 here]

Scores on the KVIQ subscales did not correlate significantly with imitation of amplitude in either group, before or after MI instructions (all $r_s < .3$; $p > .1$). In the PD group, task-specific ratings of visual MI prior to instructions correlated positively with modulation of amplitude both before (r_s (22) = .45; p = .028) and after (r_s (22) = .51; p = .01) instructions. In contrast, modulation of amplitude correlated positively with kinaesthetic imagery ratings after MI instructions in the control group (r_s (21) = .46; p = .026). There were no other significant correlations between task-specific MI ratings and amplitude modulation. There were no significant correlations between modulation and UPDRS motor score, time since diagnosis, or LEDD (all $r_s < .3$; $p > .1$).

4. Discussion

The present study demonstrated for the first time that people with PD can modulate the amplitude of their movements during imitation of observed hand actions, and that combining action observation with motor imagery increases this effect.

4.1. Effects of action observation

Reduced movement amplitude can be a debilitating consequence of PD, affecting everyday activities such as walking and handwriting. While previous studies have found that AO can influence temporal characteristics of movement in PD[7], our results provide the first quantitative evidence that people with PD can successfully adjust the amplitude of their hand movements in response to observed actions, indicating the potential for AO-based interventions to increase amplitude as well as speed.

4.2. Combined action observation and motor imagery

Combining observation and imagery has been found to increase behavioural and neural effects in healthy individuals relative to AO or MI alone[14]. However, despite evidence of motor facilitation in PD when these approaches are used separately, AO and MI have not previously been combined in studies of PD. It has been proposed that combined AO+MI may improve movement in PD by increasing corticospinal excitability, thereby enhancing premovement facilitation[8]. Here, we demonstrate that both people with PD and healthy older adults show increased imitation of hand movements when instructed to engage in MI during AO, consistent with our findings in young healthy adults[22].

The present results are complemented by our recent finding that people with PD exhibit motor resonance, whereby even without the intention to imitate, hand movements were influenced by compatibility with observed actions[27]. Action observation may therefore provide an effective external trigger for action simulation. AO may also facilitate MI by reducing the need to generate visual images, thereby allowing an increased focus on kinaesthetic elements of imagery[14]. This facilitatory effect may be somewhat independent of MI ability, as suggested by the absence of a relationship between imitation and a general MI measure (KVIQ) in the present study.

To avoid carry-over effects, whereby participants may apply MI during an ostensible AO-only condition, the task conditions were presented in a fixed order. It is thus possible that the increase in imitation with AO+MI is partly attributable to simple practice effects; however, additional analysis showed that this increase was greater following MI instructions than between pre-instruction blocks (see supplementary materials). Additionally, we have previously found that imitation of elevated movements increased in young healthy participants instructed to engage in MI, compared with a control group[22]. Moreover, any

practice effects might be expected to be counteracted by fatigue, particularly in the PD group, since the imitation task required repeated movements over multiple trials. The increase in imitation despite these demands therefore strengthens the conclusion that MI can boost the effects of AO in PD.

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Although both groups reported increased engagement in kinaesthetic and visual imagery while observing actions after MI instructions were provided, only the control group reported increased vividness of sensations and images. Additionally, imitation of movement amplitude correlated with self-reported use of kinaesthetic MI in controls, but with visual MI in the PD group. These findings suggest that participants with PD may have had difficulty in generating or effectively applying MI during AO, perhaps relying more on visual processes, consistent with neurophysiological evidence indicating possible compensatory mechanisms during MI[19]. The roles of different imagery modalities during AO in PD and healthy adults, and the relationship between MI ability and AO+MI effects, require further investigation and clarification.

4.4. Clinical implications

These findings have clear relevance for the design of interventions for PD based on AO and MI, which could offer a safe, effective and economically viable option for home-based therapy[7] that patients find acceptable[28]. Although we did not test the effects of AO+MI in the absence of dopaminergic medication, previous studies have documented benefits of AO in patients both on and off medication (e.g., [29]), and it is anticipated that AO-based therapy would improve daily activities in PD as a supplement to pharmacological treatments.

Future studies should further explore the therapeutic potential of AO+MI, including effects on meaningful everyday actions, and longer-term behavioural and neural outcomes.

The absence of a correlation between imitation and disease severity suggests that imitation and MI may not be directly influenced by motor impairment, at least in mild to moderate PD. MI has been found to be slowed but not inaccurate in PD[16], suggesting that imagery may reflect the individual's current motor repertoire[8]. However, facilitation of MI by AO offers the possibility of increasing the parameters of imagined actions beyond physical ability; combined AO+MI may thus provide a viable therapeutic option even in individuals with limited ability to overtly practice actions. Our findings also support the use of AO+MI training to improve action representation and motor control in healthy older adults[14]. Additionally, since imitation contributes to social processes, interventions based on AO and MI might improve social understanding and interaction, which may be compromised in PD[30].

In conclusion, people with PD are able to modulate the amplitude of their hand movements when imitating observed actions, and motor imagery instructions can boost this imitation. Future studies should explore potential therapeutic applications of combined AO+MI in neurorehabilitation for PD and other conditions, as well as in healthy ageing.

Funding

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1. Introduction

External sensory cues can help to overcome difficulties with movement initiation and control in Parkinson's disease (PD)[1], typically targeting gait impairments (e.g., reduced stride length, 'freezing'). However, the applicability of such cues to other functional tasks (e.g., manual actions) is limited, and the longer-term effects of cueing are unclear[2]. Observation of human movement provides another external stimulus that facilitates movement and increases motor learning in healthy individuals[3], by activating a network of fronto-parietal neural structures also engaged during motor execution[4]. Action observation (AO) training has shown encouraging effects in neurorehabilitation[5] and may help to reinforce or reorganise neural connections involved in motor control[6].

 AO can facilitate manual actions (reducing bradykinesia and temporal variability) in people with PD[7], and AO-based interventions have been found to increase functional independence, improve balance and mobility, and reduce freezing of gait, in PD[5,8]. However, such therapies rely on the ability to internally represent actions, which may be affected by PD[7]. Indeed, impaired imitation of gestures and facial expressions has been documented in PD[9,10], as well as an altered corticomotor response to observed actions[11]. Therefore, it is important to further investigate these processes in people with PD. In particular, quantitative effects on movement amplitude have not been demonstrated, despite the significant impact of reduced movement size (e.g., micrographia, shorter steps) on daily functioning.

Similar to AO, motor imagery (MI; the imagination of movement including associated images and sensations) also recruits neural regions overlapping with action execution[12], and facilitates movement and learning[13]. Recent studies of healthy participants have demonstrated greater effects on movement (e.g., sequential and rhythmic actions) when AO is combined with MI, compared with either AO or MI alone; moreover, combined AO+MI increases cortico-motor activity relative to either approach in isolation[14]. There is also some evidence of beneficial effects of combined AO+MI in stroke rehabilitation[15]; however, this has not previously been examined in PD[7]. People with PD are capable of engaging in MI[16], and MI can improve their performance of functional movements[17] and reduce freezing of gait[18]. Nevertheless, differences in neurophysiological responses during MI between people with PD and healthy controls suggest the use of compensatory (e.g., visual) mechanisms[19].

This study investigated the effects of (i) AO and (ii) combined AO+MI on hand movement amplitude in people with PD. Our first aim was to examine the effect of 'pure' AO, by comparing imitation of simple hand movements involving elevated (high) vs. direct (low) trajectories (based on Wild et al.[20]). Our second aim was to determine whether combining AO with MI increased the effects of the observed actions. Combined AO+MI was examined using the same imitation task, but explicitly instructing participants to use MI during action observation. Participants were encouraged to focus on the sensations associated with executing the action, since kinaesthetic MI produces greater sensorimotor activations than visual MI[21].

Based on previous evidence of AO and imitation in PD, we hypothesised that participants would imitate the amplitude of observed actions by modulating the height of their own movements. Moreover, if people with PD are able to engage in MI during AO, combined

AO+MI should increase imitation of movement amplitude, as found in healthy young adults[22]. Conversely, if MI is compromised, people with PD may fail to exhibit an effect of MI on imitation. We therefore also examined the relationship between imitation and self-reported MI.

2. Method

2.1. Participants

Participant characteristics are shown in Table 1. A convenience sample of 24 participants (9 females) with mild to moderate idiopathic PD (Hoehn & Yahr stage 1-3) were recruited through local neurology clinics and Parkinson's UK. All but one were taking dopaminergic medication. Participants remained on their usual medication during the study and were tested in the 'on' state where applicable. 24 control participants (13 females) with no history of neurological injury or illness were recruited from among relatives/friends of participants with PD and the local community. All participants except two in the PD group were right-handed. Participants had normal or corrected-to-normal vision and were screened for dementia using the Addenbrookes Cognitive Examination; ACE-III[23] or a brief version if they had been assessed recently for a previous study (M-ACE)[24]. Although three participants in the PD group scored within the borderline range on the M-ACE, the main results were not altered by removal of these participants, so their data were retained in the final analysis. The study was approved by a UK National Health Service Research Ethics Committee and participants provided written informed consent.

2.2.Stimuli and procedure

Imitation was examined using a video-based task[20]. Participants observed, and immediately replicated, movement sequences performed by a human hand with the index finger extended, shown as a mirror-image (right-handed participants viewed a left hand). Sequences consisted of two movements between three of four positions spaced 150 mm apart horizontally (Figure 1). In elevated trials, the hand moved between positions via an indirect trajectory, with a vertical amplitude of 130.9 mm. Direct trials showed a lower movement trajectory with an amplitude of 21.5 mm. In half of the trials, the four possible target positions were marked by small grey circles (see supplementary materials). The model's movements were paced using a metronome during recording of the stimulus videos (not audible during the imitation task).

Stimuli were projected at life-size onto a 1000 mm x 750 mm screen, positioned 1200 mm from the participant, who was seated at a table with their hand concealed from view by an occluding box (650 mm x 450 mm x 200 mm). A motion sensor was attached to the intermediate phalanx of the index finger of the dominant hand, and movements were tracked in X, Y and Z axes at 120 Hz, using a Polhemus Liberty motion tracking system with Motion Monitor software (Innovative Sports Training).

The trial sequence is illustrated in Figure 1. Following a fixation cross (4000 ms), a still image indicated the starting position for the sequence (4000 ms). The participant placed their index finger in the start position and the stimulus video was then displayed (4000 ms). The action execution phase was indicated by a go-signal (green cross and "beep"; 1000 ms), presented at a variable post-stimulus delay (1000 - 2000 ms). Finally, a blank screen was displayed (4000 ms) while the action was performed.

[Figure 1 here]

The task began with a short practice block (4 trials), followed by four blocks of 30 trials. For the first two blocks (AO), participants were given the following instruction: *"Copy what you have seen as closely as you can in terms of the timing and size of the movement".*

For the final two blocks (AO+MI), the following additional instruction was given: *"Imagine what it feels like to make the movements yourself. As you watch the hand move from one place to another, imagine what your arm, hand and finger would feel like to make the movements".*

Each block consisted of 20 test trials (10 elevated, 10 direct) containing a movement between the second and fourth positions, with 10 filler trials containing different sequences to reduce predictability. Trials were randomized within blocks. A pause halfway through each block allowed participants to take a short break.

2.3. Motor imagery

MI was assessed using a short form of the Kinaesthetic and Visual Imagery Questionnaire (KVIQ), which has been validated in people with PD[25]. Participants are asked to first perform, and then imagine performing, each of a set of simple movements, rating the clarity of images (visual subscale) and intensity of sensations (kinaesthetic subscale) using 5-point scales.

Task-specific MI was measured by asking participants to report their use and vividness of MI while watching the videos. Ratings were completed following the second block (prior to MI

instructions), and again after the final block (post MI instructions), using a 5-point scale similar to the KVIQ (see Table 2).

2.4.Data processing and statistical analysis

Kinematic data from correctly-executed movements were analysed using Matlab (Mathworks Inc.). Errors or missing data were excluded (0.7 % of trials in the PD group; none in the control group) and outliers for each trajectory condition (elevated/direct) at each time point (pre/post MI instructions) were then removed according to the procedure outlined by van Selst and Jolicoeur [26]. This resulted in the exclusion of 1.93 % individual trials in the PD group (M = 1.54 trials; range = 0-5) and 1.61 % trials in the control group (M = 1.29 trials; range = 0-3). Mean vertical amplitude was then calculated for each participant, for each trajectory and time-point. Outliers were then identified at the between-participant level using the same procedure, resulting in exclusion of data for two participants in the control group only.

To determine the effect of 'pure' AO, imitation of vertical amplitude prior to MI instructions was analysed using a Group x Trajectory ANOVA. The effect of MI instructions (AO+MI) was then analysed with a Group x Trajectory x Time ANOVA. To examine any differences in imitation of movements toward visible targets, the above analyses were repeated with Target included as an additional factor, but no main effects of Target or interactions with Trajectory or Time were found (see supplementary material).

Between-group differences in general MI (KVIQ visual and kinaesthetic subscales) and on the task-specific MI questions were analysed using Mann-Whitney U tests. Task-specific MI ratings for AO and AO+MI blocks were then compared within-group using Willcoxon signed rank tests. Finally, correlations between imitation of amplitude (elevated – direct trials) and MI measures, UPDRS motor examination, time since diagnosis and levodopa equivalent

daily dose (LEDD) were analysed using Spearman's correlation coefficient. Statistical analysis was conducted using IBM SPSS v.22, with an accepted significance level of p <.05.

3. Results

The two groups did not differ significantly in sex, but participants in the control group were significantly older (see Table 1). However, age did not correlate significantly with modulation of amplitude before or after MI instructions (all r <.4; p > .09).

[Table 1 here]

[Table 2 here]

3.1. Effects of action observation

Prior to MI instructions, there was a significant effect of Trajectory ($F(1,44) = 49.16$; $p < .001$; $\eta^2 p = .53$), with greater amplitude for elevated trials (M = 72.82 mm) than direct trials (M = 39.96 mm), demonstrating modulation in response to the observed movements (Figure 2). The effect of Group and the interaction between Group and Trajectory were not significant (see Table 2).

3.2. Effects of AO+MI

Following MI instructions (AO+MI), a significant effect of Trajectory remained ($F(1,44) = 77.90$; $p < .001$; $\eta^2 p = .64$), again reflecting greater amplitude for elevated (M = 79.69 mm) than direct (M = 39.80 mm) trials. There was a significant effect of Time ($F(1,44) = 17.73$; p

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Future studies should further explore the therapeutic potential of AO+MI, including effects on meaningful everyday actions, and longer-term behavioural and neural outcomes.

The absence of a correlation between imitation and disease severity suggests that imitation and MI may not be directly influenced by motor impairment, at least in mild to moderate PD. MI has been found to be slowed but not inaccurate in PD[16], suggesting that imagery may reflect the individual's current motor repertoire[8]. However, facilitation of MI by AO offers the possibility of increasing the parameters of imagined actions beyond physical ability; combined AO+MI may thus provide a viable therapeutic option even in individuals with limited ability to overtly practice actions. Our findings also support the use of AO+MI training to improve action representation and motor control in healthy older adults[14]. Additionally, since imitation contributes to social processes, interventions based on AO and MI might improve social understanding and interaction, which may be compromised in PD[30].

In conclusion, people with PD are able to modulate the amplitude of their hand movements when imitating observed actions, and motor imagery instructions can boost this imitation. Future studies should explore potential therapeutic applications of combined AO+MI in neurorehabilitation for PD and other conditions, as well as in healthy ageing.

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Table 1. Demographic characteristics and motor imagery scores in each group.

	PD	Control	*Statistic*	*p*
Age (M, SD)	63.5 (6.34)	68.33 (5.38)	t = 2.85	.007
Sex (% female)	37.5	54.2	$\chi^2 = 1.34$	.25
UPDRS motor score (M, SD)	38.4 (11.33)	N/A		
Hoehn & Yahr (Mdn, IQR)	2.00 (1.5)	N/A		
Years since diagnosis (M, SD)	6.8 (4.8)	N/A		
Levodopa equivalent daily dose; LEDD (mg; M, SD)	519.08 (300.77)	N/A		
KVIQ-V (Mdn, IQR)	64.23 (20.78)	79.34 (17.00)	Z = 1.89	.059
KVIQ-K (Mdn, IQR)	60.45 (17.00)	54.78 (24.56)	Z = .032	.97

Table 2. Effects of *AO* and *AO+MI* on hand movement amplitude.

	df	F	*p*	$\eta^2 p$
AO-only:				
Group	1,44	3.05	.088	.065
Trajectory	1,44	49.16	<.001	.53
Group x Trajectory	1,44	1.29	.26	.028
AO+MI:				
Group	1,44	3.54	.066	.075
Trajectory	1,44	77.90	<.001	.64
Time	1,44	17.73	<.001	.64
Trajectory x Time	1,44	12.74	.001	.22
Group x Trajectory	1,44	3.27	.078	.069
Group x Time	1,44	.22	.64	.005
Group x Trajectory x Time	1,44	2.09	.16	.045

Table 3. Task-specific MI: ratings of imagery use and vividness (median, interquartile range).

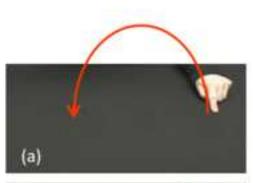| Question	Pre-instruction (AO)			Post-instruction (AO+MI)		
	PD	Control	*p*	PD	Control	*p*
1. Kinaesthetic Did you try to imagine how it would feel to make the movement yourself? (Not at all…Very much)	4.00 (2.00)	2.00 (3.00)	.34	5.00 (1.00)	5.00 (1.00)	.34
2. Kinaesthetic-Sensations How strong was your feeling (if any) of making the movement yourself? (No sensation…As intense as performing action)	3.00 (2.00)	2.00 (2.00)	.63	3.00 (1.00)	3.00 (2.00)	.63
3. Visual Did you try to imagine what it would look like to make the movement yourself? (Not at all…Very much)	3.00 (3.00)	2.00 (3.00)	.46	4.00 (1.00)	4.00 (2.00)	.98
4. Visual-Images How clear was your image (if any) of making the movement yourself? (No image…As clear as seeing action)	3.00 (3.00)	3.00 (3.00)	.34	3.50 (1.00)	3.00 (2.00)	.90

Note. Scores range from 1-5; 5 representing the highest degree of engagement (Q. 1, 3) or vividness (Q. 2, 4).
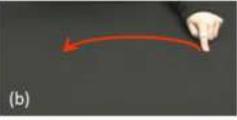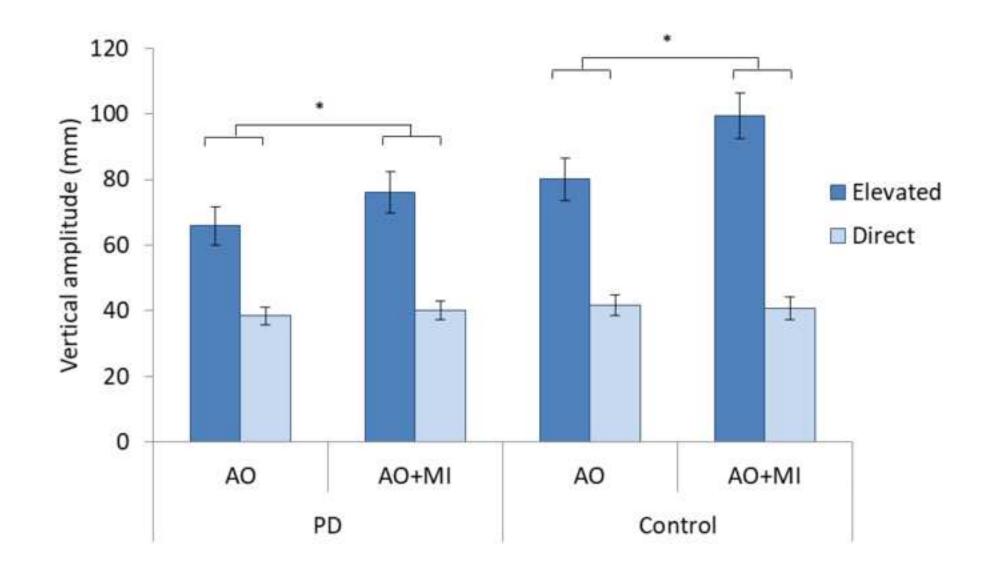
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Figure 1. Illustration of trial sequence: Participants observed videos depicting (a) elevated or (b) direct hand movement sequences, which they imitated following a short delay (1000-2000 ms).

Figure 2. Vertical amplitude was significantly greater when imitating elevated vs. direct hand movements across both PD and control groups. Both groups exhibited a significant increase in imitation of elevated trials when action observation was combined with motor imagery (*$p <$ .05). The mean elevation of stimuli with and without visible targets is shown (see Supplement). Error bars represent ±1SEM.

Still Image
(4000ms)

Observe
sequence
(4000ms)

'Go' signal
(1000ms)

Perform
movement
(4000ms)

Start position

Go

+

(a)

(b)

Optional E-Only Supplementary Files

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