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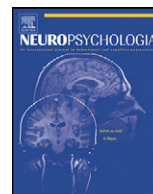
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Patients with Parkinson's disease learn to control complex systems via procedural as well as non-procedural learning

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ABSTRACT

The striatum is considered to mediate some forms of procedural learning. Complex dynamic control (CDC) tasks involve an individual having to make a series of sequential decisions to achieve a specific outcome (e.g. learning to operate and control a car), and they involve procedural learning. The aim of this study was to test the hypothesis that patients with Parkinson's disease who have striatal dysfunction, are impaired on CDC tasks only when learning involves procedural learning. 26 patients with Parkinson's disease (PD) and 26 age-matched controls performed two CDC tasks, one in which training was observation-based (non-procedural), and a second in which training was action-based (procedural). Both groups were able to control the system to a specific criterion equally well, regardless of the training condition. However, when reporting their knowledge of the underlying structure of the system, both groups showed poorer accuracy when learning took place through observation-based compared with action-based training. Moreover, the controls' accuracy in reporting the underlying structure of the systems was superior to that of PD patients. The findings suggest that the striatal dysfunction in Parkinson's disease is not associated with impairment of procedural learning, regardless of whether the task involved procedural learning or not. It is possible that the learning and performance on CDC tasks are mediated by perceptual priming mechanisms in the neocortex.

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1. Introduction

There is strong evidence that the striatum is important for a range of skill learning such as perceptual–motor skills rotary pursuit (e.g., Heindel, Salmon, Shults, Walicke, & Butters, 1989) or the serial reaction time (SRT) task (Doyon, Owen, Petrides, Sziklas, & Evans, 1996; Grafton, Hazeltine, & Ivry, 1995; Peigneux et al., 2000), perceptual skills like mirror-reading (Roncacci et al., 2002), and complex cognitive skills like the Tower of Hanoi task (Jaunt-Cyr, Taylor, & Lang, 1998) and probabilistic category learning (PCL) which is a non-motor task (Poldrack et al., 2001; Poldrack, Prabhakaran, Seger, & Gabrieli, 1999; Seger & Cincotta, 2006).

In patients with striatal dysfunction, as in individuals with Parkinson's disease (PD) or Huntington's disease, learning is shown

to be adversely affected in the SRT task (Brown et al., 2003; Doyon et al., 1997, 1998; Ferraro, Balota, & Connor, 1993; Helmuth, Mayr, & Daum, 2000; Jackson, Jackson, Harrison, Henderson, & Kennard, 1995; Kelly, Jahanshahi, & Dirnberger, 2004; Knopman & Nissen, 1991; Pascual-Leone et al., 1993; Shin & Ivry, 2003; Siegert, Taylor, Weatherall, & Abernethy, 2006; Sommer, Grafman, Clark, & Hallett, 1999; Wilkinson & Jahanshahi, 2007; Willingham & Koroshetz, 1993) and other motor-skill tasks (e.g., Haaland, Harrington, O'Brien, & Hermanowicz, 1997; Krebs, Hogan, Hening, Adomovich, & Poizner, 2001; as well as probabilistic category learning (Filoteo, Maddox, & Davis, 1998; Knowlton, Mangels, & Squire, 1996; Knowlton, Squire, et al. 1996; Sage et al., 2003; Wilkinson, Lagnado, Quallo & Jahanshahi, in press; Witt, Nuhsman, & Deuschl, 2002a) and other non-motor skill tasks (e.g., Maddox, Aparicio, Marchant, & Ivry, 2005). This pattern of findings has led some to conclude that striatal dysfunction produces general impairments in learning (e.g., Poldrack et al., 1999), and is not specific to decrements in the acquisition of novel motor skills.

However, some studies have shown normal skill learning in PD patients relative to controls. This includes studies of perceptual–motor skill learning such as rotary pursuit (e.g., Bondi & Kaszniak, 1991; Soliveri, Brown, Jahanshahi, Caraceni, & Marsden,

Abbreviations: BDI, Beck Depression Inventory; BG, basal ganglia; DA, dopamine; FB, feedback; H&Y, Hoehn & Yahr; MMSE, Mini Mental State Examination; NART, National Adult Reading Test; PD, Parkinson's disease; UPDRS, United Parkinson's Disease Rating Scale; CDC, complex dynamic control task.

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1997) and the SRT (e.g., Exner, Koschack, & Irl, 2002; Smith, Siegert, & McDowall, 2001), and studies of complex cognitive skills such as the complex dynamic control (CDC) task, which involves problem solving (e.g., Witt et al., 2006). Probabilistic classification learning (Ashby, Noble, Filoteo, Waldron, & Ells, 2003; Filoteo, Maddox, Salmpn, & Song, 2005; Schmitt-Eliassen, Ferstl, Wiesner, Deuschl, & Witt, 2007) and artificial grammar learning (AGL) (e.g., Reber & Squire, 1999; Smith et al., 2001; Witt, Nuhman, & Deuschl, 2002b) have also been shown to be unimpaired in PD patients in some studies. Differences in sample characteristics (stage of illness and disease severity, medication state of the patients) and key features of individual tasks (structure of information to be learned, presence or absence of corrective feedback, development of conscious knowledge during learning) are some of the factors that are likely to determine the magnitude of skill learning deficits in PD and may explain the inconsistent pattern of findings described above. However, what procedural learning processes are spared or impaired following striatal dysfunction, remains a contentious issue.

Many of the tasks exploring the range of skills that are spared as well as those which are impaired in Parkinson's disease patients are often described as involving procedural learning, for example; AGL, PCL and the SRT and CDC tasks. What is thought to be acquired in these tasks is "knowing how" to perform actions that are linked to specific goals/outcomes, which is different from declarative knowledge, which is "knowing that" or particular facts about the underlying actions and structural knowledge concerned with the goal itself (e.g. Anderson, 1982). Because people are able to recollect the facts and events that are acquired in a task, declarative knowledge is under voluntary control and therefore reportable. Skill learning of the kind described as procedural, often involves the incidental acquisition of new behavioral capacities through practice without the mediation of reportable knowledge (Poldrack et al., 1999). Many of the studies listed above suggest that there are learning conditions in procedural tasks on which PD patients can perform well. This raises two important questions: (1) is the learning mechanism used to acquire new skills in PD patients the same as that used by controls? (2) What are the factors that discriminate between conditions in which PD patients show impairments on procedural tasks, and conditions in which they do not?

Recent studies using complex procedural tasks have tried to address these questions. Witt et al. (2006) showed that the acquisition of a new complex problem solving skill was independent of the dopaminergic basal ganglia system affected in PD patients. One reason that Witt et al. offer as to why PD patients show equivalent levels of performance to controls in a complex cognitive skill task is the nature of the feedback procedures used in their task. Witt et al. argue in line with evidence from Shohamy et al. (2004) that complex procedural skill learning tasks in which PD patients show deficits in learning, involve trial-by-trial feedback during learning. When the nature of the feedback is changed, as in Witt et al.'s study, where PD patients received gradual feedback, or when no feedback is presented as in one condition in Shohamy et al.'s study, then this appears to assist PD patients in learning. This argument is based on the claim (Reber & Squire, 1999) that the mid-brain dopamine system (MDS) along with its cortical and sub-cortical targets is implicated in tasks where predictions about outcomes involve a reward structure (Hollerman, Tremblay, & Schultz, 2000; Vriezen & Moscovitch, 1990). Thus, procedural tasks like artificial grammar learning (Reber & Squire, 1999; Smith et al., 2001), prototype category learning (Reber & Squire, 1999) and complex control tasks (Witt et al., 2006) are successfully performed by PD patients because decisions are made without immediate feedback. By the same rationale, procedural tasks such as the SRT task (Brown et al., 2003; Doyon et al., 1997, 1998; Ferraro et al., 1993; Helmuth et al., 2000; Jackson et al., 1995; Kelly et al., 2004; Pascual-Leone et al., 1993; Shin & Ivry, 2003; Sommer et al.,

1999; Wilkinson & Jahanshahi, 2007) and PCL (Filoteo et al., 1998; Knowlton, Mangels, et al., 1996; Knowlton, Squire, et al. 1996; Sage et al., 2003; Wilkinson et al., in press; Witt et al., 2002a) reveal that PD patients have impaired learning, because information must be integrated across many trials in which feedback on the outcome of responses is presented on every trial. When PCL learning with and without feedback in PD has been directly compared, in one study patients' performance on the task improved following the removal of trial-by-trial feedback relative to when feedback was present (Shohamy et al., 2004). However, in another study, PD patients' performance remained impaired on the task even when trial-by-trial feedback was removed (Wilkinson et al., in press).

Recall, Witt et al. (2006) speculated that PD patients were not impaired at learning to control a complex system because, when compared with Shohamy et al.'s study, such learning involves gradual rather than trial-by-trial feedback. However, the tasks used by Witt et al. and Shohamy et al., although complex, differ in their underlying task structure, in the former, the task requires the ability to learn about and control a complex system, and in the latter, the task requires accurate integration of cue information to make predictive judgments. Moreover, the training phases included in both studies were not directly comparable therefore, claims concerning the effects of feedback on complex skill acquisition in PD patients are based only on comparable descriptions of the feedback structure of the tasks employed. Disentangling the contribution of the feedback structure of the tasks from the training methods involved would provide insights into whether self-generated actions are necessary in the acquisition of complex procedural skills. Therefore, in the present study we used a similar CDC task to that employed by Witt et al. in which the feedback structure of the task was constant, but training was either procedural-based (self-generated action-outcome associations) or non-procedural-based (artificially generated action-outcome associations). In so doing, we investigated what might lead to successful performance by PD patients on a complex procedural task.

There is much evidence to suggest that CDC tasks involve procedural knowledge (Berry, 1991; Berry & Broadbent, 1984, 1987, 1988; Dienes and Berry, 1997; Lee, 1995; Stanley, Mathews, Buss, & Kotler-Cope, 1989) which is dissociated from declarative knowledge of the strategies used to perform the task, and how the task itself operates. Prosaic examples of CDC tasks include using one's mobile phone or driving a car. More complex examples include operating air-traffic control systems, subway systems, and nuclear power plants. All these examples involve controlling a system that changes as a result of the actor's behaviors on that system as well as autonomously over time. In laboratory versions of these CDC tasks (see Fig. 1) participants are required to interact with a system.

In the example of a linear control system presented in Fig. 1, based on Burns and Vollmeyer's (2002) study which was also

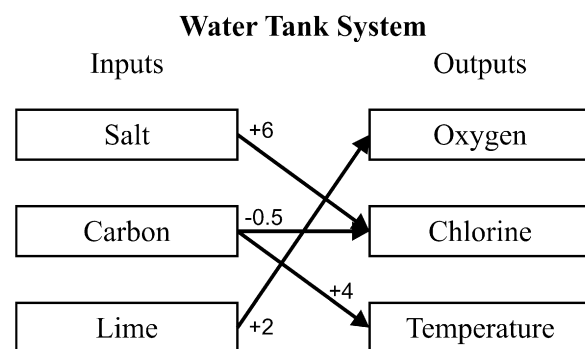


Fig. 1. Water tank system with inputs (salt, carbon, lime) and outputs (oxygenation, chlorine concentration, temperature).

used in the present study, healthy participants had to learn about, and then control a water tank purification system. Participants make decisions as to which properties of the task that they want to manipulate in order to learn about the underlying relations between inputs and outputs. Once a decision is made (e.g., change the input lime by 50 units), they then monitor the consequences of their actions on the system (e.g., output oxygenation changes by 52 units) and update their knowledge accordingly (e.g. lime affects oxygenation). It is through this exploratory process that people gain experience of how the system operates, which is then applied in test conditions, in which they are required to control the system to a specific criterion (e.g., try to reach and maintain oxygenation at the level of 150 units).

As suggested, the popular position on procedural learning in CDC tasks is that procedural knowledge and declarative knowledge are dissociated (Berry, 1991; Berry & Broadbent, 1984, 1987, 1988; Lee, 1995; Stanley et al., 1989), and that they are supported by functionally separate cognitive mechanisms (e.g., Squire, 1986). It has been shown that in healthy participants having declarative knowledge alone will impair one's later ability to perform a procedural task (Berry, 1991; Berry & Broadbent, 1984, 1987, 1988; Lee, 1995). One method used to demonstrate this involves training people on a procedural task by observing another perform it first; because the learners are monitoring what they are observing, this is claimed to generate declarative knowledge (e.g., Kelly & Burton, 2001; Kelly, Burton, Riedel, & Lynch, 2003). Berry (1991) and Lee (1995) used this method to compare the effects of action-based and observation-based learning in CDC tasks. They showed that, when participants later came to problem solve, the observers' ability to perform the procedural task was poorer than that of procedural-based learners. However, recent evidence (Osman, 2008a, 2008b, 2008c) has revealed that provided with instructions that encourage hypothesis testing strategies during learning, there is equivalent performance regardless of whether learning was observation-based or action-based.

The target question we ask in this study is: Does presence or absence of self-generated action–outcome associations determine whether or not PD patients show impairments on CDC tasks? To test this hypothesis, we presented PD patients and age matched controls with two CDC tasks: procedural learning based version, non-procedural learning based version.

In one, learning of the task required the individual to directly interact with the task, and therefore they would determine which action to take from trial to trial during learning. Participants would be actively deciding which input/outputs to change on each learning trial and are receiving direct feedback on the consequences of their interventions as a result of the changes to the output values. Given that they would be selecting the inputs to change and the values needed to be changed by, and monitoring the affects on the outputs, the output feedback was corrective in the sense that the hypotheses they would have concerning the input–output relations could be verified or falsified. Thus, at the end of each trial, participants were provided with positive or negative corrective feedback and were therefore able to revise their hypotheses about what the input–output relations were, and adapt their learning process accordingly.

In the other, learning was non-procedural-based, that is, on every learning trial participants simply observed pre-selected input changes and the consequences of these changes on the outputs, so, the action–outcomes were artificially generated, and not self-generated as with the procedural-based training version. However, consistent with the procedural-based training version, participants in the non-procedural version would see an input or several inputs change on each trial, and receive feedback in the sense that they would in turn observe the subsequent changes to the outputs based on the changes to the input/inputs on that trial. In addition,

participants could mentally simulate hypothesis testing behaviors and could test the validity of a particular hypothesis (i.e. an input–output relation) against the available information presented on any given trial.

If the procedural CDC task – with gradual feedback – recruits the striatum then CDC learning via self-generated actions will be impaired relative to non-procedural observational learning and healthy controls. If on the other hand, the CDC task does not depend on striatal structures, perhaps because of the gradual nature of the feedback and the absence of trial-by-trial feedback, as has been claimed (Witt et al., 2006) then PD patients should show equivalent control performance relative to healthy participants on both procedural and non-procedural versions of the task. In addition, if self-generated actions are critical to the acquisition of skilled knowledge in CDC tasks, as has been suggested (Berry, 1991; Lee, 1995), then we predict that age-matched controls should show poorer performance in the observation-based learning CDC task compared to the action-based learning CDC task.

2. Methods

2.1. Participants

Twenty-six individuals with a diagnosis of idiopathic PD (17 male, 9 female) aged between 52 and 71 years ($M = 62.5$, $S.D. = 7.61$) were recruited. Patients were recruited from the movement disorders clinic at the National Hospital for Neurology and Neurosurgery. They met Parkinson's Disease Society Brain Bank diagnostic criteria for PD (Hughes, Daniel, Kilford, & Lees, 1992). Disease duration ranged from 3 to 20 years ($M = 9.40$, $S.D. = 4.96$). Stage of illness and severity of the motor symptoms of PD were respectively rated by a neurologist while patients were on their usual medication using the Hoehn & Yahr (H&Y) (Hoehn & Yahr, 1967) scale and the motor section of the Unified Parkinson's Disease Rating Scale (UPDRS) (Fahn & Elton, 2005). All patients were in the mild to moderate stages of the disease, with scores on the H&Y scale of I to III.V ($M = 2.13$, $S.D. = 0.74$) and UPDRS motor scores ranging between 2 and 36.5 ($M = 17.68$, $S.D. = 10.44$). All patients were non-demented as demonstrated by scores >27 on the Mini-Mental State Examination (MMSE) (Folstein, Folstein, & McHugh, 1975). Patients were also screened for clinical depression (scores >15) on the Beck Depression Inventory (BDI) (Beck, Erbaugh, Ward, Mock, & Mendelsohn, 1961). None of the patients or controls scored above 15 on the BDI. Patients were tested on their usual medication. The majority (20/25) of PD patients were taking levodopa and other medication including dopaminergic (18/25) and/or anticholinergics (1/25). Unfortunately we were not able to ascertain the exact medications taken by 1 patient.

Twenty-six healthy volunteers (11 male, 15 female) aged between 45 and 75 years ($M = 61.38$, $S.D. = 8.02$) took part in the study. None of the controls had any neurological disorder, psychiatric illness, head injury, or alcohol or drug abuse. The study was approved by the Joint Ethics Committee of the Institute of Neurology and The National Hospital for Neurology and Neurosurgery. Informed consent was obtained prior to participation in the study from all controls and PD patients. Control participants were paid a fee of £6 per hour and the travelling expenses of patients were reimbursed. Information about controls and PD patients is presented in Table 1.

Independent samples *t*-tests were conducted to compare demographic information between the groups. All of these comparisons failed to reach significance apart from BDI score which was significantly greater in the PD group relative to the controls (see Table 1). This finding is not surprising given that having to cope with the symptoms of their disease is likely to have contributed to higher scores on this measure in PD patients.

Table 1

Demographic information for patients with Parkinson's disease and controls and clinical characteristics of the patients

	PD ($n = 26$)		Controls ($n = 26$)		<i>p</i>
	Mean	S.D.	Mean	S.D.	
Age	62.50	7.61	61.38	8.02	0.61
IQ	116.83	13.02	117.65	11.46	0.52
Mini Mental State Exam	29.27	0.96	29.50	0.91	0.32
Beck Depression Inventory	7.68	3.51	5.38	4.26	0.04
Unified Parkinson's Disease Rating Scale on medication	17.68	10.44			
Hoehn & Yahr Rating on medication	2.13	0.74			
Disease duration	9.40	4.96			

2.2. Design and materials

We employed a mixed design that included one between subject variable comparing PD patients and age matched controls and two within subject variables; one examining control performance in two CDC tasks (observation-based learning CDC task, action-based learning CDC task), the other measuring structural knowledge of the CDC task (observation-based learning CDC task, action-based learning CDC task). The order of presentation of the two CDC tasks was randomized across participants in each group. The critical manipulation was the format of the learning phase (procedural [self-generated action-outcome associations], non-procedural [artificially generated action-outcome associations]). In the procedural-based learning version all participants generated their own learning experiences by selecting the inputs they wanted to change on each learning trial. In the non-procedural-based learning version participants were presented with learning trials in which the input values and corresponding output values were pre-selected. After the learning phase of each version of the CDC-task, participants performed the same test of control in the test phase, when both procedural learners and non-procedural learners were required to demonstrate their ability to reach and maintain the same specific output values for a total of 6 trials.

2.2.1. CDC tasks

The design and underlying structure of the two CDC tasks used (Water-Tank control system, Ghost Hunting control system) were based on the Water-Tank control system (see Fig. 1). The only differences between the two problems were the visual layout of each system on the screen, and the cover story¹ (see Appendix A). In the Water-Tank control system, participants were told that, as workers of the plant, their job was to inspect the water quality of the system. The system was operated by varying the levels of salt, carbon, and lime (inputs), which then changed the three water quality indicators: oxygenation, temperature, and chlorine concentration (outputs). After the learning phase, in the test phase participants were required to control the system by reaching specific values of the water quality indicators. In the Ghost Hunting control system, participants were told that they were newly recruited ghost hunters, and had returned from a field experiment. Their job was to examine three pieces of equipment used in the field: GGH Meter, Anemometer, Trifield Meter (inputs), and the readouts of the three phenomena that these detect: Electro Magnetic Waves, Radio Waves, Air Pressure (outputs). After the learning phase, in the test phase controlling the system involved modifying the levels of the readouts of the phenomena, by manipulating the dials on each machine. Each CDC task consisted of a learning phase comprising 4 blocks of 10 trials, and a test phase in which participants were required to control the system to reach and maintain specific output criteria in the course of 10 trials.

2.2.1.1. Procedural-based learning CDC task. In the learning phase of this task, participants were presented with a computer display with three input and three output variables. Participants were free to choose to change any combination of inputs on each trial (i.e. no inputs, one input, two inputs, or all three inputs). There were a total of 40 trials. Each trial consisted of participants interacting with the system by changing any input by any value they chose, using a slider corresponding to each.² Each slider had a scale from –100 to 100 units. When participants were satisfied with their changes to the inputs, they clicked a button labelled “output readings,” which revealed the values of all three outputs. When they were ready to start the next trial, they clicked a button “next trial,” which hid the output values from view. On the next trial, the newly changed inputs affected the output values from the previous trial: thus, the effects on the outputs were cumulative from one trial to the next, but after each block of learning trials, the values of the inputs were reset to “0” and the output values reset so that Oxygenation = 100, Chlorine Concentration = 500, and Temperature = 1000.³ After the first block of 10 trials, participants were presented with structure test 1 (see Fig. 2).

¹ Osman (2008b, 2008c) contrasted observation-based and action-based learning versions of the Ghost hunting and Water tank system CDC tasks. The study revealed that the Ghost Hunting and Water-Tank system tasks were matched and revealed equivalent performance across observation-based and action-based learning versions. On this basis, the present study presented participants with an observation-based version of the Ghost hunting task, and an action-based version of the Water tank system.

² In Burns and Vollmeyer’s study, participants were shown the starting values of input and output values before they began the task. In the present experiment, participants were shown only the starting values of the input values, and not the output values, which were revealed only on the first trial, and not before. The rationale for this change was simply to encourage participants to pay special attention to the effects on the outputs resulting from the manipulations they made.

³ If a participant changed the input Salt by 50 units on Trial 1, this would in turn change the output value of Chlorine Concentration to 556 (i.e., Chlorine Concentration starting value = 500 units, +Salt value change = 50 units, +Constant added noise on input–output connection = 6 units). If on Trial 2 the input Salt was changed by 100 units, then the output value of Chlorine Concentration would be 662 (i.e., Chlorine Concentration starting value = 556 units, +Salt value change = 100 units,

A diagram of the system was shown on screen, and participants were asked to indicate which input was connected to which output. After this, participants began the next set of 10 trials. On completion of the second block, structure test 2 was presented, and so on until all 4 blocks of 10 learning trials and all four structure tests were completed.

2.2.1.2. Non-procedural-based learning CDC task. In this version the learning phase was observation-based. Instead of changing the inputs, on each trial participants pressed a button “reveal inputs,” then observed the sliders of the inputs changing automatically according to pre-specified values.⁴ Then they pressed a button “reveal outputs,” which displayed the corresponding effects on the output values. After studying them, participants clicked a button “ready for next trial,” which cleared the input and output values ready for the next trial. After each block of 10 trials participants were presented with a structure test.

2.2.1.3. Test phase of procedural-based and non-procedural-based CDC tasks. After each learning phase, participants’ ability to control the system was tested. In this phase, all participants had to change the input values to achieve and maintain set output values. In the procedural-based learning CDC task and in the non-procedural-based CDC task, for the course of 10 trials, the criterion values participants had to reach were the same, and only the labels of the outputs were different so as to correspond with the labels for that particular CDC task they were controlling: Output 1 (Water Tank = Oxygenation, Ghost Hunt = Radio Waves) = 50; Output 2 (Water Tank = Chlorine Concentration, Ghost Hunt = Electro Magnetic Waves) = 700; Output 3 (Water Tank = Temperature, Ghost Hunt = Air Pressure) = 900, for the course of 10 trials. On completing this phase, participants were presented with a further structure test.

2.2.2. Scoring

2.2.2.1. Control test scores. The procedure used was based on Burns and Vollmeyer’s scoring system. Control performance was measured as error scores in the control test. Error scores were based on calculating the difference between each target’s output value (i.e., the criterion according to the control test) and the actual output value produced by the participant for each trial of the transfer test. A log transformation (base 10) was applied to the error scores of each individual participant for each trial, to minimize the skewedness of the distribution of scores. All analyses of error scores for the control test were based on participants’ mean error, averaged over all 10 trials, across all three output variables. Success in control performance on transfer tasks is indexed by the difference between the achieved and target output values, thus lower error scores indicate better performance.

2.2.2.2. Structure scores. The method used to score performance on structure tests 1–5 computed the proportion of input–output links correctly identified for each test. A correction for guessing was incorporated, based on Vollmeyer et al.’s (1996) procedure, which was correct responses (i.e., the number of correct links included, and incorrect links avoided)—incorrect responses (i.e., the number of incorrect links included, and correct links avoided)/N (the total number of links that can be made). The maximum value for each structure score was 1. This scoring scheme was applied to score performance on all structure tests.

3. Results

This section first analyzes control performance and then structural knowledge in each CDC task. Correlation analyses examine the potential association between control performance and structural knowledge. In all analyses, a significance criterion of $\alpha = .05$ was used. The results of non-significant findings are not reported.

Because control error scores are based on difference scores, the lower the score the better the control performance. The control error scores of both PD patients and age-matched controls for the action-based learning CDC task and the observation-based learning CDC task in Fig. 3 suggests that, control performance appears to be similar across the two groups for both types of CDC task.

To analyze these data, a $2 \times 2 \times 2$ ANOVA was carried out using type of CDC task (non-procedural vs. procedural) as a within subject variable, and group (PD vs. control) and order (procedural first vs. non-procedural first) as between subject variables. The analysis

+Constant added noise on input–output connection = 6 units).

⁴ The pre-specified values of the inputs (and correspondingly the output values) that were changed on each of the 40 observation-based learning trials were generated by a high performing participant that had taken part in a piloted version of the task.

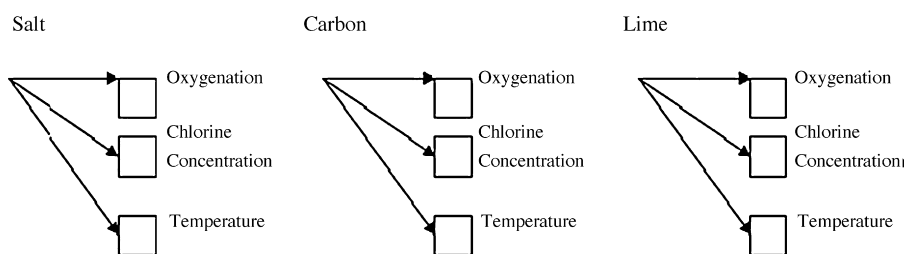


Fig. 2. Structure test.

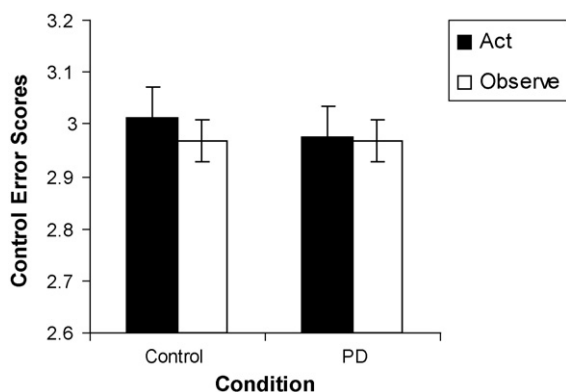


Fig. 3. Control test scores (\pm S.E.) from the control test in the action-based learning CDC task and the observation-based learning CDC task for the Parkinson's disease (PD) and healthy control groups. Successful performance is indicated by lower mean error scores.

revealed no significant main effect of type of CDC task, group, order, and no significant interactions.

For each participant, the scores from the structure tests (structure tests 1–5) were averaged across the non-procedural-based learning CDC task, and again for the procedural-based learning CDC task. The means of these scores for each group are presented in Fig. 4, which indicates that for both groups structure scores were lower (indicating worse performance) in the non-procedural than in the procedural-based-CDC task. In addition, Fig. 4 suggests that PD patients' error scores were lower (indicating poorer performance) overall than the structure scores of the age-matched controls.

These data were analyzed using a $2 \times 2 \times 2$ ANOVA on the mean of structure test 1–5 scores, using type of CDC task as a within subject variable, and group and order as between subject variables.

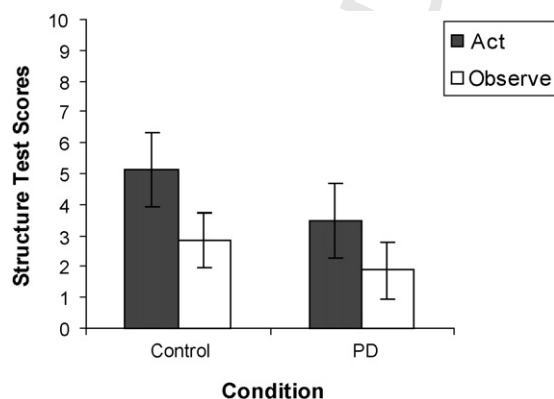


Fig. 4. Mean structure test scores (\pm S.E.) from the action-based learning CDC task and the observation-based learning CDC task for the Parkinson's disease (PD) and healthy control groups. Successful performance is indicated by higher structure scores.

There was a significant main effect of type of task, $F(1, 48) = 28.407$, $MSE = 114.08$, $p < 0.001$, $\eta^2 = 0.37$, and a significant main effect of group, $F(1, 48) = 8.91$, $MSE = 40.01$, $p < 0.005$, $\eta^2 = 0.16$. Thus, as indicated in Fig. 4, the findings suggest that overall performance in the structure tests is lower in the non-procedural relative to the procedural-based learning condition, and that overall, regardless of task type, PD patients' performance was lower than that of controls.

A correlation analysis was carried out between control scores and structure test scores (averaged across structure tests 1–5) from both the procedural and non-procedural-based learning tasks. In both groups, there was no significant relationship between control scores and structure test scores in either training version of the CDC task. In addition, we divided all participants into two groups (good structure knowledge vs. poor structure knowledge) on the basis of their structure test scores. These groups did not differ in terms of their control performance during the CDC task.

4. General discussion

PD patients showed equivalent performance to age-matched controls both in their ability to control systems which they learnt about via non-procedural-based training (artificially generated action-outcome associations) and procedural-based training (self-generated action-outcome associations) indicating that successfully learning to control a complex dynamic control task is not influenced by dysfunction of the dopaminergic basal ganglia system. Additionally, whether or not the CDC task is learned in a procedural or a non-procedural way is not a critical factor in determining the success of PD patients' control performance in complex dynamic procedural tasks. In contrast, knowledge of the underlying structure of the complex dynamic control task does seem to be affected by presence of dopaminergic basal ganglia dysfunction. PD patients had poorer knowledge about the underlying relations between the inputs and outputs of the control systems they were operating, compared with age-matched controls. Our findings are consistent with the proposal by Witt et al. (2006) that for PD patients, a procedural task involving gradual (rather than trial-by-trial) feedback facilitates successful acquisition of a new complex skill.

Successfully learning to control a complex dynamic control task does not appear to be influenced by whether learning involves self-generated action-outcome associations. These findings may provide important insights into the relationship between the basal ganglia and feelings of agency (Haggard, Clark, & Kalogeras, 2002; Kircher & Leube, 2003). In the present study, training that involved self-generated action-outcome associations would in turn produce feelings of agency, since a change in state of the system occurred as a direct consequence of the participants' decision making. In contrast, training that involved artificially generated action-outcomes would have removed any sense of agency since, any decision the participant would have taken was not associated with action-outcome associations in the task. However, despite this contrast, PD's performance on later tests of

control skills was not affected. This converges with evidence (McNamara, Durso, & Brown, 2003), suggesting PD patients showed no impairments relative to matched-controls on tests examining their sense of “self”. Spence (2003) proposes that both the sense of agency and volition are associated with premotor and basal ganglia regions, and that dopaminergic agonists used in the treatment of Parkinson’s disease have therapeutic effects that may restore volition and sense of agency, as they do in Schizophrenia. This could be explored using CDC tasks and contrasting the effects of learning through self-generated or artificially generated action-outcomes on PD patients on and off medication.

Witt et al. (2006) argued that in their study, PD patients and controls showed evidence of having learned the CDC task unconsciously for two reasons (i) both groups were able to successfully control the CDC task while, performance on subsequent tests of awareness of the CDC task was equivalent to controls but did not correlate with CDC task performance. (ii) Transfer of acquired knowledge across to a new test situation was poor (Berry & Broadbent, 1984; Squire & Frambach, 1990). Here, we take unconscious knowledge to refer to knowledge that is acquired unintentionally and is non-verbalizable, and conscious knowledge is under voluntary control and reportable. Conscious learning is considered to depend on medial temporal lobe and diencephalic brain structures, while unconscious learning is associated with the basal ganglia (Squire, 1994; Squire & Zola, 1996). One frequently used criterion for considering a task as involving unconscious learning is that patients with amnesia show intact learning on it. However, with the CDC task, Squire and Frambach (1990) found that while amnesic patients were able to learn normally early on, they showed deficits in learning in the later phases. On the basis of this and their own finding that unconscious CDC learning is intact in PD, Witt et al. (2006) suggested that learning to control a complex system relies neither on the MTL/diencephalic structures damaged in amnesia nor the basal ganglia dysfunctional in PD but instead is mediated by unconscious perceptual priming mechanisms in the neocortex (Buckner et al., 1998; Seger, Prabhakaran, Poldrack, & Gabrieli, 2000; Witt et al., 2002b).

The results from the tests of structural task knowledge in the present study are in agreement with the findings of Witt et al. as the PD patients in the present study showed evidence of intact control performance on the CDC tasks however, in contrast to Witt et al., our PD patients were more likely than controls to learn the task unconsciously—according to their task structure knowledge which was worse than controls during both CDC tasks. This apparent dissociation between performance and awareness for PD patients, regardless of whether the CDC involved procedural learning or not, may indicate that CDC task performance is mediated by the neocortex rather than the basal ganglia as hypothesised above. It is also consistent with the results of other studies reporting normal complex cognitive skill learning in PD including studies of PCL with feedback (Ashby et al., 2003; Filoteo et al., 2005; Schmitt-Eliassen et al., 2007), and AGL in PD (e.g., Reber & Squire, 1999; Smith et al., 2001; Witt et al., 2002b).

As far back as 1986, Squire proposed a reformulation of the procedural memory model and noted it to be “a collection of different abilities each dependent on its own specialized processing system... one therefore should not expect that a single lesion would affect all of procedural memory”. From a review of the empirical evidence, Soliveri et al. (1999), also concluded that procedural learning is not a unitary system, and that it is likely that different types of procedural memory such as priming, perceptual skills such as mirror reading, perceptuo-motor skills such as prism adaptation, cognitive skills such as the Tower of London/Hanoi/Toronto or motor skills such as the pursuit rotor or the serial reaction time task are mediated by different brain areas.

While the assumption has been that the striatum plays a central role in the procedural system, increasingly evidence suggests that the basal ganglia are only involved in specific types of procedural learning and that patients with Parkinson’s disease only show deficits on some procedural tasks such as unconscious sequence learning typically assessed with the serial reaction time task (e.g., Jackson et al., 1995; Wilkinson & Jahanshahi, 2007) or cognitive skills assessed with the Tower of London/Hanoi/Toronto (e.g., Saint-Cyr et al., 1998; Owen et al., 1992). The current results and those of Witt et al. (2006) showing intact learning on a CDC task by patients with PD with poor declarative knowledge of the task structure, support the fractionation of procedural memory and the involvement of the basal ganglia in only certain types of procedural learning.

Why was overall performance on tests of structural knowledge poorer when learning was observation-based (non-procedural) than action-based (procedural)? On first reflection, these findings suggest dissociation between procedural knowledge and declarative knowledge consistent with previous evidence from problem solving studies reporting that declarative knowledge of CDC tasks lags behind procedural knowledge. However, this explanation cannot account for why learning to control a CDC task via observation, which has been argued to invoke declarative knowledge, leads to equivalent performance to learning to control a CDC task via action, which has been argued to invoke procedural knowledge. Many theorists proposing dissociation between conscious and unconscious knowledge (e.g., Berry, 1991; Berry & Broadbent, 1984, 1987, 1988; Lee, 1995) would predict greater declarative knowledge for both controls and for PD patients in the observation-based learning condition than the action-based version. This is because, for the age-matched control group the learning and test conditions require the same type of knowledge, and in the PD patient group the learning conditions facilitate accurate declarative knowledge of the task because there is no feedback. Previous studies (Burns & Vollmeyer, 2002; Dandurand et al., 2004; Gonzales, 2005; Osman, 2008a, 2008b, 2008c) of CDC tasks with healthy participants have shown associations between procedural and declarative knowledge on CDC tasks. Moreover, when comparing observation-based learning and active-based learning, Osman (2008a, 2008b) reported that there are no differences between performance on measures of control performance and structural knowledge.

The evidence from the present study also suggests that, consistent with Osman’s findings (2008a, 2008b, 2008c), control performance for PD patients and controls is not affected by the training procedure used (i.e. observation-based, action-based). Furthermore, in light of these studies, the present evidence suggests that structural knowledge informs control performance, given that although weak, both PD patients and controls show evidence of a degree of accurate structural knowledge of the system. The lack of an association between structural tests of knowledge and control tests of procedural knowledge for both PD patients and controls, indicates that although structural knowledge was learnt and was likely to have informed procedural knowledge, it was not expressed as easily in tests of structural knowledge. However, given that for both groups, there was an advantage in learning about the system procedurally on expression of declarative knowledge, more practice with the actual system may have led to a strengthening of the declarative knowledge that was used to support it.

5. Conclusions

In the present study we investigated what might lead to successful performance by PD patients on a CDC task and whether the type of feedback received during training (procedural vs. non-procedural) does indeed mediate performance. The main findings were that

- PD patients showed equivalent performance to age matched controls based on a measure of their ability to control a complex dynamic task.
- PD patients and controls showed equivalent procedural knowledge regardless of whether their training of the task was through self or artificially generated action-outcome associations.
- Overall both groups showed poorer knowledge of the structure of the system when their learning was observation-based than action-based.
- PD patients showed poorer declarative knowledge than age-matched controls for both observation-based and action-based versions of the CDC task. Thus while PD patients can acquire knowledge of the underlying rules of the task and could use it effectively in operating the task, they were unable to express this knowledge as effectively as controls.

The findings indicate that the striatal dysfunction in PD is not associated with learning deficits in CDC tasks regardless of whether or not learning involved self or artificially generated action-outcome associations.

Q5 Uncited reference

Brown, Redondo-Verge, Chacon, Lucas, and Channon (2001).

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Appendix A

A.1. Water Purification Tank Control System

Observation instructions: You are a trainee laboratory technician working in a water filtration unit. As part of your training you will learn to control the water tank system by managing three water quality measures: Oxygenation; Chlorine CL concentration; Temperature. The quality measures are known as outputs and are used to monitor three system inputs: Salt; Carbon; Lime. In the following task you will be presented with a series of trials in which you will see a diagram of the 'Malwart' water filtration unit, which you will learn to control. The system is set so that the quality measures change according to the values chosen by one of the workers of the water plant. You will see the amount of Salt, Carbon, and Lime inputs change automatically according to those set by the worker; this is indicated by a slider corresponding to each input moving either to the left or the right. You will see a total of 40 trials divided into four sessions of 10 trials each. For each trial, you should watch carefully the changes to the inputs. When you have examined the changes to the inputs you can check the output levels by pressing the button labeled 'Output readings.' This will reveal the concentration levels of the quality measures. After you have studied these you should press the 'Input levels' button to begin the next trial. You should try and pay close attention to the values of the inputs that are entered and the output levels; this is because you will be required to imitate the worker's behavior later. Good Luck!

A.2. Ghost Hunting Control System

General instructions: Newspaper Report: Hillside, NJ Investigations, Utah State Library.

Library worker John, his brother, and wife all reported seeing odd shadows out of the corner of their eyes. Most unusual was the report of the phone calls that came at 7:15 AM, certain mornings that were riddled with static and no one on the other end of the call. The team of paranormal investigators went to investigate yesterday and was fully equipped with a Trifield meter, a Anemometer, a GGH meter. The investigation took place from 6:30 AM till approximately 8:30 AM. Regular recordings were made. You were part of the team. You have done all the hard work and are back at the lab processing the data from the difference pieces of equipment you have used. Since you are new to this you are not quite sure which of the three pieces of equipment (GGH meter, Anemometer, Trifield meter) actually registers air pressure, radio waves, and the electro magnetic field—which are all disrupted when a ghost is present.

Standard action instructions: You have a total of 40 trials divided in to 4 sessions of 10 trials each in which you can test the equipment by altering the values of the meters and examining the computer readout for each of the output values: air pressure, radio waves, and electro magnetic field. For each trial, you should try to change only one input; however this is only a recommendation and you may choose to use a different strategy. Once you have changed the value of an input you can then check the output readings levels by pressing the button labeled 'show me readings'; this will reveal the computer readings. After you have studied these you should press the 'restart' button to begin the next trial. You should try and pay close attention to the values you chose for the meters and the effects on the output readings. Good Luck!

References

- Anderson, J. R. (1982). Acquisition of cognitive skill. *Psychological Review*, 89, 369–406.
- Ashby, F. G., Noble, S., Filoteo, J. V., Waldron, E. M., & Ellis, S. W. (2003). Category learning deficits in Parkinson's disease. *Neuropsychology*, 17, 115–124.
- Beck, A. T., Erbaugh, J., Ward, C. H., Mock, J., & Mendelsohn, M. (1961). An inventory for measuring depression. *Archives of General Psychiatry*, 4(6), 561.
- Berry, D. (1991). The role of action in implicit learning. *Quarterly Journal of Experimental Psychology*, 43, 881–906.
- Berry, D., & Broadbent, D. E. (1984). On the relationship between task performance and associated verbalizable knowledge. *Quarterly Journal of Experimental Psychology*, 36, 209–231.
- Berry, D., & Broadbent, D. E. (1987). The combination of implicit and explicit knowledge in task control. *Psychological Research*, 49, 7–15.
- Berry, D. C., & Broadbent, D. E. (1988). Interactive tasks and the implicit-explicit distinction. *British Journal of Psychology*, 79, 251–272.
- Buckner, R. L., Goodman, J., Burock, M., Rotte, M., Koutstaal, W., Schacter, D., et al. (1998). Functional-anatomic correlates of object priming in humans revealed by rapid presentation event-related fMRI. *Neuron*, 20(2), 285–296.
- Bondi, M. W., & Kaszniak, A. W. (1991). Implicit and explicit memory in Alzheimer's disease and Parkinson's disease. *Journal of Clinical Experimental Neuropsychology*, 13, 339–358.
- Brown, R. G., Jahanshahi, M., Limousin-Dowsey, P., Thomas, D., Quinn, N. P., & Rothwell, J. C. (2003). Pallidotomy and incidental sequence learning in Parkinson's disease. *Neuroreport*, 14(1), 21–24.
- Brown, R. G., Redondo-Verge, L., Chacon, J. R., Lucas, M. L., & Channon, S. (2001). Dissociation between intentional and incidental sequence learning in Huntington's disease. *Brain*, 124, 2188–2202.
- Brown, B. D., & Vollmeyer, R. (2002). Goal specificity effects on hypothesis testing in problem solving. *Quarterly Journal of Experimental Psychology*, 55, 241–261.
- Doyon, J., Gaudreau, D., Laforce, R., Castonguay, M., Bedard, P. J., Bedard, F., et al. (1997). Role of the striatum, cerebellum, and frontal lobes in the learning of a visuomotor sequence. *Brain and Cognition*, 34(2), 218–245.
- Doyon, J., Laforce, R., Bouchard, G., Gaudreau, D., Roy, J., Poirier, M., et al. (1998). Role of the striatum, cerebellum and frontal lobes in the automatization of a repeated visuomotor sequence of movements. *Neuropsychologia*, 36(7), 625–641.
- Doyon, J., Owen, A. M., Petrides, M., Sziklas, V., & Evans, A. C. (1996). Functional anatomy of visuomotor skill learning in human subjects examined with positron emission tomography. *European Journal of Neuroscience*, 8(4), 637–648.
- Exner, C., Koschack, J., & Irl, E. (2002). The differential role of premotor frontal cortex and basal ganglia in motor sequence learning: Evidence from focal basal ganglia lesions. *Learning and Memory*, 9, 376–386.

- Fahn, S., & Elton, R. L. (2005). UPDRS Development Committee. Unified Parkinson's disease rating scale. In S. Fahn, C. D. Marsden, D. Calne, & M. Goldstein (Eds.), *Recent developments in Parkinson's disease*. Florham Park, NJ: Macmillan Publishing Co. Inc.
- Ferraro, F. R., Balota, D. A., & Connor, L. T. (1993). Implicit memory and the formation of new associations in nondemented Parkinson's-disease individuals and individuals with senile dementia of the Alzheimer type—a serial reaction-time (Srt) investigation. *Brain and Cognition*, 21(2), 163–180.
- Filoteo, J. V., Maddox, W. T., & Davis, J. (1998). Probabilistic category learning in patients with amnesia, Huntington's disease, or Parkinson's disease: The role of the hippocampus and basal ganglia. *Journal of Cognitive Neuroscience*, 108–1108.
- Filoteo, J. V., Maddox, W. T., Salpmn, D. P., & Song, D. (2005). Information-integration category learning in patients with striatal dysfunction. *Neuropsychology*, 19, 212–222.
- Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). Mini-mental state—Practical method for grading cognitive state of patients for clinician. *Journal of Psychiatric Research*, 12(3), 189–198.
- Grafton, S. T., Hazeltine, E., & Ivry, R. (1995). Functional mapping of sequence learning in normal humans. *Journal of Cognitive Neuroscience*, 7(4), 497–510.
- Gold, K. Y., Harrington, D. L., O'Brien, S., & Hermanowicz, N. (1997). Cognitive-motor learning in Parkinson's disease. *Neuropsychology*, 11, 180–186.
- Haggard, P., Clark, S., & Kalogeras, J. (2002). Voluntary action and conscious awareness. *Nature Neuroscience*, 5, 382–385.
- Heindel, W. C., Salmon, D. P., Shults, C. W., Walicke, P. A., & Butters, N. (1989). Neuropsychological evidence for multiple implicit memory systems: A comparison of Alzheimer's, Huntington's and Parkinson's disease patients. *Journal of Neuroscience*, 9, 582–587.
- Helmuth, L. L., Mayr, U., & Daum, I. (2000). Sequence learning in Parkinson's disease: A comparison of spatial-attention and number-response sequences. *Neuropsychologia*, 38(11), 1443–1451.
- Hoehn, M. M., & Yahr, M. D. (1967). Parkinsonism—Onset progression and mortality. *Neurology*, 17(5), 427.
- Hollerman, J. R., Tremblay, L., & Schultz, W. (2000). Involvement of basal ganglia and orbitofrontal cortex in goal-directed behaviour. *Progress in Brain Research*, 126, 193–215.
- Hughes, A. J., Daniel, S. E., Kilford, L., & Lees, A. J. (1992). Accuracy of clinical-diagnosis of idiopathic Parkinson's disease—A clinicopathological study of 100 cases. *Journal of Neurology Neurosurgery and Psychiatry*, 55(3), 181–184.
- Jackson, G. M., Jackson, S. R., Harrison, J., Henderson, L., & Kennard, C. (1995). Serial reaction-time learning and Parkinson's disease—Evidence for a procedural learning deficit. *Neuropsychologia*, 33(5), 577–593.
- Kelly, S., & Burton, A. M. (2001). Learning complex sequences: No role for observation. *Psychological Research*, 65, 15–23.
- Kelly, S., Burton, A. M., Riedel, B., & Lynch, E. (2003). Sequence learning by action and observation: Evidence for separate mechanisms. *British Journal of Psychology*, 94, 355–372.
- Kelly, S. W., Jahanshahi, M., & Dirnberger, G. (2004). Learning of ambiguous versus hybrid sequences by patients with Parkinson's disease. *Neuropsychologia*, 42(10), 1350–1357.
- Knopman, D., & Nissen, M. J. (1991). Procedural learning is impaired in Huntingtons-disease—Evidence from the serial reaction-time-task. *Neuropsychologia*, 29(3), 245–254.
- Knowlton, B. J., Mangels, J. A., & Squire, L. R. (1996). A neostriatal habit learning system in humans. *Science*, 273(5280), 1399–1402.
- Knowlton, B. J., Squire, L. R., Paulsen, J. S., Swerdlow, N. R., Swenson, M., & Butters, N. (1996). Dissociations within nondeclarative memory in Huntington's disease. *Neuropsychology*, 10(4), 538–548.
- Krebs, H. I., Hogan, N., Hening, W., Adomovich, S. V., & Poizner, H. (2001). Procedural motor learning in Parkinson's disease. *Experimental Brain Research*, 141, 425–437.
- Kircher, T. T., & Leube, D. T. (2003). Self-consciousness, self-agency, and schizophrenia. *Consciousness and Cognition*, 12, 656–669.
- Lee, Y. (1995). Effects of learning contexts on implicit and explicit learning. *Memory and Cognition*, 23, 723–734.
- Maddox, T. W., Aparicio, P., Marchant, N. L., & Ivry, R. B. (2005). Rule-based category learning is impaired in patients with Parkinson's disease but not in patients with cerebellar disorders. *Journal of Cognitive Neuroscience*, 17, 707–723.
- McNamara, P., Dursio, R., & Brown, A. (2003). Relation of “sense of self” to executive function performance in Parkinson's disease. *Cognitive and Behavioral Neurology*, 14, 139–148.
- Osman, M. (2008a). Observation can be as effective as action in problem solving. *Cognitive Science*, 32, 162–183.
- Osman, M. (2008b). Evidence for positive transfer and negative transfer/anti-learning of problem solving skills. *Journal of Experimental Psychology: General*, 137, 97–115.
- Osman, M. (2008c). Seeing is as good as doing. *Journal of Problem Solving*, 2, 1.
- Pascual-Leone, A., Grafman, J., Clark, K., Stewart, M., Massaquoi, S., & Lou, J. S. (1993). Procedural learning in Parkinson's-disease and cerebellar degeneration. *Annals of Neurology*, 34(4), 594–602.
- Peigneux, P., Maquet, P., Meulemans, T., Destrebecqz, A., Laureys, S., Degueldre, C., et al. (2000). Striatum forever, despite sequence learning variability: A random effect analysis of PET data. *Human Brain Mapping*, 10(4), 179–194.
- Poldrack, R. A., Clark, J., Pare-Blagoev, E. J., Shohamy, D., Moyano, J. C., Myers, C., et al. (2001). Interactive memory systems in the human brain. *Nature*, 414(6863), 546–550.
- Poldrack, R. A., Prabhakaran, V., Seger, C. A., & Gabrieli, J. D. E. (1999). Striatal activation during acquisition of a cognitive skill. *Neuropsychology*, 13(4), 564–574.
- Reber, P. J., & Squire, R. L. (1999). Intact learning of artificial grammars and intact category learning by patients with Parkinson's disease. *Behavioural Neuroscience*, 1235–242.
- Savage, J. A., Taylor, A. E., & Lang, A. E. (1998). Procedural learning and neostriatal dysfunction in man. *Brain*, 111, 941–959.
- Sage, J. R., Anagnostaras, S. G., Mitchell, S., Bronstein, J. M., De Salles, A., Masterman, D., et al. (2003). Analysis of probabilistic classification learning in patients with Parkinson's disease before and after pallidotomy surgery. *Learning and Memory*, 10(3), 226–236.
- Schmitt-Eliassen, J., Ferstl, R., Wiesner, C., Deuschl, G., & Witt, K. (2007). Feedback-based versus observational classification learning in healthy aging and Parkinson's disease. *Brain Research*, 1142, 178–188.
- Seger, C. A., & Cincotta, C. M. (2006). Dynamics of frontal, striatal, and hippocampal systems during rule learning. *Cerebral Cortex*, 16(11), 1546–1555.
- Seger, C. A., Prabhakaran, V., Poldrack, R. A., & Gabrieli, J. D. E. (2000). Neural activity differs between explicit and implicit learning of artificial grammar strings: An fMRI study. *Psychobiology*, 28(3), 283–292.
- Shin, J. C., & Ivry, R. B. (2003). Spatial and temporal sequence learning in patients with Parkinson's disease or cerebellar lesions. *Journal of Cognitive Neuroscience*, 15, 1232–1243.
- Siebert, 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(4), 490–495.
- Smith, J., Siebert, R. J., & McDowall, J. (2001). Preserved implicit learning on both the serial reaction time task and artificial grammar in patients with Parkinson's disease. *Brain and Cognition*, 43, 378–391.
- Soliveri, P., Brown, R. G., Jahanshahi, M., Caraceni, T., & Marsden, C. D. (1997). Learning manual pursuit tracking skills in patients with Parkinson's disease. *Brain*, 120, 125–137.
- Sommer, M., Grafman, J., Clark, K., & Hallett, M. (1999). Learning in Parkinson's disease: Eyeblick conditioning, declarative learning, and procedural learning. *Journal of Neurology Neurosurgery and Psychiatry*, 67(1), 27–34.
- Spence, S. A. (2003). Cognitive neurobiology of volition and agency in schizophrenia. In T. W. Robbins (Ed.), *Disorders of brain and mind* (pp. 223–242). Cambridge University Press.
- Squire, L. (1986). Mechanisms of memory. *Science*, 232, 1612–1619.
- Squire, L. R., & Zola, S. M. (1990). Cognitive skill learning in amnesia. *Psychobiology*, 18, 109–117.
- Squire, L. R., & Zola, S. M. (1996). Structure and function of declarative and non-declarative memory systems. *Proceedings of the National Academy of Sciences of the United States of America*, 93(24), 13515–13522.
- Stanley, W. B., Mathews, R. C., Buss, R. R., & Kotler-Cope, S. (1989). Insight without awareness: On the interaction of verbalization, instruction, and practice in a simulated process control task. *Quarterly Journal of Experimental Psychology*, 41, 533–577.
- Vriezen, E. R., & Moscovitch, W. (1990). Memory for temporal order and conditional associative-learning in patients with Parkinson's disease. *Neuropsychologia*, 28, 1283–1293.
- Wilkinson, L., & Jahanshahi, M. (2007). The striatum and probabilistic implicit sequence learning. *Brain Research*, 1137(1), 117–130.
- Wilkinson, L., Lagnado D.A., Quallo, M., & Jahanshahi, M. (in press). The effect of corrective feedback on non-motor probabilistic classification learning in Parkinson's disease. *Neuropsychologia*.
- Willingham, D. B., & Koroshetz, W. J. (1993). Evidence for dissociable motor-skills in Huntingtons-disease patients. *Psychobiology*, 21(3), 173–182.
- Witt, K., Daniels, C., Daniel, V., Schmitt-Eliassen, J., Volkmann, J., & Deuschl, G. (2006). Patients with Parkinson's disease learn to control complex systems – an indication for intact implicit cognitive skill learning. *Neuropsychologia*, 44, 2445–2451.
- Witt, K., Nuhsmann, A., & Deuschl, G. (2002a). Dissociation of habit-learning in Parkinson's and cerebellar disease. *Journal of Cognitive Neuroscience*, 14(3), 493–499.
- Witt, K., Nuhsmann, A., & Deuschl, G. (2002b). Intact artificial grammar learning in patients with cerebellar degeneration and advanced Parkinson's disease. *Neuropsychologia*, 40(9), 1534–1540.