CHAPTER IV
DISCUSSION

PD patients commonly showed dysfunction of movement plans (11, 152), as measured by reaction time (RT), and movement execution skills (59) in daily activities including reach-to-grasp (RTG) task (4-6). However, there still be controversial findings if these patients have RTG deficits in planning, kinematics and transport-grasp coordination (4, 12, 14, 15), because these studies used different protocols and participants' characteristics. Thus, in the first experiment, researcher investigated the RTG planning, kinematics and coordination by controlling all possibly influential factors and used the RTG under barrier avoidance condition which was tested the RTG kinematics and coordination in previous studies (20, 22, 23). All mean values of each variable in PD group were compared to those in non-disabled control group.

Then, researcher continuously examined the effect of trainings RTG action in PD group. However, the training protocol should be able to enhance motor learning which was impaired in these PD including slow acquiring the skill, poorer retained performance and inability to transfer their skill to other tasks when compared to non-disabled controls (see review 24-26). Action observation (AO) combined with motor training could enhance acquisition, retained performance and transferred capability when learned prehensile task in non-disabled and stroke individuals (29-32, 35). Therefore, the second study aimed to examine the effect of action observation (AO) combined with motor training in 3 aspects: 1) improvement in acquisition phase; 2) performance in retention test which compose of retained and saving capability; and 3) transferred capability to untrained-task when compared to placebo (P) and control (C) groups. For measuring the motor learning in these 3 aspects, participants were tested the capability in trained- and untrained- tasks before training (Pretest), after training immediately (Posttest) and 45 minutes later (Retention test). The untrained task was RTG under barrier avoidance condition (similar to first experiment) which could measure RTG planning, kinematics and transport-grasp coordination.

Then, the possibly underlying mechanisms of AO were analyzed by questionnaire regarding the advantages of training condition such as the action understanding, enhancing memory, error detection, error correction, motivation, directing attention, increasing of self-confidence, excitement of training, and willing to receive alternative treatments beyond medications.

5.1 Methods and participants

5.1.1 First experiment

It is still controversial if PD patients have RTG impairments in planning, kinematics of transport and grasp and transport-grasp coordination (4, 12, 14, 15). Therefore, this study efforted to re-examine RTG performance in PD population by controlling the possibly influential factors including severity or stage of disease, more affected side, task condition and difficulty, and measurement for reach-to-grasp kinematics and coordination.

The recruited individuals with PD had bilateral mild to moderate impairment of upper extremity, and had more affected on right side. Most of the previous studies frequently recruited participants with mild impairment (Hoehn and Yahr stage I) and did not concern regarding the more affected side (e.g., 14, 16, 153). The different stage of disease might have differential impact on reaching and grasping performance (17, 153). Moreover, regarding the more affected side, hemiparkinsonian patients showed slowed planning or RT and movement time only when bad or affected side was right side (154). Similarly, an another previous study indicated that hemiparkinson's disease patients have preserved kinematics of reaching and grasping (155). Therefore, PD participants in this first experiment were recruited when they had more affected hand on right side which were their dominant hand.

The current study used a challenging RTG action, which is reaching and precision grasping with fast speed and avoiding a barrier, to investigate movement deficits in PD patients. RTG performance was measured by planning (measured by reaction time; RT), kinematics in transport (movement time; MT, maximum transport velocity; V_{max}, absolute and relative time to maximum transport velocity; TV_{max}, and absolute and relative deceleration time; DT) and grasp component (maximum aperture; A_{max}, absolute and relative time to maximum aperture; TA_{max}, absolute and relative aperture closure time; ACT, and aperture closure distance; ACD), and transport-grasp coordination (highest cross correlation coefficient; r_{max} and associated time lag; T_{max}).

We chose the precision grasp which was commonly used in elders (156) and chose the sensitive cross correlation analysis to detect impaired coordination (23, 50, 76). The results represent that PD patients had deficient planning, kinematics and coordination in both temporal and spatial aspects except all relative values, ACD and r_{max}.

This study composed of 9 non-disabled controls and 19 PD participants. The amount of the participants was calculated by the formula of sample size calculation (Appendix N). The means and standard deviations of all variables were selected to this calculation. The enough amount of participants per group for RT, MT, V_{max}, absolute TV_{max}, and absolute DT, A_{max}, absolute TA_{max}, absolute ACT, and T_{max} were 3 – 18 persons per group. The amount of participants that were used in this study could found the significant differences between non-disabled and PD groups. In contrast when considering all relative values, ACD and r_{max}, the sample size were 25 – 40 persons per group. These findings indicate that all relative values, ACD and r_{max} were preserved in PD participants when compare to non-disabled adults.

The characteristics of all participants have been shown in Table 4.1. They consisted of age, Mini Mental State Examination score which is cognitive capability, and depression and anxiety scores. There was no significant difference in those factors between non-disabled and PD groups. The recruitment was initiated by inviting the PD individuals first and then inviting the non-disabled controls who were matched in age (±5 years) with the PD patient. Therefore, this technique could minimize the influential factor such as aging which affect the RTG performance (156-160).

5.1.2 Second experiment

Because of the remaining impairment of RTG actions in PD individuals although they took their normal medicine, therefore they require alternative treatment to rehabilitate their deficits. All parkinsonian participants in first experiment and further recruitment were asked to participate in second experiment.

The training protocol was chosen in this study is action observation (AO) combined with motor training. AO when coupled with motor training resulting in enhancing the retention of performance (32, 43, 44) and inducing brain plasticity (161, 162). In our study, there were 3 training groups: Action observation (AO), Placebo (P) and Control (C) groups. The group allocation used stratified randomization for minimizing the bias. In AO group, participants observed 6 hand actions in 6 minutes or 1 minutes per action. This duration (6 minutes) is the enough time for activating the mirror neurons (MNs) and enhancing motor learning in previous studies (e.g.,(34, 42, 163). Thus, in other 2 groups which are double control groups also used 6 minutes for observing 6 landscape perspectives in P group or resting in C group. In P group, we selected the 6 natural landscapes because these landscapes might have no effect on observers' performance. In contrast, the control group in previous studies chose and applied foot action (39) and acoustic cue (34). There are evidences supported that hearing the action's sound (48) and foot action could activate MNs (164). Therefore, AO protocol in this study in only one group which could be the protocol using MNs concepts.

If considering the video in AO group, two models were mild PD individuals (Hoehn and Yarh stage I) consisted of a PD had affected hand on right side and another on left side. The hand actions were recorded in PD models because previous evidences indicated that facilitation effect was found only observing unskilled model (165) or parkinsonian model (39). In addition, the sound of actions when models were performing the hand actions were louden. Hearing the action's sound is an important ingredient in AO protocol (48). The tasks that model did in video clips were purposive hand-object interaction tasks which could enhance motor programing in primary motor cortex of specific muscle (108, 162).

The total training duration was approximately 45 minutes which is enough time to induce rapid plasticity in human brain (e.g., 45, 46). PD individuals were trained in ON-state of medication which promote the retention performance in PD for 45 minutes (34). Therefore, these protocols should be able to promote the learning in acquisition and retention phase (including retained and saving capability), and might be able to transfer to another task.

Moreover, observers' attention was controlled by asking the question before observing in both AO and P groups. The questions were shown following: 1) How many and what actions or landscapes that you will observe?, 2) How many repetitions of fourth actions or landscapes will be presented?, 3) How many repetitions of fifth actions or landscapes will be presented?, 4) How many repetitions of sixth actions or landscapes will be presented?. The purpose of these questions was enhancing directing attention to observed video, thus the answers were not used in analyses. However, there is no criteria to exclude patients who have attention problems in the present study. It is well known that attention is the important ingredient in AO training (e.g., 166).

The testing composed of test in trained- and untrained- task. The test in trained-task was total time and time in each item of Wolf motor function test (WMFT). The test in untrained-task was planning, kinematics and coordination variables during performing RTG under barrier avoidance condition as using in first experiment.

5.2 First experiment: effects of Parkinson's disease on reach-to-grasp actions.

RTG planning, kinematics in transport and grasp component, and transport-grasp coordination were compared between non-disabled and PD groups. The variables in these domains were shown in previous part (5.1.1 First experiment).

5.2.1 Reach-to-grasp planning

Previous studies which used simple reaction time (RT) to assessed PD patients found conflict results (12, 167, 168). In this study demonstrated delayed response to visual signal or RT when compare to non-disabled controls. The task which assessed participants in this study required performing complex goal-directed movement with fast speed. The increased task difficulty i.e. fast speed or high accuracy task resulting in increasing the RT (160), while obstacle appearance did not affect RT (169, 170). The prolonged RT in PD patients indicates difficulty in movement initiation or "akinesia" (39, 152). Goodrich and colleagues concluded that persons with PD have impaired recruitment attentional resources to prepare and speed their RT (171).

5.2.2 Transport and grasp kinematics

Participants with PD demonstrated prolonged movement time and lower maximum wrist velocity. It represent bradykinesia which is the result of internal programming deficits (15). Moreover, patients with PD have a slower force development which leads to impaired scaling of movement parameters (172). PD participants demonstrated deficits in all spatial and raw values of temporal domains of transport and grasp components. These impairments of PD patients were also found in other studies (4, 12, 16, 41). However, other studies found conflict results regarding maximum aperture, some studies found smaller maximum aperture size (12, 41) while others did not found (4, 14, 16, 173). The possible factors might be the different stages of PD and different task difficulty. The present study excluded mild stage patients (Hoehn and Yarh stage I) whereas previous studies recruited these mild patients (e.g., 14, 16) and used a challenging task (the barrier task with small object, and fast speed). This resulted in significantly smaller aperture than controls. Reduced maximum grasp aperture amplitude reflects hypometric movement which commonly occur in patients during performing hand movement such as writing (174, 175). These deficits indicate the important role of the basal ganglia in controlling movement timing (e.g., 176, 177) and amplitude (60, 152).

Contrast with aforementioned findings, all relative values of both transport and grasp components, and the distance from the initiation of aperture closure to object (reflected by aperture closure distance; ACD) are similar to those of the non-disabled control. These findings were inconsistent with previous studies. For relative value in transport component, the varied results were found. A study reported normal relative time to maximum velocity (TV_{max}) (16) while another found significantly decreasing (4) and another found significantly increasing (173). None of reports regarding relative deceleration time (DT). The relative DT was computed by subtraction between total time (100%) and relative TV_{max}. In case of ACD, this study found controversial result when compare to a previous study which demonstrated shorter ACD (41). The authors concluded that basal ganglia may be involved in specify closure distance (41). Thus the altered closure distance might reflect basal ganglia dysfunction in controlling closing of aperture. The possible reason why all relative values were not changed after suffering PD is that they prolonged in all time parameters including MT, TV_{max}, DT, TA_{max}, ACT for maintaining their motor programming by consistent ratio of duration in each component relative to total movement time or relative values (178). For ACD, it was calculated by location of the hand relative to the target object during initiating aperture closure. This distance correlate to transport velocity and maximum aperture size. The increased aperture closure distance resulting from grater maximum aperture size and faster wrist velocity at the time of maximum aperture (179). Therefore, if ACD depend on this control law, ACD in PD groups should be smaller than non-disabled group. However, the possible explanation is task constraint. Because the task which used in this study is barrier task, thus participants opened their hand with maximal aperture amplitude when pass the barrier and then start to close their hand with limited distance (from barrier to object). Very short distance for closing the hand in barrier condition also induce smaller ACD in healthy adults (180).

5.2.3 Transport-grasp coordination

The control group demonstrated tight temporal coupling between the components of transport and grasp. In contrast, in the PD group it was delayed by approximately 170 milliseconds. Thus, individuals with PD showed disrupted temporal coordination. This impaired coordination might result from a failure to execute the reach and grasp components in a parallel manner. Previous neurophysiological studies have reported that the basal ganglia integrates somatosensory and visual information (181). Thus, deficient integration of proprioceptive information derived from the transport component and visual information regarding object recognition form the grasp would result in inability to control both transport and grasp simultaneously in persons with PD. However, our participants preserved spatial coordination. This finding could be explained by “Speed/accuracy trade-off” theory (182). PD participants spent a longer time coordinating transport velocity and grasp aperture in order to have a perfectly coupled pattern of movements.

All PD participants in this study were noted the amount and type of medicine that they normally take (as shown in Appendix K). Although the dose and type of medication were varied across patients and testing was done in ON-medication state, the results still be demonstrated the consistent RTG impairments. Therefore, these remained deficits require the training for regaining patient's RTG capability into normal level.

5.3 Second experiment: Effects of AO on motor learning of RTG actions (both trained- and untrained- task)

The Fagg-Arbib-Rizzolatti-Sakata or FARS model (Figure 2.3) which describe the linkage between circuit of visuomotor transformation and mirror neurons postulate the role of each area of the brain when observing the grasping actions. The premotor (PM) area is the part for planning reaching (dorsal PM) and grasping (ventral PM) program. Adjacent area including supplementary motor area (SMA), prefrontal cortex and basal ganglia also have connections to ventral PM for planning the sequential movement, storing into working memory and error processing. This model could explain why the AO has benefit to PD observers.

This study investigated the learning effect of action observation combined with physical training on speed of trained-task. When considering to each task, the tasks that were improved by training with AO consisted of lifting can, stacking checkers, flipping cards, and turning key. Although the lifting can is a simple RTG with whole hand grasping, it could be improved by AO. The possible explanation is that the lifting can is common daily living activity and then lead the performer to be expert in this task. An evidence support that the mirror neurons were strongly activated when observer familiar to and was the expert of observed skill (183). For the improvement in stacking checkers, flipping cards, and turning key, these skills are sequential movements that are controlled by basal ganglia and SMA (130, 133). Therefore, the activation of mirror neurons during observing these skills might enhance the activation of SMA and leading to improve these skills.

We also determine the transferred capability from trained- to untrained-RTG with barrier avoidance task. In this task, the planning time (RT), spatial and temporal kinematics of RTG movement, and RTG coordination were measured. The main findings in AO protocol when compare to other protocols present the following: 1) movement speed in trained-task was able to improve with a larger extent and retained overtaken performances for 45 minutes; 2) In untrained-task, there were improvement in temporal RTG kinematics, and coordination in both acquisition and retention phases.

A previous evidence demonstrated that PD observers increased their movement rate significantly and maintained that improvement for 45 minutes when training with observing repetitive finger movement from a third person perspective for 6 minutes and followed by 2 minutes execution of the same actions (34). The present study was adjusted some parameters from that study for maximizing the learning effects as demonstrate in aforementioned discussion.

Considering the trained-task, the extent of improving the speed and retained and saving capability were larger in AO group. Although RTG under barrier avoidance condition was not trained, all temporal RTG kinematics was improved and retained after training with all protocols. But the facilitation effect on saving capability was found only in AO training group. Importantly, retained capability of deceleration time (DT) and temporal coordination could maintained for at least 45 minutes only in AO group. Previous evidences (e.g., 60) and result in first experiment in current study demonstrated that PD patients, when compare to the controls, had slowness in planning and bradykinesia (as evidenced by prolonged RT and MT), more relying on visual feedback represented by longer DT, hypometria (reduced amplitude of maximum velocity and grip aperture) and poor anticipatory control of grasping (as evidenced by later TA_{max}) during performing RTG actions. Whereas, there were no impairment in spatial kinematics (except grasp aperture) and coordination in PD (result in first experiment). Therefore, the training with AO in this study could minimize aforementioned impairments, except planning deficits and small aperture. The greatest effect of AO was found in DT and temporal coordination, especially in retention phase. Aforementioned findings indicates that AO could minimize bradykinesia, improve all temporal kinematics and coordination, and reduce the dependence of visual feedback in PD. In summary, the AO enhance the improvements in acquisition phase, maintaining those improvements in retention phase and transferring to untrained-task.

5.4 Second experiment: Underlying mechanisms of AO on motor learning of RTG actions.

This paragraph explains the advantages and possible underlying mechanisms of the AO protocols. Basal ganglia is the internal timing system in human brain for controlling movement timing or temporal information (e.g., 176, 177). The evidences support that basal ganglia was activated during observing hand movement (184-186). Therefore, this activation might be the reason why movement timing was improved. As we mentioned in previous paragraph that our protocol could activate the MNs which enhance action recognition and understandings the goals of model's movements (111). During observing the actions, the visual information is sent to higher order association areas for sophisticated cognitive mechanisms and compared with previously stored data and then observer would understand what the other person is doing (see review(110). This might be the reason why PD patients reduced their relying on visual feedback after observing. Observation also enhance retention performance by facilitating formation of motor memories (42, 110). The participants in this study also express that action observation could facilitate their action understanding and memory, although there were not significant between groups (but nearly reach significant level). The FARS model (Figure 2.3) support that prefrontal cortex stores the working memory during observing, whereas the ventral PM is the part for action recognition. Thus, AO could enhance memory and action understanding.

In this study, the findings in questionnaire demonstrate the obvious advantages of AO which are promoting error detection and preventing. The observation model's performance with knowledge of result (KR) feedback regarding model's errors enhanced error detection process of observer (187). Beside from KR, the observer also able to detect recognize error in movement timing of model (188). There is an evidence indicated that prefrontal cortex was activated for error detection process during observing model's performance (189). Therefore, prefrontal cortex could promote detecting the errors PD patients, who have the deficit in basal ganglia, via observing error in motor timing of model and use this detection to prevent their own errors.

Furthermore, there is an evidence support that AO could promote the transferred capability to untrained task in non-disabled people (35). The possible mechanism is that observer acquire movement information from observing and achieve the exact movement after followed by physical training, then could generate the appropriate movement when performing similar untrained task (35). These findings demonstrate that the present study is the preliminary demonstration of the transferred effect of AO in PD on another similar untrained-task referred to as near transfer (190).

Our study demonstrates beneficial effects of AO on all temporal parameters, while no effect on spatial domain. The possible explanation is that our AO training has not the instruction regarding movement amplitude e.g. aperture size during observing or testing. Farley and Koshland revealed "speed–amplitude relations", which indicate that practicing with amplitude cue result in both bigger and faster movements while velocity cues result in mostly faster movements (but not bigger) (191). It might be the reasons why spatial kinematics were not improved by our training. Therefore, further study with AO training using amplitude cue should be assessed. Moreover, the retention of those improvements was assessed only at 45 minutes after training. Further study should investigate effect of the training with AO concept at longer retention test.

5.5 Clinical implication

Parkinson's disease (PD) is the most common neurodegenerative movement disorders in elderly population. The cardinal symptoms in patients with PD including bradykinesia, tremor, rigidity and postural instability affect the functional performance in daily living activities. Beside from walking, the clumsy hand is frequently complained in these patients. The results in this study indicate the impairments of reach-to-grasp (RTG) action in the domain of planning, spatial and temporal kinematics of transport and grasp components and transport-grasp coordination. Although the patients took their normal medication, these impairments were observed. It indicated that medication could not regain their normal RTG planning, kinematics and coordination. Therefore, these patients need the alternative treatment for improve their capabilities of RTG actions.

Additionally, the barrier avoidance task which was used in this study is a challenging RTG actions and appropriate to investigate the RTG impairment in PD populations. This task could disturb the transport component. Therefore, this perturbation task induce obvious deficits in transport-grasp coordination.

Similarly, Wolf motor function test (WMFT) is also a sensitive and easily applied measurement to detect RTG impairments. In this study, PD participants were tested by six items of WMFT including lifting can, lifting pencil, lifting paper clip, stacking checker, flipping cards, and turning key. The results demonstrated that the times for lifting can, stacking checker, flipping cards, and turning key were improved by training and were retained for 45 minutes. Although WMFT was initially used in stroke population, findings in this study indicates the advantage of WMFT to detect the change or improvement after rehabilitation sessions in PD participants.

Physical therapy is a way to rehabilitate them without harmfulness. Because of poor motor learning in both skill acquisition and retention performance in PD patients, the training in rehabilitation session is not enough. Patients need to practice home programming at their places. One of practical way is the motor training combine with action observation (AO). This protocol is easy to apply and be trained. Moreover, this protocol is the effective training for enhancing motor learning in non-disabled and individuals with stroke populations. Similarly, AO combined with motor training in current study could improve skill acquisition and retention performance in both trained- and untrained- tasks, represents transferred capability to other tasks, of PD participants when compare to control and placebo group.

However, the therapists should carefully apply this protocol to their treatments, because recruited patients was selected by specific criteria such as mild to moderate arm impairment (Hoehn and Yarh stage II – III) and aged between 49 – 80 years. In addition, the task used in the study was RTG actions in Wolf Motor Function test including lifting can, pencil and paper clip, stacking checkers, flipping cards, and turning key and RTG under barrier avoidance condition. It is still unclear whether dyad training can be applied to other task, or to other environment and/or to patients with other characteristics apart from in this study. In addition, the retention test was done at 45 minutes after training. It is still be questionable if this protocol could enhance retained performance more than 45 minutes. Thus, applying AO combined with motor training in patients with other characteristics such as severe impairment, other age ranges, in the other tasks or environment and longer retention test are suggested for further studies.

5.6 Limitations in this study

5.6.1 Participants aspect

5.6.1.1 Although PD participants in second experiment were allocated by stratification with age range, Hoeh and Yarh stage and more affected side, the baseline performance still be different between groups. Therefore, the level of impairment by considering Unified Parkinson's Disease Rating Scale (UPDRS) score and disease duration might minimize this different.

5.6.1.2 There is upper limit for disease duration. Some patients were suffered from PD more than 10 years. These patients also have slight limb dyskinesia, although medical record did not report wearing-off phenomenon. It is unclear if limb dyskinesia has any effect to RTG performance.

5.6.2 Protocols aspect

5.6.2.1 For the protocol in second experiment, there are 6 hand actions in both observation and motor training period. The 6 actions might be the one factor affect the learning performance in PD participants who have poor adaptation during switching tasks (e.g.,(192).

5.6.2.2 The instruction gave to patients in second study focus to movement timing and accuracy which were “as immediately and as fast as possible without collision of barrier”. There was no instruction to spatial domain i.e. open your hand with as wider as possible.

5.7 Further studies

All results reveal the beneficial effect of action observation combined with motor training protocol on motor learning in individuals with Parkinson’s disease. However, further study could determine what any other conditions of action observation protocol could lead to greater advantages or effectiveness, other treatment protocols which able to improve planning and maximum aperture size. Therefore, the further studies should:

1. Controlling the homogeneity of participants prior to allocate to training by matching or stratifying the PD participants by other scales which are more elaborated than Hoehn and Yahr stage i.e. UPDRS.

2. The awareness regarding the effect of dyskinesia in PD patients on training effect. Researcher should control or exclude the patients who have dyskinesia. In contrast, the studies of the effect of action observation in PD patients with and without motor complication including dyskinesia might be benefit to general clinical situation.

3. The training with observation of fewer hand actions instead of 6 actions.

4. The training with action observation and using instruction in both movement timing and amplitude.

5. The further studies with other technique or larger sample size might be required to investigate the effect of training on aperture size of PD patients.

6. The training with action observation and adding external feedback of model's performance including knowledge of results, timing, and amplitude which could promote the motor learning in non-disabled adults in previous studies (187, 188).

7. The longer retention test after training with action observation should be investigated.