

**EFFECTS OF PRACTICE ON LEARNING AND RETENTION OF TOOL-RELATED
MOTOR SKILLS IN PARKINSON'S DISEASE**

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Abstract

Previous research revealed that individuals with Parkinson's disease (PD) show preserved learning of tool-related motor skills within a session. However, as a possible result of striatal dysfunction, retention has been found to be impaired after a 3-week delay. The goal of the current study was to further examine motor skill impairments related to complex tool use in PD by investigating the effects that different delays and extensive practice have on performance. PD participants and controls were trained on novel tools over four sessions, and motor skill performance was investigated by examining patterns of learning and forgetting over time. Results showed that PD participants were unimpaired in motor skill learning within sessions, but they did not retain these skills between sessions. In spite of forgetting, with practice, individuals with PD still demonstrated improvement across sessions. These findings indicate that people with PD may benefit from extensive practice when learning tool-related motor skills.

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Introduction

Parkinson's disease (PD) results from striatal dysfunction caused by degeneration of dopamine-producing cells in the basal ganglia, leading to disruptions of voluntary movements. Physical symptoms may include tremor, rigidity, gait disturbances, and bradykinesia (i.e., slowed movements; Rodriguez-Oroz et al., 2009). Although PD is primarily characterized by these motor difficulties, cognitive impairments can also be present even in non-dementing individuals (Lewis, Dove, Robbins, Barker, & Owen, 2003; McFadden, Mohr, Sampson, Mendis, & Grimes, 1996). More specifically, findings generally suggest that individuals in the early stages of PD show impaired procedural memory (i.e., skill-based learning; Squire, 1992), both on motor and non-motor tasks (Knowlton, Mangels, & Squire, 1996; Shohamy, Myers, Kalanithi, & Gluck, 2008; Werheid, Zysset, Muller, Reuter, & Yves von Cramon, 2003). However, their declarative memory for consciously accessible information remains largely intact (Davidson et al., 2006), although deficits in some aspects of declarative memory have been found (Cohn, Moscovitch, & Davidson, 2010). Procedural memory plays an important role in learning and retaining motor skills, and this ability may be negatively affected in PD (Albouy, King, Maquet, & Doyon, 2013; Roy, in progress). However, it is currently unknown whether long-term learning and retention of motor skills could be improved in individuals with PD.

There is recent evidence that impaired motor skill performance extends to the use of complex tools in PD (Roy, in progress). Complex tools are defined as objects that transform motor output into advantageous mechanical actions to achieve a goal when acting on a recipient object (e.g., using a knife to slice bread; Frey, 2007). We often rely on familiar complex tools, but there are also situations in which we must learn new skills, using a novel tool, to achieve a goal. Although complex tool use may seem relatively straightforward, this ability relies on a

multitude of skills and knowledge, mediated by different memory systems. The use of both familiar and unfamiliar novel complex tools is important because it allows us to fulfill various everyday activities that would otherwise be difficult or impossible to accomplish (Ambrose, 2001).

Of particular importance to the current study, Roy (in progress) showed that in learning how to use novel complex tools, people with PD demonstrated intact learning of motor skills within a session; however, unlike healthy controls, PD participants did not retain these skills after a 3-week delay. This pattern of preserved within-session learning but impaired long-term retention has been previously reported in PD using a variety of tasks (Bedard & Sanes, 2011; Marinelli et al., 2009; Mochizuki-Kawai et al., 2004). At this point, the neural and psychological processes underlying this impairment remain unresolved. It is also unclear whether it is possible to improve tool-related motor skill learning and retention in PD, and whether individuals with PD would show impaired performance after a shorter delay. Thus, the aim of the current study was to further investigate the findings by Roy (in progress) by examining the effects of shorter delays and more extensive practice on motor skill performance in PD. Prior to describing the current study in more detail, I will first provide an overview of human memory systems, and examine how they may interact in PD. I will then discuss how declarative and procedural memory may specifically mediate complex tool use, and describe how procedurally mediated tasks, such as motor skill learning, can be impaired in PD. Finally, I will consider whether more extensive practice may result in long-lasting retention of motor skills in PD.

Overview of Human Memory Systems

Declarative and procedural memory systems are functionally and neurally distinct. Encoding of declarative memories is dependent on the hippocampal complex, although it

remains controversial whether the hippocampal complex is required for the maintenance and retrieval of such memories (Moscovitch et al., 2005; Squire, 1992). It has been hypothesized that declarative memories are flexible and can be rapidly acquired (Squire, 2009; Squire & Zola, 1996; Tulving, 1985), and a distinction in declarative memory has been made between semantic memory and episodic memory. Semantic memory comprises general knowledge about the world and oneself, whereas episodic memory involves the recollection of subjective events and experiences that are specific to a time and place (Renoult, Davidson, Palombo, Moscovitch, & Levine, 2012). Procedural memory is a type of nondeclarative memory, which is implicit, and it is believed to be less flexible and less rapidly acquired than declarative memory (Squire, 2009; Tulving, 1985). Although less is known about the neural underpinnings of procedural memory, motor skill learning is thought to be mediated by cortico-cerebellar and cortico-striatal systems (Doyon, Penhune, & Ungerleider, 2003). It is also important to note that although declarative and procedural memory systems are thought to rely on different neurological areas, both types of memory may require executive functions (i.e., control processes required for planning, monitoring, coordinating, etc.) mediated by the frontal lobes (Salthouse, Atkinson, & Berish, 2003). For instance, changes in executive functioning have been shown to affect performance on tasks mediated by declarative memory (see Buckner, 2004 for a review), and performance on procedurally mediated tasks may require cognitive aspects involving executive functions (Beaunieux et al., 2006).

A key functional difference between the two memory systems involves the retention of knowledge over time. Declarative memory is not always reliable because it is susceptible to forgetting as a result of decay over time or interference effects (Ellenbogen, Payne, & Stickgold, Mitchell, 2006; Brown, & Murphy, 1990). On the other hand, procedural memory appears to be

more robust to these effects, and performance on tasks that are procedurally mediated tends not to be susceptible to interference, or decline with time (Gabrieli, Corkin, Mickel, & Growdon, 1993; Mitchell et al., 1990, though see Brashers-Krug, Shadmehr, & Bizzi, 1996).

It was initially believed that declarative and nondeclarative (e.g. procedural) memory systems operated independently (Squire, Knowlton, & Musen, 1993). Evidence for this hypothesis stemmed from early studies demonstrating impaired declarative memory, but preserved procedural learning in amnesic individuals with medial temporal lobe damage (Cohen & Squire, 1980; see Squire & Zola, 1996 for a review). Additional support came from studies that demonstrated a double dissociation of declarative and nondeclarative memory using probabilistic classification learning, such as on the weather prediction task. This task relies on nondeclarative memory processes as participants learn to associate visual cues from four cards that are probabilistically associated with a weather outcome. Findings showed that amnesic individuals demonstrated preserved performance on this task, as they learned at the same rate as control participants. However, despite intact performance, they were unable to answer explicit, factual questions about the training procedure (Knowlton, Squire, & Gluck, 1994). On the other hand, individuals with basal ganglia dysfunction, as a result of Huntington's disease (Knowlton, Squire, Paulsen, Swerdlow, Swenson, & Butters, 1996), and nondementing PD (Knowlton, Mangels, Squire, 1996), were impaired in learning the probabilistic classification task even though they could recall explicit details about training.

Though the above mentioned patient studies originally suggested that declarative and nondeclarative memory systems operated independently, more recent evidence suggests that the two memory systems can interact with modulation from the prefrontal cortex (Poldrack et al., 2001; see Poldrack & Rodriguez, 2004 for a review). It now appears that different types of

interactions can exist between declarative and nondeclarative (e.g., procedural) memory systems. For example, the two memory systems have been shown to interact *cooperatively*, which occurs when more than one system is simultaneously required to mediate performance, and the systems do not compete with each other (e.g., Sadeh, Shohamy, Levy, Reggev, & Marial, 2011). Conversely, memory systems can also interact *competitively*, which occurs when one system has an inhibitory influence over the other system (Packard & Goodman, 2013).

Competitive interactions between the hippocampus and striatum were described from functional magnetic resonance imaging (fMRI) studies using probabilistic classification learning where increased activation in the striatum, and decreased activation in the medial temporal lobes has been reported (Poldrack, Prabhakaran, Seger, & Gabrieli, 1999; Seger & Cincotta, 2006). This antagonistic activity between the two systems has also been described during motor sequence learning. Generally, hippocampal activity increases during initial learning. However, with learning, striatal activation increases, whereas hippocampal activity decreases (Albouy et al., 2012; Schendan, Searl, Melrose, & Stern, 2003). Notably, during the early phases of motor sequence learning, cooperative interactions may actually hinder performance. For instance, parallel increasing activation in the striatum and hippocampus was shown to correlate with poorer performance in older adults (Rieckmann, Fischer, & Backman, 2010) and younger, slower learners (Albouy et al., 2008). It is important to note that with a competitive relationship between memory systems, *compensatory* interactions may also occur, whereby the dysfunction of a competing system results in a greater use of the preserved system (Packard & Goodman, 2013). For example, a compensatory relationship has been observed in people with PD when performing tasks that normally rely procedural memory. Compared to healthy control participants, individuals with PD may make greater use of their declarative system, mediated by

the hippocampus, possibly because of an impaired procedural system, mediated by the striatum (Gobel et al., 2013; Moody, Bookheimer, Vanek, & Knowlton, 2004). As motor skill learning is mediated by the striatum, it is possible that compensatory interactions may occur in people with PD, but further research is needed.

Memory Systems in Tool Use

Both declarative and procedural memory are required for complex tool use (Creem & Proffitt, 2001; Roy & Park, 2010; Silveri & Ciccarelli, 2009). It has been proposed that tool-related skills and knowledge can be divided into four main components: 1) recalling a tool's function and attributes, 2) grasping a tool for use, 3) skillfully using a tool to achieve a goal, and 4) executing the motor skills associated with a tool (Roy & Park, 2010). Findings suggest that some of this tool-related knowledge relies primarily on declarative memory, while other aspects of performance rely predominantly on procedural memory. Conversely, other aspects of tool use may require an interaction of both types of memory.

In a previous study, Roy and Park (2010) specifically examined how declarative and procedural memory systems mediate complex tool use. Using novel tools, the researchers examined tool use by an individual with profound hippocampal amnesia, D.A., and a matched sample of controls during three sessions, with three days between sessions 1 and 2, and three weeks between sessions 2 and 3. Compared to controls, D.A. was impaired in recalling a tool's attributes and demonstrating its correct grasp after the delays, suggesting that these aspects are mediated, at least in part, by declarative memory. These findings were consistent with previous research suggesting that recalling conceptual knowledge about objects (Hodges, Bozeat, Ralph, Patterson, & Spatt, 2000) and tool grasping (Creem & Proffitt, 2001) rely on semantic memory.

For motor skill performance, D.A. learned how to use the tools during training trials within a session, during which he watched a video demonstrating a tool's use, and then he immediately completed the task he had just observed. D.A. learned motor skills associated with the tools at the same rate as controls during the first training session. Also, after a 3-day and 3-week delay, D.A. completed additional training sessions, and his performance did not decline from the previous sessions. Roy and Park (2010) concluded that motor skill learning during training was mediated by procedural memory, which is consistent with previous studies (Corkin, 1968; Harrington, Haaland, Yeo, & Marder, 1990; Krebs, Hogan, Hening, & Adamovich, 2001; Siegert, Taylor, Weatherall, & Abernethy, 2006).

Conversely, D.A.'s performance during skilled tool use (i.e., the intentional use of a tool to achieve a goal) suggested that the task might require an interaction of both declarative and procedural memory systems. Although skilled tool use is similar to motor skill learning during training, as both require the execution of a motor skill to achieve a goal, skilled tool use may be more declaratively demanding because one must know how to accurately use a tool from memory (i.e., there is a delay between viewing the video demonstrating how to use a tool and using the tool at a later time). Compared to controls, D.A. was severely impaired in his ability to accurately demonstrate a tool's use after a delay, suggesting that declarative memory was required. However, once the experimenters provided D.A. with a non-motor, visual cue (i.e., the starting position of the object that the tool acted on, referred to as the *recipient*), he could properly execute the required motor skills, and his completion time (i.e., the time it took to successfully complete the task) was no longer impaired relative to controls. This finding suggests that providing a visual cue may have helped D.A. access procedural memory, allowing him to execute the motor skills associated with the tool.

Further support for the relationship between declarative and procedural memory systems in various aspects of tool use emerged from a follow-up study examining novel tool use in a sample of people with mild-moderate PD, and healthy age and education-matched controls (Roy, in progress). Similar to Roy and Park (2010), participants were tested on four main components of tool use, but there were two sessions that were spaced three weeks apart. The results of the study were important because they provided evidence of a double dissociation where individuals with PD showed the opposite pattern of performance than the hippocampal amnesic case, D.A.: namely, impaired retention of motor skill learning, but unimpaired recall of tool attributes and function, and unimpaired grasp demonstration. Importantly, individuals with PD showed improved motor skill performance across training trials in session 1, and their rate of improvement did not differ from that of controls. However, in contrast to D.A., motor skill performance of individuals with PD declined after the 3-week delay, and was not significantly better than the first training trial in session 1.

Participants also completed a test that assessed skilled tool use ability. Similar to training, participants carried out the motor skill associated with the tool to complete a task, but they were required to do so from memory. For this task, compared to controls, individuals with PD were unimpaired in their ability to accurately demonstrate a tool's use. However, PD participants demonstrated impairments in the time it took them to complete the task. Though individuals with PD demonstrated intact learning within a session, they did not retain their completion time performance, and unlike controls, PD participants were significantly slower after the 3-week-delay. Taken together, performance during skilled tool use provided evidence that this ability may require an interaction of both declarative and procedural memory systems.

Regarding motor skill performance during training, Roy (in progress) proposed a possible explanation for the performance pattern where individuals with PD showed intact learning within a session, but impaired retention over time. It was suggested that deficits in motor skill retention in PD might have resulted from impaired procedural processing due to striatal dysfunction. The experimenters proposed that due to an impaired procedural system, individuals with PD might have compensated by instead relying on declarative memory when learning motor skills. Thus, within a session, participants with PD were able to learn motor skills, but they were not able to retain this knowledge because their declarative memory declined over the 3-week delay. Though this type of compensation may have occurred, further investigation into motor skill performance in PD is required.

Motor Skill Learning and Retention in Parkinson's disease

Intact learning within a session has been consistently reported in previous studies that examined motor skill learning in PD on a variety of tasks (see Nieuwboer, Rochester, Muncks, & Swinnen, 2009 for a review). However, fewer studies have examined the effects of delay on motor skill retention, and findings have been less consistent. It is important to note that factors such as the complexity of the task, the amount and type of training, and the retention intervals varied across studies, so mixed results could be attributable to such differences. For example, Marinelli and colleagues (2009) and Bedard and Sanes (2011) reported normal rates of learning within a session, but impaired retention after a 24-hour delay on visuomotor adaptation tasks in individuals with PD. In contrast, individuals with PD have shown unimpaired retention after 48 hours on a rapid-arm reaching task (Behrman, Cauraugh, & Light, 2000). In addition, Smiley-Oyen, Lowry and Emerson (2006) reported unimpaired retention on movement sequence tasks

after two days and three weeks in individuals with PD. It is worth noting that in this study participants completed extensive training over a three-week period, which may have contributed to unimpaired retention performance.

Acquisition and long-term retention of a newly learned motor skill in PD was also investigated by Mochizuki-Kawai and colleagues (2004). In this study, participants with PD learned and practiced a motor skill during four sessions over 18 months. Overall, the study demonstrated that people with PD could acquire new motor skills, as they had unimpaired learning within a session, and they retained performance up to a month later. However, they did not retain these skills over longer delays, and they were unable to perform the skills after 3 and 18 months. Based on these findings, the experimenters concluded that the striatum is required for motor skill consolidation. They proposed that because PD participants had a compromised striatal system, they were unable to form long-lasting motor skills that were retained over time. However, the authors also suggested that more frequent training might be beneficial, as individuals with PD retained their performance for up to one month after training.

Can Practice Modulate the Relative Use of Different Memory Systems?

As individuals with PD demonstrate impaired motor skill retention, it is important to consider factors that may improve long-lasting performance of skills. One factor may be the amount of practice that individuals with PD are given. It has been proposed that there are three distinct phases in motor learning: 1) a fast, early learning phase, mediated by declarative memory, when considerable improvement occurs initially, 2) a consolidation stage where motor skills become resistant to decay or interference, and 3) a slower, later learning phase, mediated by procedural memory, when practice leads to smaller improvements over time (Albouy et al., 2013). In healthy younger adult participants it has been shown that as practice with motor

learning increases, striatal activation also increases, whereas hippocampal activation decreases (Albouy et al., 2008; Albouy et al., 2013). Thus, it could be argued that in motor learning more extensive practice may result in an increasing role for procedural memory, and a decreasing role for declarative memory, at least in younger, healthy adults.

However, as individuals with PD have striatal dysfunction, they may be impaired in switching from a declaratively mediated fast learning phase to a procedurally mediated slow learning phase. In support of this possibility, Shohamy, Myers, Onlaor and Gluck (2004) examined performance of individuals with PD and controls during the weather prediction task. Results showed that individuals with PD were impaired on the task during later training trials, but not in early training trials. Their analysis suggested that during early learning both controls and individuals with PD used “sub-optimal” strategies mediated by declarative processes. However, with practice in later learning, healthy controls, but not individuals with PD, switched to an “optimal” strategy using stimulus-response associations mediated by the basal ganglia. Thus, practice may be an important factor to consider in motor skill learning because it has been shown to increasingly engage procedural memory processing in healthy adults. However, the adoption of an “optimal,” striatally mediated strategy may be impaired in individuals with PD, but this has not yet been investigated in motor skill learning and retention with novel complex tools.

It has also been reported that although additional practice may not result in unimpaired retention, it may benefit people with PD in overall learning. For example, Leow, Loftus and Hammond (2012) showed that in a motor adaptation task, compared to controls, people with PD were impaired during within-session learning and retention after a 24-hour delay even after overlearning (i.e., repetitive practice). However, despite these impairments, individuals with PD

showed some improvement that was indicative of learning over time. Most critically, the results showed that people with PD did not have an absolute deficit in learning; though they had a slower learning rate and retained less over time, they still demonstrated attenuated learning that benefitted performance.

Overview and Rationale of the Current Experiment

The purpose of the current study was to extend the findings from Roy (in progress) by investigating factors that may affect motor skill learning and retention in complex tool use in PD. Specifically, the current experiment examined the effects that additional practice and shortened retention intervals have on performance. These factors have been shown to affect procedural memory impairments in individuals with PD, although the previously discussed studies used different tasks, different retention intervals and different amounts of practice. One goal of the current study was to provide a better understanding of the motor skill impairment in individuals with PD and clarify whether long-term motor skill performance can be improved. Additionally, the findings could help to better understand the neural and psychological processes that underlie tool-related motor skill performance in PD (i.e., whether there may be an interaction between the declarative and procedural memory systems). Specifically, I examined (a) whether individuals with PD demonstrate motor skill learning over time with more extensive training and (b) whether individuals with PD retain their motor skill performance after delays.

To assess these questions, a similar experimental procedure as described in Roy (in progress) was used, but participants were given more extensive training and were tested at shorter delays. Memory for various aspects of tool use (i.e., recall of tool attributes and function, grasp of tool, skilled tool use, and motor skill learning/retention) was tested in a sample of individuals with PD and a group of healthy age and education-matched controls, with the

primary focus on motor skill performance during training. Participants were tested over four sessions, with one day, approximately one week, and approximately three weeks between the sessions, respectively.

Based on the assumption that individuals with PD are impaired on procedural processing that is striatally mediated the following hypotheses were proposed. First, I hypothesized that compared to controls, individuals with PD would demonstrate equivalent motor skill learning within each of the four training sessions, as Roy (in progress) reported intact learning within one session. Second, I predicted that compared to healthy controls, people with PD would be impaired in their retention of these motor skills, even after a 1-day delay. If individuals with PD relied on declarative memory to learn motor skills, it was expected that their performance would decline between sessions, as their declarative memory may deteriorate over time. Third, I investigated whether individuals with PD would still demonstrate some overall learning across sessions as a result of more extensive training, despite forgetting between sessions. As proposed by Leow and colleagues (2012), people with PD may still be able to learn motor skills with more practice, but demonstrate attenuated benefits due to striatal dysfunction. However, it was unclear whether people with PD would show a similar pattern of improvement with novel tools, as the nature of task differed from the previously used motor adaptation task.

In addition to examining motor skills, performance on recall of tool attributes, grasp and skilled tool use was also investigated. As performance of the recall and grasp measure are proposed to be mediated by declarative memory (Roy & Park, 2010; Roy, in progress), it was hypothesized that performance would also decline over the delays, and would not differ between the two groups. However, skilled tool use may be mediated by both declarative and procedural

memory systems, and because it was unclear how practice would affect performance, there were not any detailed predictions for skilled tool use performance.

Method

Participants

Eighteen participants with a diagnosis of idiopathic PD and 18 healthy aged and education-matched controls were recruited to complete the study. Participants with PD were recruited from the Sun Life Financial Movement Disorders Research Centre (MDRC), affiliated with Wilfred Laurier University in Waterloo, Ontario, Canada. Control participants were recruited through advertising within local communities. Participants with PD did not significantly differ from control participants on any characteristics, which are displayed in Table 1.

All participants were required to be right-handed, fluent English speakers, and between the ages of 50 and 85. Participants were excluded from the study if they had a reported history of any neurological illness (besides PD in the patient group), a history of serious head injury, current anxiety or depression as assessed by the Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983), general cognitive deterioration as demonstrated by a score below 26 on the Mini-Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975), or colour blindness. Additional exclusion criteria included: difficulty using right hand as a result another condition or injury; severe tremor in the right hand (or severe tremor in the left hand, which affected ability to use the right hand); severe bradykinesia; or severe rigidity in the right wrist or hand. To assess these criteria, prior to participation, participants answered questions about their daily functioning, and current scores from the motor section of the Unified Parkinson's Disease Rating Scale (UPDRS III; Fahn & Elton, 1987) were examined for participants with PD.

Participants remained on their regular medication throughout the study and were tested during their optimal medication levels. Seventeen PD participants were taking dopaminergic drugs, and one PD participant was not taking any medication. The study was approved by the relevant ethics review boards, and all participants gave written consent prior to participation.

Materials

Novel Tools. Nine novel complex tools were created for the study. The tools were constructed from a children's building toy, K'NEX (see Figure 1). The tools were modeled after those developed by Roy & Park (2010), but some of the tools in the current study differed in their design and function. Each novel tool was unique in its appearance and function, and was constructed so that its function and manner of grasping could not be inferred from its appearance. The tools were designed to be grasped unimanually, and performed a specific task by acting on an object, known as the recipient. For example, one of the tools picked up and moved a ring (the recipient) to a designated area, and another tool was used to balance a cylindrical object, as the tool moved in a counterclockwise, circular motion. Each tool was painted a different color and pilot testing showed that the function, grasp and use of the tool could not be determined based on the physical appearance of the tool. The tools were randomly divided into three equal tool sets (Set A, B, and C).

Training Videos. Each tool had an instructional video to explain its correct use. The videos were approximately 30 seconds in length and were played on a laptop. Each video featured a demonstration of the task and audio instructions, which provided enough information and detail to enable participants to understand how the task was performed.

Recall Test. A cued Recall test was used to assess knowledge of tool attributes and function. The retrieval cue consisted of three different grey-scale images for each tool, which

were presented on one page. In response to each cue, participants gave verbal responses to questions inquiring about 1) the function of the tool 2) the colour of the tool 3) the recipient of the tool 4) the colour of the recipient and 5) the number of recipients used in that task. Each response was recorded by the experimenter.

Grasp-to-command Test. One at a time, each tool was placed in front of the participant. Using their right hand, participants were instructed to grasp the tool in the correct way if they were to use it. To ensure no cues were given as to the correct grasp, the experimenter placed the tools down using an overhand grasp in one of three random orientations. Feedback was not provided during this task.

Use-to-command Test. The Use-to-command test was a measure of skilled tool use. During the task, the experimenter placed the tool and its associated materials (e.g., the recipient) in front of the participant. Participants were then instructed to demonstrate the correct use of the tool and to inform the experimenter once they completed the task. It is important to note that tools were placed in the correct starting location, but the associated recipients were placed in a designated location, which was the same for all tools. Thus, to accurately complete the task, the recipient had to be placed in the correct starting location prior to carrying out the task. Participants had a 120-second time limit to complete one errorless attempt, and timing began once the tool made contact with the recipient. During this task, participants did not receive any feedback on their performance.

Neuropsychological Tests. All participants with PD completed a battery of standardized neuropsychological tests, which was administered during a 60-minute session that was separate from the four experimental sessions. This battery consisted of the Brief Visuospatial Memory Test Revised (BVMT-R; Benedict, 1997), Hopkins Verbal Learning Test-Revised (HVLTR;

Benedict, Schretlen, Groninger, & Brandt, 1998), Stroop test - Victoria version (Troyer, Leach, & Stauss, 2006), Boston Naming Test (BNT; Kaplan, Goodglass, & Weintraub, 1983), Rey-Osterrieth Complex Figure Test (ROCF; Osterrieth, 1944; Fastenau, Denburg, & Hufford, 1999), FAS Verbal Fluency Test (Spreen & Benton, 1977), Animal Naming Test (Tombaugh, Kozak & Rees, 1999), Trail Making Test (Reitan & Wolfson, 1985; Tombaugh, Rees, & McIntyre, 1998), selected tests from the Wechsler Adult Intelligence Scale (WAIS-IV; Wechsler, 2009), and Grooved-Pegboard test (Matthews & Klove, 1964). Test results for each participant were combined, and an overall cognitive profile for the PD group is displayed in Table 2. As shown in Table 2, participants with PD performed in the normal range on all neuropsychological test scores, with the exception of the Grooved Pegboard Test, which is a test requiring dexterity, processing speed and other psychological processes (Strauss, Sherman, & Spreen, 2006). Control participants did not complete formal cognitive testing.

Design and procedure

Participants were tested individually during four sessions (S1, S2, S3, S4). S1 and S2 occurred one day apart, S2 and S3 occurred 6-7 days apart, and S3 and S4 occurred 20-22 days apart¹. Each session was identical in design and format, and consisted of the Pre-test, Training and Post-test. Across participants and trials, the order within a tool set was fixed, but the administration of the sets (i.e., A, B, and C) was counterbalanced.

Six tools (i.e., two sets) were used for each participant to minimize fatigue and keep sessions within one hour. Consequently, only three tools were included in the Pre-test and Post-test. A detailed description of the study's design is provided in Figure 2. Additionally, an example of the procedure for a given participant will be described in the sections below.

¹ Participants with PD completed an additional, separate session for neuropsychological testing.

Pre-test. The Pre-test consisted of a Recall test followed by Grasp-to-command and Use-to-command tests. For each participant, only one set of the tools was used (e.g., Set A), but the tool set varied across participants and each set was tested an equal number of times. The Pre-test in S1 was used to determine that the attributes, function, grasp and use of the tools could not be inferred prior to Training. The Pre-tests in S2, S3 and S4 were used to investigate retention of knowledge and performance after the delays.

Training. Once the Pre-test was completed, participants were trained on two tool sets (e.g., Set B and Set A). During Training, one at a time, the tool and its associated objects were placed in front of the participant, in the same way they were positioned in the Training video. Participants then viewed the video, which demonstrated the proper grasp and use of the tool. Participants were not allowed to handle the tool while the video was playing. Immediately after viewing the video, participants were instructed to use the tool in the same way as in the video, and to complete the task as quickly as possible while minimizing errors. Participants had a 120-second time limit to complete one errorless attempt. Timing began once the tool made contact with the recipient. During this time, the experimenter provided feedback if any errors were made (e.g., incorrect grasp, recipient placement or task order), and participants were asked to start over. Immediately after completing the first Training trial or once the 120 seconds elapsed, the task was reset so that the tools and associated objects were positioned as they were at the start of the video, and participants completed a second training trial.

Post-test. Like the Pre-test, the Post-test consisted of the Recall, Grasp-to-command and Use-to-command tests. The tool set used in the Post-test was the set used in Training that was not administered in the Pre-test (e.g., Set B). In addition, the tool set assessed in the Post-test was the set that was administered first in Training session in order to reduce recency effects, and to

examine recall and performance after a short delay. For example, a participant completed the Pre-test on Set A and was then trained on Set B and Set A. The post-test was then conducted using Set B (refer to Figure 2 for full counterbalancing of administration).

At the end of the Post-test during S4, participants completed a training trial on the tool set that had not been used in the previous sessions (e.g., Set C). This extra trial on the untrained tool set was included to determine whether previous training with the other tools generalized to improvement in performance with other novel tools.

Scoring

During Training, motor skill performance was measured as completion time. This measure reflects the amount of time required to complete one errorless, successful attempt. Timing began once the tool made contact with the recipient. If the task could not be successfully completed within the time limit, participants received the maximum score of 120 seconds. Also, the number of attempts was recorded, which accounts for the number of errors that were made prior to successfully performing one errorless trial.

For the Recall test, performance was measured as the percentage of accurate responses to the items in each trial. Participants received one point for a correct answer and zero points for an incorrect answer. A scoring rubric of accurate responses was developed from previous pilot testing.

Grasp-to-command performance was measured as the percentage of accurate grasps in each trial, where one point was awarded for every correct grasp. A second independent rater scored 25% of the data, and inter-rater reliability was 94.07% (calculated as percentage of agreement).

Use-to-command performance was assessed by accuracy and time. Accuracy was measured as the percentage of accurate tool demonstrations. One point was awarded if the task was performed successfully within the 120-second time limit. A second independent rater scored 25% of the data, and inter-rater reliability was 94.98% (calculated as percentage of agreement). Similar to Training scoring, Use-to-command time was measured as completion time, which reflected how quickly participants successfully performed the task.

Overview of Statistical Analyses

The purpose of the data analyses was to compare the effects of practice and duration of delay on performance of PD participants relative to controls. Specifically, two different patterns of performance were examined: 1) Patterns of learning and 2) Patterns of forgetting. To investigate the effects of practice on learning, I analyzed whether participants improved their performance across days (i.e., the four sessions), as well as within each session. To examine forgetting, I analyzed whether the number of days delayed between sessions affected differences in performance. These two patterns of interest were examined using different models (Model 1 and Model 2, respectively). Linear mixed models were used to assess these questions because the data are longitudinal, and some of the independent variables are continuous (Shek & Ma, 2011). The analyses for Model 1 and Model 2 were performed using the mixed model procedure in SPSS 17.0 statistical software. For each model, the fixed effects were examined using the maximum likelihood method. The design of Model 1 differed for the Training task than the other tests (i.e., Use-to-command, Recall and Grasp-to-command) because Training performance had a non-linear pattern, which will be subsequently described in more detail. The design of Model 2 was similar for all tool measures. For all analyses, only statistically significant results are reported.

Results

Training

Model 1: Learning

For Training, the outcome variable for Model 1 was completion time. The fixed effects associated with GROUP (PD participants vs. controls), DAY (the day each session was completed, where S1= day 1, S2 = day 2, S3 = day 8 or 9, S4 = day 29 or 30)², and TRIAL within each session (the first vs. second Training trial) were examined. In the analyses, day and trial were treated as continuous variables, and group was treated as a categorical factor. To account for the curvilinear pattern in Training performance, the data were linearized by performing a negative inverse transformation on the DAY variable [$-(1/X)$, where X= the day each session was completed], referred to as LINEARIZED DAY. The fixed effects of the interactions of GROUP by LINEARIZED DAY, GROUP by TRIAL, and LINEARIZED DAY by TRIAL were also examined. Thus for Training, Model 1 had a total of seven predictors.

The three predictor variables (i.e., GROUP, LINEARIZED DAY and TRIAL) were centered. To facilitate the interpretation of the findings, for the GROUP variable, the value of 0 was assigned to controls (and PD participants = 1), to allow control participants to be the reference group. The TRIAL variable was centered, so the first trial in each session was assigned a value of 0, and the second trial was given a value of 1. The LINEARIZED DAY variable was also centered by adding 1 to the term (i.e., $-(1/DAY) + 1$), so the first session began when DAY = 0. Thus by centering the variables, the intercept represents the completion time of the PD group at the first trial in the first session (i.e., the beginning of the study).

² There was slight variation in the days participants were tested in S3 and S4. The exact day each participant was tested was entered into the analysis.

There were four main questions to assess learning: 1) Did the effect of group contribute to performance (e.g., Was there a difference between PD participants and controls in their completion time during Training?); 2) Did the effect of days contribute to performance (e.g., Did performance on Training improve over sessions?); 3) Did the effect of trial contribute to performance (e.g., Did participant improve their completion time from the first to second Training trail within each session?); and 4) Did these variables interact in any way?

Learning Analysis. To evaluate whether participants benefited from practice and improved their Training performance, completion time was analyzed as the outcome variable with the seven specified fixed effects for Model 1³⁴. Figure 3 shows Training performance measured as the mean completion in seconds for both training trials within the four sessions (i.e., after a 1-day, 7-day and 21-day delay). There was a main effect of group [$F(1, 216) = 19.88, p < .001$] indicating that overall, PD participants were slower than controls. More critically, there was a significant effect of linearized day [$F(1, 216) = 12.91, p < .001$], which shows that participants became faster over the four sessions. However, there was no significant interaction between group and linearized day, suggesting that improvement did not differ across groups. In addition to overall learning, there was a significant effect of trial [$F(1, 216) = 9.17, p = .003$], showing that participants became faster from the first trial to the second trial within a session. Conversely, there was not a significant interaction between group and trial, indicating that within-session improvement did not differ between groups.⁵

³ In order to ensure that average time scores were not inflated by incomplete attempts (i.e., maximum time scores of 120 seconds), incomplete attempts were removed before conducting analyses on completion time for both Training and Use-to-command

⁴ Performance was also examined using total completion time, which assessed the total time required to complete the task, from the beginning of the first attempt to the end of the errorless attempt. Similar patterns of performance were obtained for both Training and Use-to-command data.

In summary (see Table 3), PD participants were slower than controls, but both groups benefited from practice by improving similarly within and across sessions.

Model 2: Forgetting

Model 2 investigated the effects of delay between sessions on performance. The outcome variable for Model 2 was a difference score, which was calculated as the difference in completion time from the first training trial in one session and the second training trial in the preceding session. Specifically, for Training data, scores were computed for the differences in completion time from T3 to T2 (a one-day delay), T5 to T4 (a 7- day delay), and T7 to T6 (a 21- day delay).

The fixed effects associated with GROUP, DELAY (the number of days between each session), and the interaction of GROUP by DELAY were examined. There were three main questions to assess forgetting: 1) Did the effect of delay contribute to forgetting (e.g., Did participants retain their speed of performance during Training after the delays?); 2) Did the effect of group contribute to performance (e.g., Was there a difference in the amount of forgetting between PD participants and controls?); and 3) Did these variables interact in any way?

Forgetting Analysis. Figure 4 displays the differences in Training performance measured as the mean differences in completion time across the three delays (i.e., 1 day, 7 days and 21 days) for PD participants and controls. Mixed linear model analyses showed that there was a significant effect of group [$F(1, 108) = 4.74, p = .033$] demonstrating a difference in the amount of forgetting between PD participants and controls (see Table 3). As shown in Figure 4, PD participants were much slower after each delay, as their completion time increased. However, controls appeared to maintain their performance, as their completion times were similar before and after the delays.

In summary from Model 1 and Model 2 the findings showed that both PD participants and controls demonstrated learning because their Training performance improved over time. However, despite this similarity in overall learning, the groups showed different patterns of forgetting; controls retained their performance between sessions whereas PD participants were slower after each delay.

Error Analysis: Number of Attempts

Learning. Figure 5 presents the mean number of attempts made during Training. To assess if unsuccessful attempts affected performance, the mean number of attempts was examined as the outcome variable with the six specified fixed effects. None of the effects were significant (see Table 4). Therefore, there was not a difference in the number of errors made by PD participants and controls, and the number of errors did not significantly decrease across trials or sessions.

Forgetting. The mean differences in the number of attempts during Training are shown in Figure 6. The outcome variable was the difference in the number of attempts from the Post-test in one session and the Pre-test in the previous session, and the three previously specified fixed effects were examined. There were no significant effects (see Table 4), demonstrating that participants did not make more errors after the delays, and this pattern was not different for PD participants and controls.

Tool-specific Improvements in Motor Skill Learning

To examine whether motor skills acquired during Training were tool-specific, completion time in T1 was compared to the untrained tool set (completed in S4). A two-way mixed ANOVA was used with training trial (T1 and UT) and group (PD and control) as factors, and completion time as the dependent variable. For the PD group, the average completion time (in seconds) was

33.13 ($SD = 10.82$) for Trial 1, and 32.02 ($SD = 10.65$) for the untrained set. For the control group, the average completion time (in seconds) was 25.21 ($SD = 10.27$) for Trial 1, and 25.76 ($SD = 11.72$) for the untrained set. The analysis showed that there was a main effect of group $F(1, 34) = 4.33, p = .045, \eta^2 = .11$), but no significant interaction, or main effect of trial. Thus, although controls were faster than PD participants overall, there were no differences in completion time between T1 and untrained tools. Therefore, skills acquired during training did not generalize to other novel tools.

Overview of Analyses: Use-to-command, Recall and Grasp-to-command Tests

Model 1: Learning

For the remaining tests (i.e., Use-to-command, Recall and Grasp-to-command), a similar Model 1 was used to assess learning. However, as performance patterns were already linear, a transformation was not performed on the DAY variable. The outcome variable for Model 1 was the dependent variable that corresponded to each task (i.e., completion time or accuracy). The fixed effects associated with GROUP, DAY and TRIAL (the Pre-test vs. Post-test) were assessed, as well as the fixed effects of the interaction between GROUP by DAY, GROUP by TRIAL, and DAY by TRIAL. Thus, Model 1 had a total of 6 predictors.

As expected, none of the participants were able to accurately complete any of the tool tasks in S1 Pre-test because the tools were novel and they had not completed any training. Thus, the mean completion time was 120 seconds for both groups, and the mean accuracy scores for all remaining measures were 0. As a result, S1 was excluded, so the Model 1 analyses only included S2, S3 and S4 in the DAY variable.

In addition, similar to the Training data, the predictor variables were centered to aid in the interpretation of our results. Thus, control participants served as the reference group, and

time began (i.e., DAY = 0) at the first trial in the second session (because the first session was excluded). The goal of the Model 1 analyses was to assess the same four questions outlined in the Training data.

Model 2: Forgetting

For Use-to-command, Recall and Grasp-to command, Model 2 was identical to the model used for the Training data.

Use-to-command Completion Time

Learning. Figure 7 presents Use-to-command time measured as the mean completion time in seconds. To assess whether participants improved how quickly they performed the Use-to-command test, completion time was examined as the outcome variable with the six specified fixed effects for Model 1. There was an effect of group [$F(1, 216) = 3.91, p = .05$], revealing that overall PD participants were slower than controls. However, there was not a significant interaction or main effect of day, indicating that the groups did not become faster over sessions (see Table 5). Thus, participants maintained a consistent completion time throughout the study.

Forgetting. The outcome variable was the difference in completion time from the Post-test in one session and the Pre-test in the preceding session (i.e., S2 Pre-test – S1 Post-test, S3 Pre-test – S2 Post-test, S4 Pre-test – S3 Post-test). The fixed effects of group, delay and their interaction were assessed. The mean differences in completion time are presented in Figure 8.

There were no significant effects for the three predictor variables in the model (see Table 4). Most importantly, there was not a main effect of group, demonstrating that the amount of forgetting did not differ between PD participants and controls. Therefore, participants did not get significantly slower after the delays, and this retention pattern did not differ between PD participants and controls.

In summary, Use-to-command completion time remained consistent over time and within the four sessions (Model 1), and participants maintained their speed across delays (Model 2).

Use-to-command Accuracy

S1 Learning. To examine initial learning during S1, performance was investigated using a two-way ANOVA with Use-to-command accuracy as the dependent variable, and group (PD and controls) and test trial (S1 Pre-test and S1 Post-test) as factors (Figure 9). There was only a main effect of test trial demonstrating that Use-to-command accuracy improved from S1 Pre-test to S1-Post test [$F(1, 34) = 372.53, p < .001, \eta^2 = .92$], and this improvement did not differ between groups. Thus, participants could not initially use the tools accurately, but their performance significantly improved after they completed Training.

Learning. Figure 9 shows Use-to-command performance measured as the mean accuracy scores. To assess whether participants improved their Use-to-command performance, accuracy was examined as the outcome variable with the six specified fixed effects. Overall, none of the effects were significant (see Table 6). Thus, PD participants and controls did not differ in their accuracy for the Use-to-command task. Additionally, performance did not become more accurate over time. However, this overall lack of improvement must be considered within the context of forgetting, which was assessed in Model 2.

Forgetting. The mean differences in Use-to-command accuracy scores are presented in Figure 10. The outcome variable in the analysis was the difference in Use-to-command accuracy from the Post-test in one session and the Pre-test in the preceding session with the fixed effects of the three previously specified variables. There was only a significant effect of delay [$F(1, 108) = 3.78, p = .05$] (see Table 5 for a summary). Both PD participants and controls were less accurate over the delays, but the amount of forgetting did not differ between the groups.

In summary, PD participants and control did not demonstrate learning over time, as their accuracy score did not significantly improve (Model 1). However, this lack of improvement was affected by the delays between sessions, whereby participants did not retain their performance over the delays (Model 2). Most importantly, this performance pattern was similar for both groups.

Recall Accuracy

S1 Learning. Initial learning in Recall was investigated using a two-way ANOVA with accuracy as the dependent variable, and group (PD and controls) and test trial (S1 Pre-test and S1 Post-test) as factors (Figure 11). There was only a main effect of test trial [$F(1, 34) = 1245.70, p = < .001, \eta^2 = .97$], which shows that Recall accuracy improved from S1 Pre-test to S1-Post test, and this improvement did not differ between groups. Therefore, participants could not accurately answer questions about the tools attributes and function initially, but their performance significantly improved after Training.

Learning. Figure 11 presents the mean accuracy scores for the Recall test. To assess whether participants improved their Recall performance, accuracy was assessed as the outcome variable with the six specified fixed effects. None of the effects were significant (see Table 7), demonstrating that PD participants and controls did not differ in their Recall performance. Moreover, participants did not become more accurate over time. However, this lack of learning may reflect forgetting between sessions (Model 2).

Forgetting. The mean differences in Recall accuracy scores are presented in Figure 12. In the analysis, the outcome variable was the difference in Recall accuracy from the Post-test in one session and the Pre-test in the preceding session, and the fixed effects were group, delay and their interaction. There was only a significant effect of days delayed [$F(1, 108) = 4.47, p = .04$]

(see Table 7 for a summary). Therefore, both PD participants and controls were less accurate over the delays. However, the amount of forgetting did not differ between the groups.

Overall, in the Recall task, participants did not improve significantly over sessions (Model 1). However, this lack of learning was affected by delays, as both PD participants and controls similarly demonstrated forgetting between sessions (Model 2).

Grasp-to-command Accuracy

S1 Learning. Performance was investigated using a two-way ANOVA with Grasp accuracy as the dependent variable, and group (PD and controls) and test trial (S1 Pre-test and S1 Post-test) as factors (Figure 13). There was a only main effect of test trial [$F(1, 34) = 190.86, p = < .001, \eta^2 = .85$], showing that Grasp accuracy improved from S1 Pre-test to S1-Post test for all participants. Thus, participants could not accurately demonstrate the grasp for the tools initially, but their performance significantly improved after Training.

Learning. Figure 13 presents the mean accuracy scores for the Grasp-to-command test. To assess whether participants improved their Grasp performance, accuracy was examined as the outcome variable with the six specified fixed effects. There was only a significant effect of the interaction between days and trial [$F(1, 216) = 4.84, p = .03$]. Thus, there was no significant improvement over sessions, and performance did not differ between groups (see Table 8). As shown by Figure 11, the significant interaction indicates that participants improved more from the Pre-test to the Post-test trial as days increased. This pattern of greater within-session improvement as time increased may be due to the pattern of forgetting across participants.

Forgetting. The mean differences in Grasp accuracy scores are shown in Figure 14. The outcome variable was the difference in Grasp accuracy from the Post-test in one session and the Pre-test in the previous session, and the three previously specified fixed effects were examined.

There was only a significant effect of delay [$F(1, 108) = 16.51, p < .001$] (see Table 8), demonstrating forgetting between sessions. As shown in Figure 14, both groups appeared to forget more as the length of the delay increased.

In summary, for the Grasp-to-command test, participants did not improve across sessions (Model 1). However, both group appeared to show greater within-session improvement as time increased. This increasing effect of trial over days was likely affected by the pattern of forgetting whereby participants forgot more as the delays increased (Model 2). Therefore, because participants retained less over time, they had the opportunity to make greater improvements within sessions.

Discussion

The current study examined the effects of delay and practice on tool-related motor skills. A sample of PD participants and healthy controls were trained on a set of novel complex tools over four sessions. Motor skill performance was examined during Training and memory for other aspects of tool use was examined during Recall, Grasp-to-command and Use-to-command tests. The purpose of the study was to determine whether more extensive training and shorter delays than used in Roy (in progress) would result in improvements with overall learning and retention, and further clarify the neural and psychological processes underlying motor skill performance in PD.

In assessing motor skill performance during Training, it was hypothesized that compared to controls, PD participants would demonstrate preserved learning within each of the four sessions. However, it was predicted that individuals with PD would be impaired in retaining these skills, by demonstrating slower completion times after delays. I also examined the possibility that despite forgetting, individuals with PD might still show some overall

improvement with more extensive training because practice has been previously shown to improve long-term learning of motor skills, although previous studies did not involve the use of novel tools (e.g., Leow et al., 2012). The analysis for learning showed that overall participants improved from the first to the second training trial within sessions. Thus, PD participants were not impaired during within-session learning. Results also revealed that PD participants appeared to benefit from practice because they became significantly faster across sessions. However, despite overall learning, unlike controls, PD participants also demonstrated forgetting between sessions: they became significantly slower even after a 1-day delay. Taken together, PD participants were able to improve their motor skill performance with practice, though they also exhibited significant forgetting.

Accuracy performance on Recall and Grasp-to-command tests was also examined. It was predicted that for both PD participants and controls accuracy would decline between sessions because performance on these tasks has been shown to be mediated by declarative memory, and it was hypothesized that this type of knowledge would deteriorate over the delays (Roy, in progress; Roy & Park, 2010). Results showed that for these tasks, both groups demonstrated significant forgetting between sessions, and possibly for that reason, participants also did not show improvement across sessions. Findings regarding accuracy for these aspects of tool use are consistent with previous studies suggesting that declarative knowledge is required for recalling information about a tool's attributes, and accurately demonstrating its correct grasp (Roy, in progress; Roy & Park, 2010).

Skilled tool use was assessed by the Use-to-command test where participants were required to demonstrate a tool's use without any cues or assistance after a delay. The task had two components: accuracy and completion time. The accuracy score indicated whether or not

participants performed the task accurately, whereas completion time indicated how quickly the successful task was performed. Results showed that for Use-to-command accuracy, both PD participants and control demonstrated forgetting over the delays, suggesting this aspect of the task was mediated, at least in part, by declarative memory. For completion time, the results were unexpected. Although individuals with PD were slower overall, their performance did not differ from that of controls. Both groups did not demonstrate learning within sessions because they did not get faster from the Pre-test to the Post-test, and participants did not show significant improvement across sessions. At the same time, participants did not demonstrate forgetting between sessions, as they did not get slower after the delays. Overall, participants' completion times remained consistent throughout the entire study, which is not consistent with a purely declarative or purely procedural performance pattern.

Tool-related Motor Skill Performance in Parkinson's disease

For performance during Training, individuals with PD were unimpaired in motor skill learning within sessions, which is consistent with Roy (in progress), and other studies examining within session motor skill learning in PD on different tasks (Nieuwboer et al., 2009). It is possible that individuals with PD demonstrated preserved performance because the striatum is not heavily required in early stages of motor skill learning. Instead, the cortico-cerebellar circuit and hippocampus have been found to be important in early learning phases during motor skill acquisition (Albouy et al., 2013; Doyon et al., 2009). However, in the later stages of learning when there is greater automaticity in performing the skill, the striatum has been shown to have greater activity, while activity decreases in the cortico-cerebellar circuit (Doyon et al., 2002) and hippocampus (Albouy et al., 2013).

Although people with PD demonstrated intact within-session learning, results indicated that compared to controls, PD participants were impaired in retaining their motor skill performance across the delays. This memory performance pattern of improved acquisition within session and memory loss after a delay is consistent with properties of declarative memory (Eichenbaum, 1997; Mitchell 1990; Squire, 2009), and with the performance pattern on the Recall and Grasp-to-command tests, which are mediated declarative memory (Roy & Park, 2010). Thus, one possibility is that individuals with PD used a compensatory strategy where they relied more heavily on declarative memory, mediated by the hippocampus, when performing tool-related motor skills, as a result of impaired procedural processing, mediated by the striatum. Thus, within a session, learning was preserved, but it was not retained over time because declarative memory declined over the delays. This possibly may have occurred because declarative and procedural memory have been previously shown to interact competitively during motor skill learning in healthy adults (Albouy et al., 2013). Additionally, previous studies have suggested that people with PD may have used a compensatory strategy during tasks that normally rely on the striatum. For instance, this type of compensatory relationship was demonstrated in a study examining performance of individuals with PD on the weather prediction task (Moody et al., 2004). Though the study did not find behavioural impairments in PD participants, neuroimaging analyses showed that there was decreased activation in the striatum, and increased activation in the medial temporal lobes in PD participants relative to controls. Thus, when the striatal system was compromised in PD, the hippocampal system appeared to be utilized to a greater extent.

A compensatory relationship in PD has also been reported from a study that examined nondeclarative learning in a perceptual-motor sequencing task, Serial Reaction Time (SRT)

(Gobel et al., 2013). Overall participants with mild cognitive impairment (MCI) were unimpaired on the SRT task whereas participants with PD were impaired. However, two participants with PD displayed an interesting pattern of performance that suggested they might have employed a declarative strategy to complete the task. Thus, the authors speculated that individuals with PD might compensate impaired nondeclarative learning by relying more on declarative processing.

An alternative possibility may be that performance was not retained due to inefficient procedural processing. Participants in the current study had mild-moderate PD, so they may have had some intact procedurally processing that was not functioning as efficiently as healthy controls. PD participants may have partially used procedural memory during learning, but due to some dysfunction, their performance deteriorated between sessions. The possibility of partially intact procedural processing is supported by the overall learning pattern where people with PD demonstrated significant improvement across sessions that did not differ from controls. The prospect that individuals with PD may not have an absolute deficit in procedural memory is important because it suggests that people with PD may still be able to show some long-lasting performance of motor skills; the findings from current study demonstrate individuals with PD can acquire and improve upon new motor skills, but require more extensive practice possibly because their striatal system functions less efficiently.

Shohamy and colleagues (2008) proposed a similar explanation for impaired performance on probabilistic category learning in PD. In their study, the experimenters used computational modeling to examine the effects of extensive practice on the weather prediction task by individuals with PD. The model revealed that early in the task (i.e., after 600 trials), the PD group had a slower learning rate compared to the control group, so they displayed impaired performance. However, after extensive amounts of practice (i.e., 3000 trials), the PD group

showed similar performance compared to the control group. Thus, Shohamy and colleagues argued that people with PD might have a generalized slowing, but not an absolute loss, in nondeclarative learning.

The extent to which individuals with PD may still be able to use procedural memory when performing motor skills warrants further investigation. To examine whether it is possible to bias the use of procedural memory, one could investigate whether inhibiting the use of declarative memory during Training would result in a greater reliance on procedural memory. Support for this possibility comes from a study by Foerde, Knowlton and Poldrack (2006) that examined whether the use of a distracting secondary task affected declarative and procedural memory involvement during probabilistic classification learning. Their results showed that activity in the striatum was strongly correlated with performance during the dual-task condition, whereas activation in the hippocampus was strongly correlated with performance when the secondary task was not performed concurrently during probabilistic classification learning. These findings suggest that it is possible to bias the use of a certain memory system through the use of a secondary task, which could be used to further investigate tool-related motor skill learning in PD, and the underlying neural and psychological processes.

Performance During Skilled Tool Use

Unlike performance patterns during Training and the other tool tests, findings for Use-to-command (i.e., skilled tool use) were somewhat puzzling. In their Use-to-command accuracy scores, both PD participants and controls demonstrated forgetting between sessions. However, during completion time performance, PD participants did not demonstrate learning within sessions or forgetting between delays, which is inconsistent with findings from Roy (in progress). Regarding completion time during the Use-to-command test, Roy's (in progress)

findings suggested that this aspect of the task may be mediated by procedural memory because PD participants became faster within a session, and unlike controls, people with PD did not retain their performance after a 3-week delay. However, the current study's findings suggest that the sample of participants did not use procedural memory because they did not show any learning.

It is unclear why this inconsistency exists, but one possible explanation is that participants in the two studies used different strategies to complete the Use-to-command test. Previous research suggests that skilled tool use requires an interaction of both memory systems (Roy & Park, 2010; Roy, in progress), and a number of factors may bias the extent to which participants use declarative and procedural memory. Additionally, within the current study's patient sample, it may be that different PD participants relied on different memory systems during their tool use demonstration. For example, for PD participants' Use-to-command completion time, there was considerable variability in their forgetting performance, as demonstrated by large standard errors (refer to Figure 6). The variability in performance raises the possibility that in the current study, participants with PD might have shown different patterns of learning. For instance, it may be the case that some individuals with PD showed a procedural learning pattern, where forgetting did not occur between delays, whereas other people with PD showed a declarative learning pattern, where they became significantly slower after delays. This variability in people with PD has been reported by Gobel and colleagues (2013), who suggested that two participants might have used a declarative strategy to complete a nondeclarative motor-skill learning task, whereas the other 13 participants appeared to rely on procedural memory. The possibility that these differences may have occurred within the PD group in the current study will be examined shortly.

Conclusion

The current study demonstrated that practice could benefit tool-related motor skill learning in PD. Although within-session gains may not be fully retained over delays, it is critical to note that motor skill performance of people with PD improved with more extensive training. The findings suggest that people with PD may still have partially intact striatal functioning and procedural memory, as they demonstrated some improvement that was robust to the effects of time. However, the lack of retention between delays also suggests that individuals with PD may have compensated for deficits in procedural memory by relying more heavily on declarative memory when learning motor skills. Although these are reasonable possibilities, the current study has limitations, as the findings cannot lead to decisive conclusions about the underlying neural and psychological mechanisms.

Having the ability to learn and improve upon newly learned motor skills might have important implications for rehabilitation. Although individuals with PD may have impaired striatal functioning, this does not necessarily result in a complete inability to learn and retain new motor skills. Though people with PD may not fully retain performance over time, the current study showed that individuals with PD demonstrated improvement with more extensive training in learning new motor skills.

References

- Albouy, G., King, B. R., Maquet, P., & Doyon, J. (2013). Hippocampus and striatum: Dynamics and interaction during acquisition and sleep-related motor sequence memory consolidation. *Hippocampus*, *23*, 985-1004. doi: 10.1002/hipo.22183
- Albouy, G., Sterpenich, V., Vandewalle, G., Darsaud, A., Gais, S., Rauchs, G.,... Maquet, P. (2012). Neural correlates of performance variability during motor sequence acquisition. *Neuroimage*, *60*, 324–331. doi: 10.1016/j.neuroimage.2011.12.049
- Albouy, G., Sterpenich, V., Balteau, E., Vandewalle, G., Desseilles, M., Dang-Vu, T.,...Maquet, P. (2008). Both the hippocampus and striatum are involved in consolidation of motor sequence memory. *Neuron*, *2*, 261-272. doi: 10.1016/j.neuron.2008.02.008
- Ambrose S. H. (2001). Paleolithic technology and human evolution. *Science*, *291*, 1748-1753. doi: 10.1126/science.1059487
- Beaunieux, H., Hubert, V., Witkowski, T., Pitel, A., Rossi, S., Danion, J.,...Eustache, F. (2006). Which processes are involved in cognitive procedural learning? *Memory*, *14*, 521-539. doi: 10.1080/09658210500477766
- Bedard, P., & Sanes, J. N. (2011). Basal ganglia-dependent processes in recalling learned visual-motor adaptations. *Experimental Brain Research*, *209*, 385-393. doi: 10.1007/s00221-011-2561-y
- Behrman, A. L., Cauraugh, J. H., & Light, K. E. (2000). Practice as an intervention to improve speeded motor performance and motor learning in Parkinson's disease. *Journal of Neurological Sciences*, *174*, 127-136. doi: 10.1016/S0022-510X(00)00267-7
- Benedict, R. H. B. (1997). *Brief Visuospatial Memory Test - Revised*. Professional manual. Odessa, Fla: Psychological Assessment Resources.

- Benedict, R. H. B., Schretlen, D., Groninger, L., & Brandt, J. (1998). The Hopkins Verbal Learning Test - Revised: Normative data and analysis of interform and test-retest reliability. *The Clinical Neuropsychologist, 12*, 43-55. doi: 10.1076/clin.12.1.43.1726
- Brashers-Krug, T., Shadmehr, R., & Bizzi, E. (1996) Consolidation in human motor memory. *Nature, 382*, 252-255. doi: 10.1038/382252a0
- Buckner, R. (2004). Memory and executive function in aging and AD: Multiple factors that cause decline and reserve factors that compensate, *Neuron, 44*, 195-208. doi: 10.1016/j.neuron.2004.09.006
- Cohn, M., Moscovitch, M., & Davidson, P. S. R. (2010). Double dissociation between familiarity and recollection in Parkinson's disease as a function of encoding tasks, *Neuropsychologia, 48*, 4142-4147. doi: 10.1016/j.neuropsychologia.2010.10.013
- Cohen, N. J., & Squire, L. R. (1980). Preserved learning and retention of pattern-analyzing skill in amnesia: Dissociation of knowing how and knowing that. *Science, 210*, 207-210. doi: 10.1126/science.7414331
- Corkin, S. (1968). Acquisition of motor skill after bilateral medial temporal lobe excision. *Neuropsychologia, 6*, 255-265. doi: 10.1016/0028-3932(68)90024-9
- Creem, S. H., & Proffitt, D. R. (2001). Grasping objects by their handles: A necessary interaction between cognition and action. *Journal of Experimental Psychology: Human Perception and Performance, 27*, 218-228. doi: 10.1037/0096-1523.27.1.218
- Davidson, P. S., Anaki, D., Ciaramelli, E., Cohn, M., Kim, A. S., Murphy, K. J.,...Levine, B. (2008). Does lateral parietal cortex support episodic memory? *Neuropsychologia, 46*, 1743-1755. doi: 10.1016/j.neuropsychologia.2008.01.011
- Doyon, J., Penhune, V., & Ungerleider, L. G. (2003). Distinct contribution of the cortico-striatal

- and cortico-cerebellar systems to motor skill learning. *Neuropsychologia*, *41*, 252-262.
doi: 10.1016/S0028-3932(02)00158-6
- Doyon, J., Song, A. W., Karni, A., Lalonde, F. Adam, M. M., & Ungerleider, L. G. (2002).
Experience-dependent changes in cerebellar contributions to motor sequence learning.
Proceedings of the National Academy of Science, USA, *99*, 1017-1022. doi:
10.1073/pnas.022615199
- Eichenbaum, H. (1997). Declarative Memory: Insights from Cognitive Neurobiology. *Annual
Review of Psychology*, *48*, 547-572. doi: 10.1146/annurev.psych.48.1.547
- Ellenbogen, J. M., Payne, J. D., & Stickgold, R. (2006). The role of sleep in declarative memory
consolidation: passive, permissive, active or none? *Current Opinion in Neurobiology*, *16*,
1-7. doi: 10.1016/j.conb.2006.10.006
- Fastenau, P. S., Denburg, N. L., & Hufford, B. J. (1999). Adult norms for the Rey-Osterrieth
complex figure test and for supplemental recognition and matching trails from the
extended complex figure test. *The Clinical Neuropsychologist*, *13*, 30-47. doi:
<http://dx.doi.org/10.1076/clin.13.1.30.1976>
- Foerde, K., Knowlton, B. J., & Poldrack, R. A. (2006). Modulation of competing memory
systems by distraction. *Proceedings of the National Academy of Sciences*, *103*, 11778-
11783. doi: 10.1073/pnas.0602659103
- Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). "Mini-mental state": A practical
method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric
Research*, *12*, 189-198. doi: 10.1016/0022-3956(75)90026-6
- Frey, S. H. (2007). What puts the how in where? Tool use and the divided visual streams
hypothesis. *Cortex*, *43*, 368-375. doi: 10.1016/S0010-9452(08)70462-3

- Gabrieli, J. D., Corkin, S., Mickel, S. F., & Growdon, J. H. (1993). Intact acquisition and long-term retention of mirror-tracing skill in Alzheimer's disease and in global amnesia. *Behavioral Neuroscience, 107*, 899-910. doi: 10.1037/0735-7044.107.6.899
- Gobel, E. W., Blomeke, K., Zadikoff, C., Simuni, T., Weintraub, S., & Reber, P. J. (2013). Implicit perceptual-motor skill learning in mild cognitive impairment and Parkinson's disease. *Neuropsychology, 27*, 314-321. doi: 10.1037/a0032305
- Harrington, D. L., Haaland, K. Y., Yeo, R. A., & Marder, E. (1990). Procedural memory in Parkinson's disease: Impaired motor but not visuoperceptual learning. *Journal of Clinical and Experimental Neuropsychology, 12*, 323-339. doi: 10.1080/01688639008400978
- Hodges, J. R., Bozeat, S., Lambon Ralph, M. A., Patterson, K., & Spatt, J. (2000). The role of conceptual knowledge in object use. Evidence from semantic dementia. *Brain, 123*, 1913–1925. doi: 10.1093/brain/123.9.1913
- Kaplan, E., Goodglass, H. Weintraub, S. (1983). *Boston Naming Test*. Philadelphia: Lea & Febiger.
- Knowlton, B. J., Mangels, J. A., & Squire, L. R. (1996). A neostriatal habit learning system in humans. *Science, 273*, 1399–1402. doi: 10.1126/science.273.5280.1399
- Knowlton, B. J., Squire, L. R., & Gluck, M. A. (1994). Probabilistic classification learning in amnesia. *Learning & Memory, 1*, 106-120. doi: 10.1101/lm.1.2.106
- Knowlton, B. J., Squire, L. R., Paulsen, J. S., Swerdlow, N., Swenson, M. & Butters, N. (1996). Dissociations within nondeclarative memory in Huntington's disease. *Neuropsychology, 10*, 538-548. doi: 10.1037/0894-4105.10.4.538
- Krebs, H. I., Hogan, N., Hening, W., & Adamovich, S. V. (2001). Procedural motor learning in Parkinson's disease. *Experiential Brain Research, 141*, 425-437. doi: 10.1007/s002210100871

- Leow, L., Loftus, A. M., & Hammond, G. R. (2012). Impaired savings despite intact initial learning of motor adaptation in Parkinson's disease. *Experimental Brain Research*, *218*, 295-304. doi: 10.1007/s00221-012-3060-5
- Lewis, S. J. G., Dove, A., Robbins, T. W., Barker, R. A., & Owen, A. M. (2003). Cognitive impairments in early Parkinson's disease are accompanied by reductions in activity in frontostriatal neural circuitry. *The Journal of Neuroscience*, *23*, 6351-6356.
- Marinelli, L., Crupi, D., Di Rocco, A., Bove, M., Eidelberg, D., Abbruzzese, G., & Felice Ghilardi, M. (2009). Learning and consolidation of visuo-motor adaptation in Parkinson's disease. *Parkinsonism & Related Disorders*, *15*, 6-11. doi: 10.1016/j.parkreldis.2008.02.012
- Matthews, C. G., & Kløve, H. (1964). Instruction manual for the adult neuropsychology test battery. University of Wisconsin Medical School, Madison.
- McFadden, L., Mohr, E., Sampson M., Mendis T., & Grimes, J. D. (1996). A profile analysis of demented and nondemented Parkinson's disease patients. *Advances in Neurology*, *69*, 339-341.
- Mitchell, D. B., Brown, A. S., & Murphy, D. R. (1990). Dissociations between procedural and episodic memory: effects of time and aging. *Psychology and Aging*, *5*, 264-276. doi: 10.1037/0882-7974.5.2.264
- Mochizuki-Kawai, H., Kawamura, M., Hasegawa, Y., Mochizuki, S., Oeda, R., Yamanaka, K., & Tagaya, H. (2004). Deficits in long-term retention of learned motor skills in patients with cortical or subcortical degeneration. *Neuropsychologia*, *42*, 1858-1863. doi: 10.1016/j.neuropsychologia.2004.03.012
- Moody, T. D., Bookheimer, S. Y., Vanek, Z., & Knowlton, B. J. (2004). An implicit learning

- task activates medial temporal lobe in patients with Parkinson's disease. *Behavioral Neuroscience*, *118*, 438–442. doi: 10.1037/0735-7044.118.2.438
- Moscovitch, M., Rosenbaum, R. S., Gilboa, A., Addis, D. R., Westmacott, R., Grady, C.,...Nadel, L. (2005). Functional neuroanatomy of remote episodic, semantic and spatial memory: a unified account based on multiple trace theory. *Journal of Anatomy*, *207*, 35-66. doi: 10.1111/j.1469-7580.2005.00421.x
- Nieuwboer, A., Rochester, L., Muncks, L., & Swinnen, S. P. (2009). Motor learning in Parkinson's disease: limitations and potential for rehabilitation. *Parkinsonism and Related Disorders*, *15S3*, S53-S58. doi: 10.1016/S1353-8020(09)70014-8
- Osterrieth, P.A. (1944). "Filetest de copie d'une figure complex: Contribution a l'etude de la perception et de la memoire [The test of copying a complex figure: A contribution to the study of perception and memory]". *Archives de Psychologie*, *30*, 286–356.
- Packard, M. G., & Goodman, J. (2013). Factors that influence the relative use of multiple memory systems. *Hippocampus*, *23*, 1044-1052. doi: 10.1002/hipo.22178
- Poldrack, R. A., Clark, J., Pare-Blagoev, E. J., Shohamy, D., Moyano, C., & Gluck, M. A. (2001). Interactive memory systems in the human brain. *Nature*, *414*, 546-550. doi: 10.1038/35107080
- Poldrack, R. A., Prabhakaran, V., Seger, C. A., & Gabrieli, J. D. (1999). Striatal activation during acquisition of a cognitive skill. *Neuropsychology*, *13*, 564-574. doi: 10.1037/0894-4105.13.4.564
- Poldrack, R. A., & Rodriguez, P. (2004). How do memory systems interact? Evidence from human classification learning. *Neurobiology of Learning and Memory*, *82*, 324–332. doi: 10.1016/j.nlm.2004.05.003
- Rieckmann, A., Fischer, H., & Backman, L. (2010). Activation in striatum and medial temporal

- lobe during sequence learning in younger and older adults: Relations to performance. *Neuroimage*, *50*, 1303-1312. doi: 10.1016/j.neuroimage.2010.01.015
- Reitan, R.M., & Wolfson, D. (1985). *The Halstead-Reitan Neuropsychological test battery: Theory and clinical interpretation*. Tucson, AZ: Neuropsychology Press.
- Renoult, L., Davidson, P. S., Palombo, D. J., Moscovitch, M., & Levine, B. (2012). Personal semantics: at the crossroads of semantic and episodic memory. *Trends in Cognitive Neuroscience*, *16*, 550-558. doi: 10.1016/j.tics.2012.09.003
- Rodriguez-Oroz, M. C., Jahanshahi, M., Krack, P., Litvan, I., Macias, R., Bezard, E., & Obeso, J. A. (2009). Initial clinical manifestations of Parkinson's disease: features and pathophysiological mechanisms. *The Lancet Neurology*, *8*, 1128-1139. doi: 10.1016/S1474-4422(09)70293-5
- Roy, S. (in progress). *Interaction of declarative and procedural memory systems during acquisition of tool-related knowledge and skills in Parkinson's disease* (Unpublished doctoral dissertation). York University, Toronto, ON.
- Roy, S., & Park, N. W. (2010). Dissociating the memory systems mediating complex tool knowledge and skills. *Neuropsychologia*, *48*, 3026-3036. doi: 10.1016/j.neuropsychologia.2010.06.012
- Sadeh, T., Shohamy, D., Levy, D. R., Reggev, N., & Marial, A. (2011). Cooperation between the hippocampus and the striatum during episodic encoding. *Journal of Cognitive Neuroscience*, *23*, 1597-1608. doi: 10.1162/jocn.2010.21549
- Salthouse, T. A., Atkinson, T. M., & Berish, D. E. (2003). Executive functioning as a potential mediator of age-related cognitive decline in normal adults. *Journal of Experimental Psychology*, *4*, 566-594. doi: 10.1037/0096-3445.132.4.566

- Seger, C. A., & Cincotta, C. M. (2006). Dynamics of frontal, striatal, and hippocampal systems during rule learning. *Cerebral Cortex*, *16*, 1546-1555. doi: 10.1093/cercor/bhj092
- Schendan, H. E., Searl, M. M., Melrose, R. J., & Stern, C. E. (2003). An fMRI study of the role of the medial temporal lobe in implicit and explicit sequence learning. *Neuron*, *37*, 1013–1025. doi: 10.1016/S0896-6273(03)00123-5
- Shek, D. T. L., & Ma, C. M. S. (2011). Longitudinal data analyses using linear mixed models in SPSS: Concepts, procedures and illustrations. *The Scientific World Journal*, *11*, 42-76. doi: 10.1100/tsw.2011.2
- Shohamy, D., Myers, C. E., Kalanithi, J., & Gluck, M. A. (2008). Basal Ganglia and dopamine contributions to probabilistic category learning. *Neuroscience and Biobehavioral Reviews*, *32*, 219-236. doi: 10.1016/j.neubiorev.2007.07.008
- Shohamy, D., Myers, C. E., Onlaor, S., & Gluck, M. A. (2004). Role of the basal ganglia in category learning: How do patients with Parkinson's disease learn? *Behavioral Neuroscience*, *111*, 676-686. doi: 10.1037/0735-7044.118.4.676
- Siegert, R. J., Taylor, K. D., Weatherall, M., & Abernethy, D. A. (2006). Is implicit sequence learning impaired in Parkinson's disease? A meta- analysis. *Neuropsychology*, *20*, 490–495. doi: 10.1037/0894-4105.20.4.490
- Silveri, M. C., & Ciccarelli, N. (2009). Semantic memory in object use. *Neuropsychologia*, *47*, 2634-2641. doi: 10.1016/j.neuropsychologia.2009.05.013
- Smiley-Oyen, A. L., Lowry, K. A., & Emerson, Q. R. (2006). Learning and retention of movement sequences in Parkinson's disease. *Movement Disorders*, *21*, 1078-1087. doi: 10.1002/mds.20906
- Spreeen, O., & Benton, A. L. (1977). Neurosensory Center Comprehensive Examination for

- Aphasia. Victoria, BC: Neuropsychology Laboratory, University of Victoria.
- Strauss, E., Sherman, E. M. S., & Spreen, O. (2006). *A compendium of neuropsychological tests: Administration, norms and commentary*. New York, NY: Oxford University Press.
- Squire, L. R. (1992). Memory and the hippocampus: a synthesis from findings with rats, monkeys, and humans. *Psychological Review*, *99*, 195-231. doi: 10.1037/0033-295x.99.2.195
- Squire, L. R. (2009). Memory And Brain Systems: 1969-2009. *Journal of Neuroscience*, *29*, 12711-12716. doi: 10.1523/JNEUROSCI.3575-09.2009
- Squire, L. R., Knowlton, B., & Musen, G. (1993). The structure and organization of memory. *Annual Review of Psychology*, *44*, 453-495. doi: 10.1146/annurev.ps.44.020193.002321
- Squire, L. R., & Zola, S. M. (1996). Structure and function of declarative and nondeclarative memory systems. *Proceedings of the National Academy of Science, USA*, *93*, 13515-13522. doi: 10.1073/pnas.93.24.13515
- Tombaugh, T. N., Kozak, J., & Rees, L. (1999). Normative data stratified by age and education for two measures of verbal fluency: FAS and animal naming. *Archives of Clinical Neuropsychology*, *14*, 167-177. doi: 10.1093/arclin/14.2.167
- Tombaugh, T. N., Rees, L., & McIntyre, N. (1998). Normative data for the Trail Making Test. Personal communication cited in Spreen and Strauss. *A compendium of neuropsychological tests: Administration, norms and commentary* (2nd ed.). New York: Oxford University Press.
- Tulving, E. (1985). How many memory systems are there? *American Psychologist*, *40*, 385-398. doi: 10.1037/0003-066X.40.4.385

- Troyer, A. K., Leach, L., & Strauss, E. (2006). Aging and response inhibition: Normative data for the Victoria Stroop Test. *Aging, Neuropsychology, and Cognition*, *13*, 20-35. doi: 10.1080/138255890968187
- Wechsler, D. (2009). Wechsler Memory Scale—Fourth Edition: San Antonio, TX: Pearson.
- Werheid, K., Zysset, S., Müller, A., Reuter, M., & Yves von Cramon, D. (2003). Rule learning in a serial reaction time task: An fMRI study on patients with early Parkinson's disease. *Cognitive Brain Research*, *16*, 273-284. doi: 10.1016/S0926-6410(02)00283-5
- Zigmond, A. S., & Snaith, R. P. (1983). The Hospital Anxiety And Depression Scale. *Acta Psychiatrica Scandinavica*, *67*, 361-370. doi: 10.1111/j.1600-0447.1983.tb09716.x

Table 1.

Participant Characteristics

Variable	PD (n = 18)		CON (n = 18)		p-value
	M	SD	M	SD	
Age	66.3	10.2	67.8	11.18	.67
Education (years)	14.9	3.9	13.2	2.8	.16
Gender (M/F)	13/5		12/6		
MMSE (/30)	28.7	1.1	28.8	1.1	.77
HADS (/42)	9.2	4.2	7.9	3.11	.33
HADS-anxiety (/21)	4.8	2.5	4.1	2.2	.36
HADS-depression (/21)	4.2	2.2	3.8	2.1	.58
Years Since Onset	7.2	5.4			
UPDRS motor section	22.6	7.3			
Side Affected (L/R/B)	10/5/3				
LED (mg/day)	647.83	374.21			

PD, Parkinson's disease; CON, Controls; MMSE, Mini-mental State Examination; HADS, Hospital Anxiety and Depression Scale; UPDRS, Unified Parkinson's Disease Rating Scale; L/R/B, Left/Right/Both; LED, levodopa-equivalent dose.

Table 2

Standardized z-scores for Participants with Parkinson's disease^a

Neuropsychological Test	M (SD)	p-value ^b
<i>WAIS-IV (selected subtests)</i>		
Digit Span	.09 (.80)	.63
Matrix Reasoning	.35 (.87)	.11
Information	.28 (.68)	.10
<i>HVLT-R</i>		
Total Recall (T1-T3)	-.22 (.81)	.28
Delayed Recall	-.36 (.80)	.07
Percent Retained	-.24 (.76)	.19
Recognition Discrimination	-.16 (1.11)	.55
<i>BVMT-R</i>		
Total Recall (T1-T3)	-.10 (1.11)	.71
Delayed Recall	-.01 (1.39)	.97
<i>ROCF</i>		
Copy	-.02 (.89)	.93
Immediate	.48 (1.18)	.10
Delayed	.16 (1.22)	.60
<i>Trail Making Test</i>		
Part A	-.70 (1.84)	.12
Part B	-.88 (2.17)	.11
B-A	-.29 (.88)	.18
<i>Stroop Test (Victoria version)</i>		
Dots	-.07 (.89)	.74
Words	-.35 (.91)	.12
Colour Words	.22 (.77)	.23
<i>Phonemic fluency</i>	-.10 (.56)	.46
<i>Semantic fluency</i>		
Animals	.34 (1.01)	.16
Supermarket	.45 (1.05)	.09
<i>Boston Naming Test</i>	-.14 (.92)	.52
<i>Grooved Pegboard</i>		
Dominant hand	-2.42 (.70)	< .001
Non-dominant hand	-2.11 (1.05)	< .001

WAIS-IV = Wechsler Adult Intelligence Scale – Fourth Edition; HVLT-R = Hopkins Verbal Learning Test – Revised; BVMT-R = Brief Visuospatial Memory Test – Revised; ROCF = Rey Osterrieth Complex Figure.

^aScores represent mean z-scores across participants for each cognitive test. Raw scores on each test were first scored according to appropriate normative data for each participant and were then converted to z-scores.

^bA one-sample t-test was conducted to obtain p-values.

Table 3

Linear Mixed Model Analyses of Learning and Forgetting for Training Completion Time

Model	Fixed Effects	Estimate	<i>t</i>	<i>p</i>
Model 1: Learning	Group	-9.51	-4.46	< .001
	Day	0.02	0.26	.79
	Linearized Day	-8.11	-2.97	.003
	Trial	-7.26	-3.40	.001
	Group * Linearized Day	-.94	-0.35	.73
	Group * Trial	3.17	1.55	.12
	Linearized Day * Trial	2.54	.95	.34
Model 2: Forgetting	Group	-2.73	-2.18	.03
	Delay	0.11	1.58	.12
	Group * Delay	-.08	-0.80	.43

Table 4

Linear Mixed Model Analyses of Learning and Forgetting for Training: Number of Attempts

Model	Fixed Effects	Estimate	<i>t</i>	<i>p</i>
Model 1: Learning	Group	-0.14	-0.97	.33
	Day	-0.01	-1.2	.23
	Linearized Day	-0.08	-0.40	.69
	Trial	-.13	-0.84	.40
	Group * Linearized Day	-0.08	-0.44	.66
	Group * Trial	-.08	-0.59	.56
	Linearized Day * Trial	0.25	1.32	.19
Model 2: Forgetting	Group	0.21	0.86	.39
	Delay	0.003	0.28	.79
	Group * Delay	-.04	-1.80	.07

Table 5

Linear Mixed Model Analyses of Learning and Forgetting for Use-to-command Completion Time

Model	Fixed Effects	Estimate	<i>t</i>	<i>p</i>
Model 1: Learning	Group	-5.37	-1.98	.05
	Day	0.10	0.82	.42
	Trial	0.10	0.04	.97
	Group * Day	-.012	-0.90	.37
	Group * Trial	1.73	0.55	.59
	Day * Trial	-0.15	-1.14	.26
Model 2: Forgetting	Group	1.35	0.45	.65
	Delay	0.27	1.65	.10
	Group * Delay	-0.30	-1.29	.20

Table 6

Linear Mixed Model Analyses of Learning and Forgetting for Use-to-command Accuracy

Model	Fixed Effects	Estimate	<i>t</i>	<i>p</i>
Model 1: Learning	Group	1.75	0.34	.74
	Day	-0.19	-0.88	.38
	Trial	6.48	1.24	.22
	Group * Day	0.07	0.25	.80
	Group * Trial	-1.32	-0.22	.83
	Day * Trial	0.47	1.80	.07
Model 2: Forgetting	Group	1.72	0.23	.82
	Delay	-0.55	-1.32	.19
	Group * Delay	0.04	-.08	.94

Table 7

Linear Mixed Model Analyses of Learning and Forgetting for Recall Accuracy

Model	Fixed Effects	Estimate	<i>t</i>	<i>p</i>
Model 1: Learning	Group	1.57	0.40	.69
	Day	0.09	0.54	.59
	Trial	1.32	.34	.74
	Group * Day	0.005	0.02	.98
	Group * Trial	-1.06	-0.23	.82
	Day * Trial	0.25	1.26	.21
Model 2: Forgetting	Group	5.00	1.06	.29
	Delay	-0.25	-0.93	.36
	Group * Delay	-0.30	-0.81	.42

Table 8

Linear Mixed Model Analyses of Learning and Forgetting for Grasp-to-command Accuracy

Model	Fixed Effects	Estimate	<i>t</i>	<i>p</i>
Model 1: Learning	Group	-3.76	-0.70	.49
	Day	-0.35	-1.49	.14
	Trial	6.95	1.30	.20
	Group * Day	0.12	0.44	.66
	Group * Trial	2.98	0.47	.64
	Day * Trial	0.59	2.20	.03
Model 2: Forgetting	Group	-1.80	-0.27	.79
	Delay	-1.09	-2.88	.005
	Group * Delay	0.01	0.01	.99

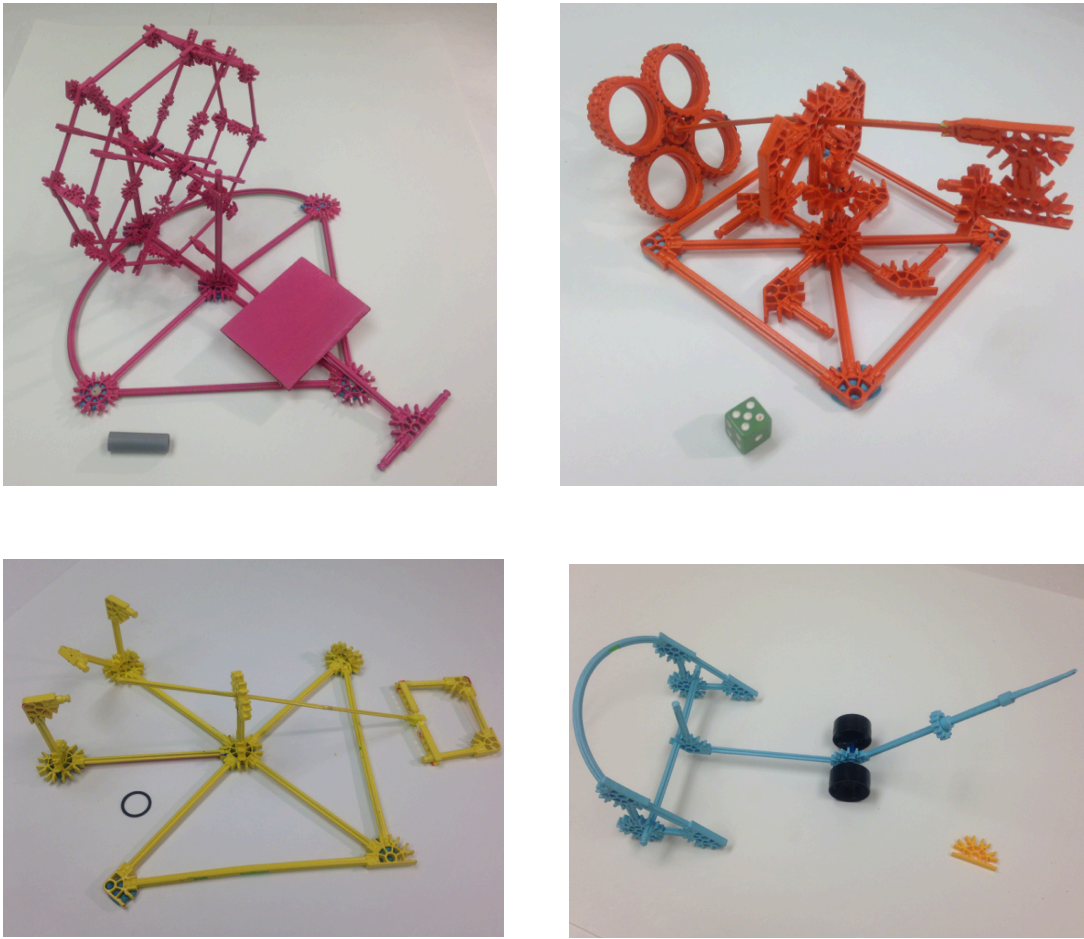
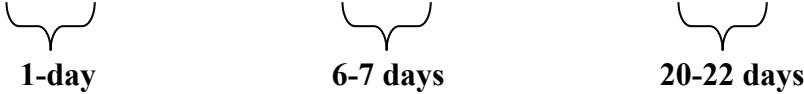


Figure 1. Examples of tools and their associated recipients that were developed for the study.

#	Session 1			Session 2			Session 3			Session 4			
	Pre-test	Training T1 T2	Post-test	Pre-test	Training T3 T4	Post-test	Pre-test	Training T5 T6	Post-test	Pre-test	Training T7 T8	Post-test	Un-trained
1	A	B A	B	B	A B	A	A	B A	B	B	A B	A	C
2	B	C B	C	C	B C	B	B	C B	C	C	B C	B	A
3	C	A C	A	A	C A	C	C	A C	A	A	C A	C	B



1-day **6-7 days** **20-22 days**

Figure 2. Illustration of experimental design to demonstrate counterbalancing order of the three tool sets used in the study (i.e., Sets A, B, and C) across experimental sessions for each version (i.e., Version 1, 2 and 3).

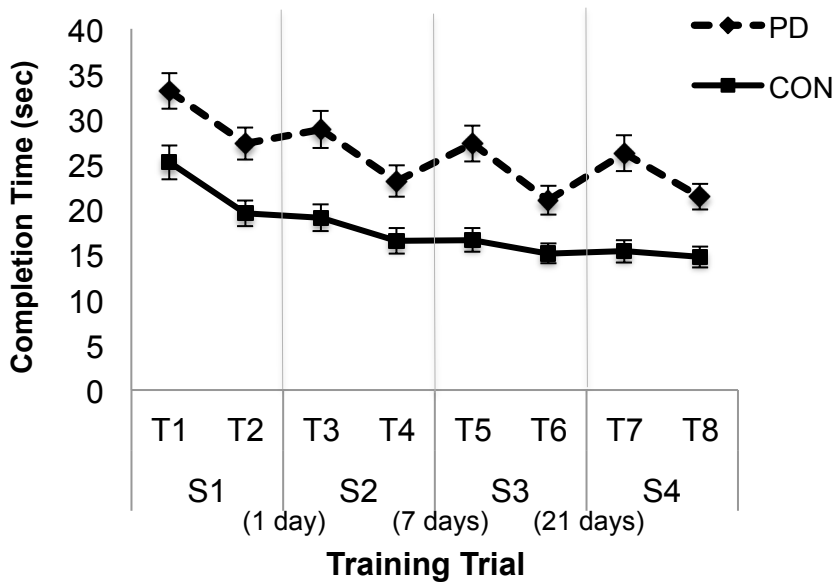


Figure 3. Mean completion time (\pm SE) across Training trials. PD and control participants showed similar learning, as both groups displayed improvement within sessions and over time.

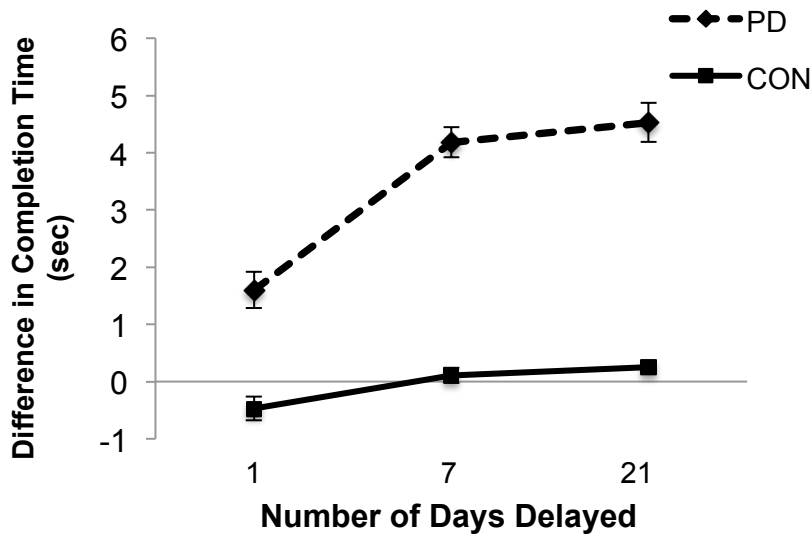


Figure 4. Differences in mean completion time for Training trials (\pm SE) across days delayed. PD participants showed significant slowing between sessions. However, control participants retained their level of performance across the delays.

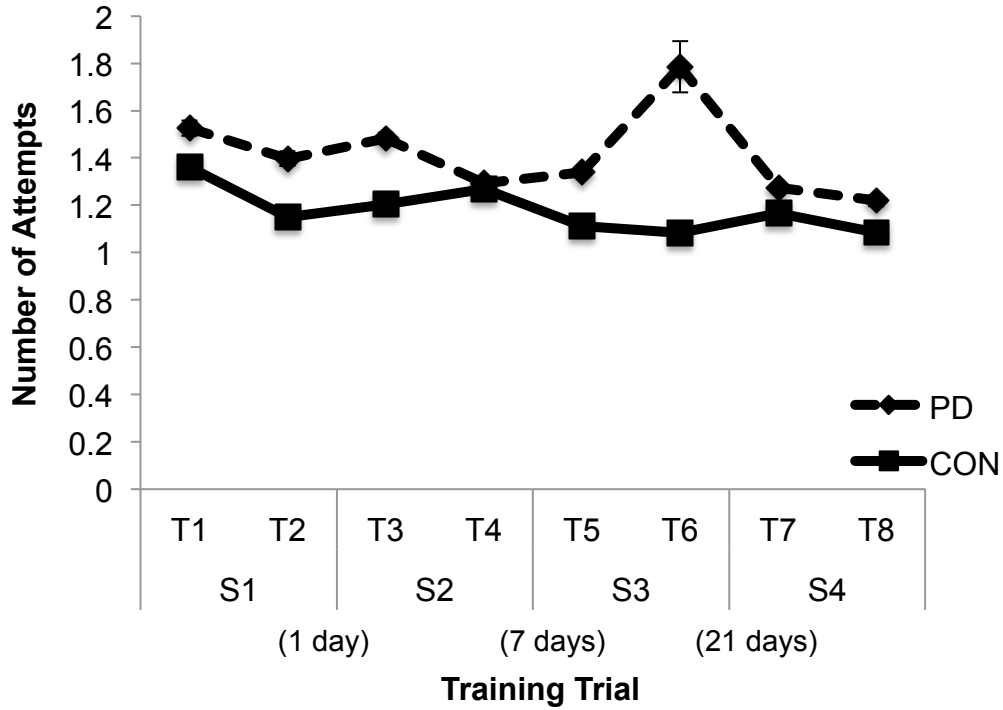


Figure 5. Mean number of attempts (\pm SE) across Training trials. PD and control participants did not make significantly less errors across trails or sessions.

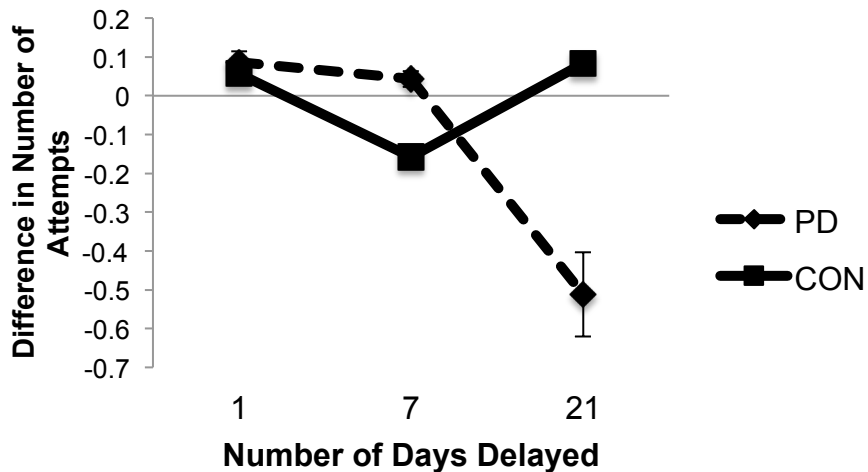


Figure 6. Differences in mean number of attempts during Training (\pm SE) across days delayed. PD and control participants did not make more errors after the delays.

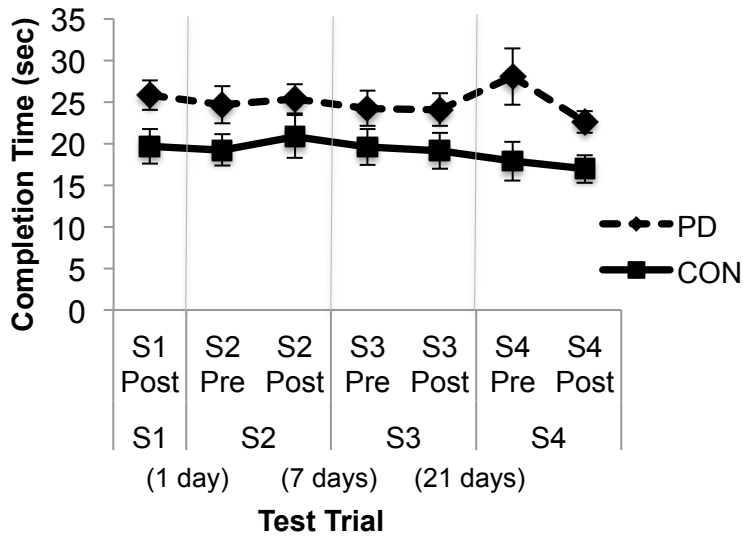


Figure 7. Mean completion time during Use-to-command (+/- SE) across test trials. Although PD participants were slower overall than controls, both groups displayed consistent performance over time; participants did not become faster within a session, and they maintained their speeds after the delays.

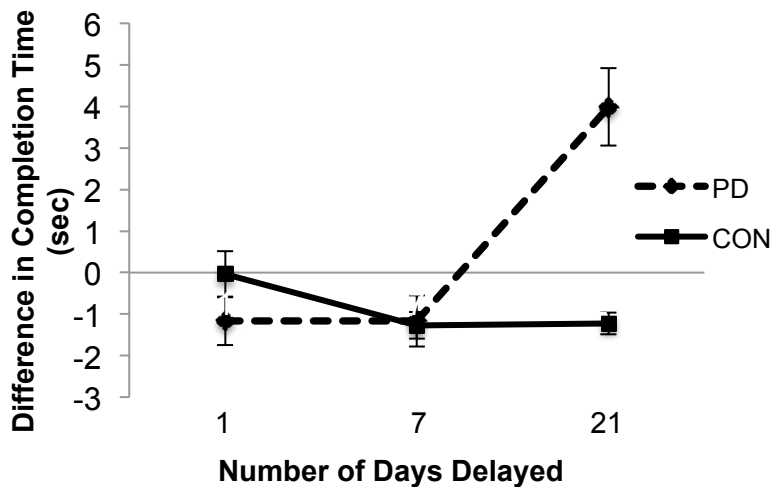


Figure 8. Differences in mean completion time for Use-to-command (+/- SE) across days delayed. Both PD and control participants retained their performance over the delays, and there was not a significant difference in forgetting between the groups.

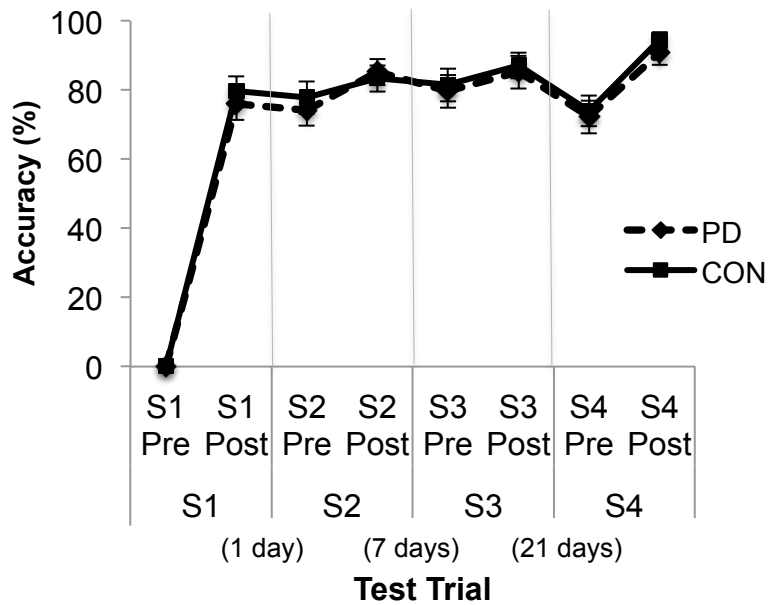


Figure 9. Percentage of correct demonstrations for Use-to-command (+/- SE) across test trials. PD and control participants did not demonstrate significant learning over time. There was not any improvement within or between sessions. The lack of overall improvement may be due to forgetting that occurred over the delays.

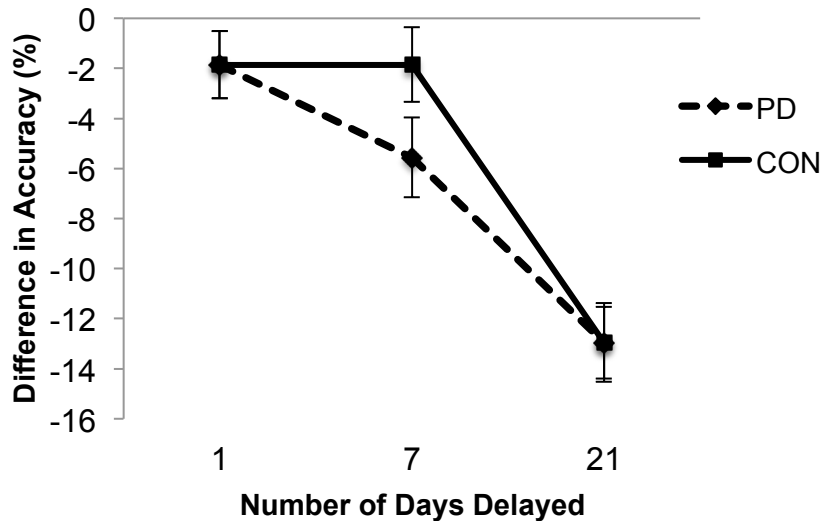


Figure 10. Differences in mean accuracy scores for Use-to-command (+/- SE) across days delayed. PD and control participants did not retain their performance over the delays. However, the amount of forgetting did not differ between the groups.

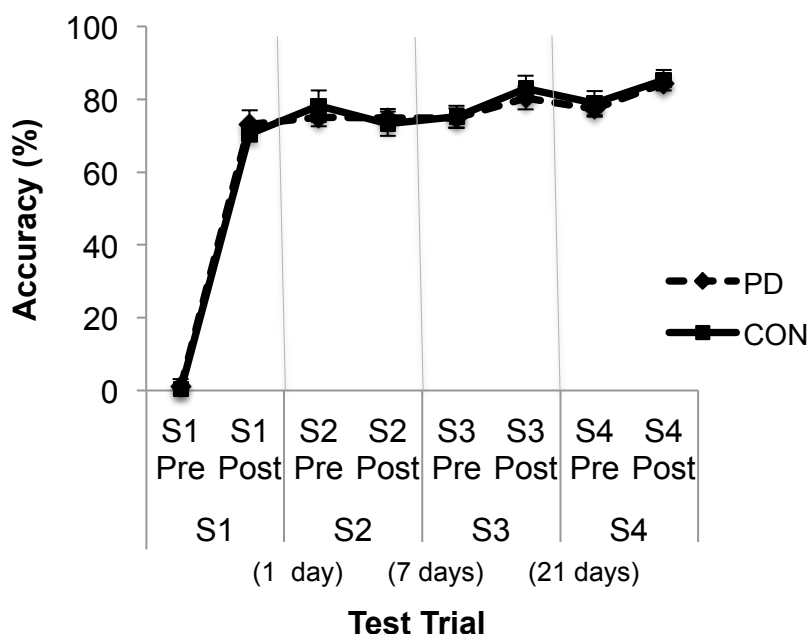


Figure 11. Percentage of correct responses (+/- SE) for Recall test items across test trials. Both groups showed a similar pattern of performance. Additionally, PD and control participants did not improve their accuracy within sessions or over time. The lack of overall learning may be due to forgetting that occurred between sessions.

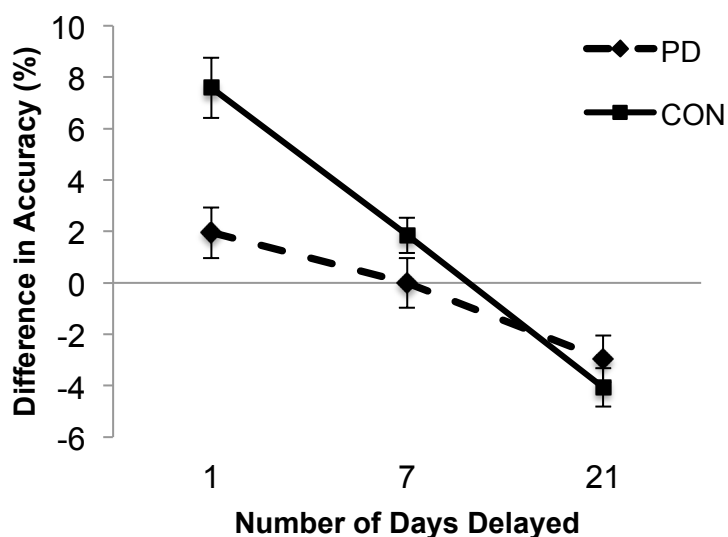


Figure 12. Differences in mean accuracy scores for Recall test items (+/- SE) across days delayed. Overall, participants displayed forgetting over the delays. Importantly, the amount of forgetting was similar for both groups.

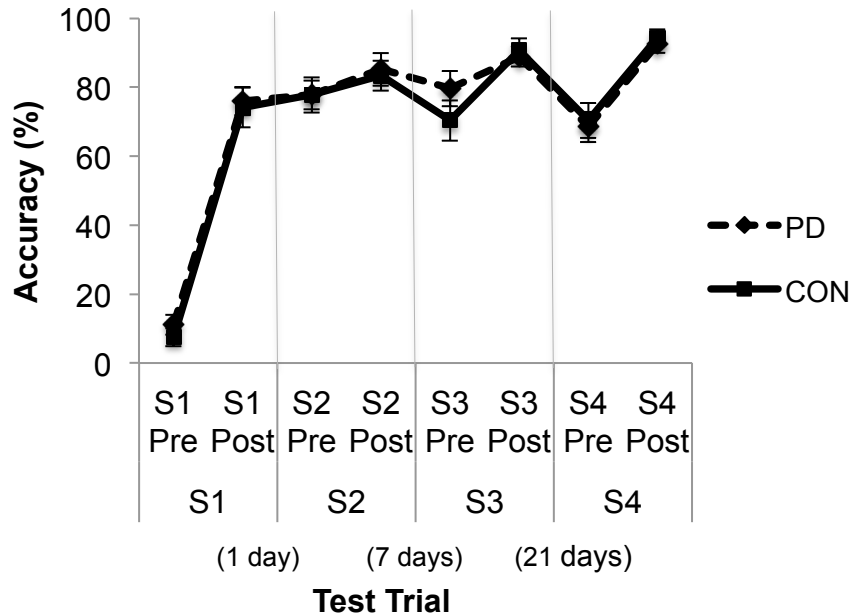


Figure 13. Percentage of correct demonstrations of Grasp-to-command (\pm SE) across test trials. Overall, performance of PD and controls participants did not differ, and both groups did not show significant improvement over time. However, participants improved more from the Pre-test to the Post-test trial as time increased.

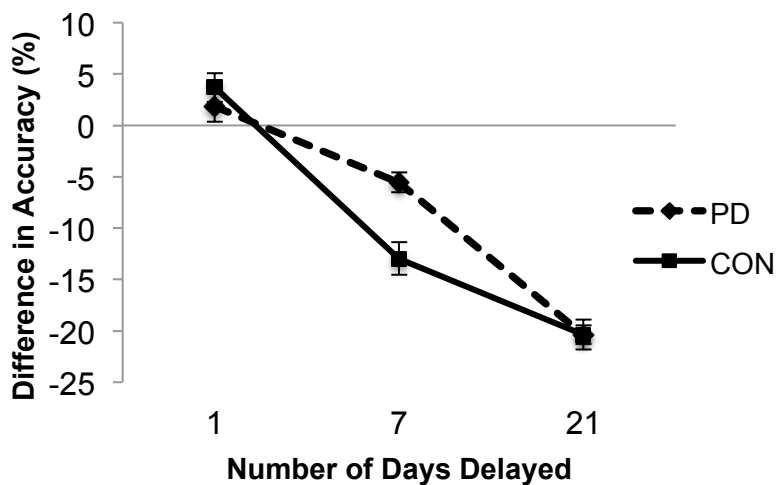


Figure 14. Differences in mean accuracy scores for Grasp-to-command (\pm SE) across days delayed. Overall, participants demonstrated forgetting over the delays, and the amount of forgetting was not different for PD and control participants.