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Role of the Basal Ganglia in Category Learning: How Do Patients With Parkinson's Disease Learn?

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The purpose of the present study was to gain a deeper understanding of the role of the basal ganglia in learning and memory by examining learning strategies among patients with basal ganglia dysfunction. Using a probabilistic category learning task (the "weather prediction" task) previously shown to be sensitive to basal ganglia function, the authors examined patterns of performance during learning and used mathematical models to capture different learning strategies. Results showed that patients with Parkinson's disease exhibit different patterns of strategy use. Specifically, most controls initially used a simple, but suboptimal, strategy that focused on single-cue–outcome associations; eventually, however, most controls adopted a more complex, optimal learning strategy, integrating single-cue associations to predict outcomes for multiple-cue stimuli. In contrast, the majority of individuals with Parkinson's disease continued to rely on simple single-cue learning strategies throughout the experiment.

The basal ganglia have traditionally been associated with motor control. However, studies in the past decade have also implicated the basal ganglia in cognition. Neuroanatomical studies have shown that the basal ganglia form reciprocal loops with highly cognitive regions in the frontal cortex (Alexander, DeLong, & Strick, 1986). Electrophysiological findings have demonstrated that dopamine neurons in the basal ganglia play an important role in reward-related learning (Schultz, 1998; Schultz, Dayan, & Montague, 1997). Behavioral studies have also provided evidence for the role of the basal ganglia in cognition, demonstrating that basal ganglia damage leads to a range of cognitive deficits in animals (Kesner, Bolland, & Dakis, 1993; Kim & Baxter, 2001; McDonald & White, 1993; Packard, 1999; Packard, Hirsch, & White, 1989; Packard & McGaugh, 1996) and humans (Downes et al., 1989; Jackson, Jackson, Harrison, Henderson, & Kennard, 1995; Owen et al., 1993; Saint-Cyr, Taylor, & Lang, 1988; Swainson et al., 2000).

Most behavioral studies view the basal ganglia as supporting a procedural, or habit, learning system (Eichenbaum & Cohen, 2001; Gabrieli, 1998; Jog, Kubota, Connoly, Hillegaart, & Graybiel, 1999; Knowlton, Mangels, & Squire, 1996; Mishkin, Malamut, & Bachevalier, 1984; Robbins, 1996; Squire, 1994; Squire & Zola, 1996). *Procedural learning* is defined as learning that is acquired over many trials, without requiring explicit conscious awareness (e.g., Gabrieli, 1998); an example would be learning to ride a bicycle, where the ability to consciously verbalize the knowledge bears little relationship to the learning of the skill itself. This procedural learning system has been dissociated both functionally and anatomically from a medial temporal lobe system thought to be important for declarative memory, which is typically defined as explicit and conscious recollection of facts or events (e.g., Gabrieli, 1998; Knowlton et al., 1996; Squire, 1994).

Evidence supporting a role for the basal ganglia in procedural learning comes from findings that animals with basal ganglia lesions show deficits on behavioral tasks thought to rely on procedural learning. For example, animals with basal ganglia damage are impaired at gradual learning of cue–outcome relations (cf. Packard et al., 1989), or stimulus–response associations (Packard, 1999; Packard & McGaugh, 1996).

Further evidence for the role of the basal ganglia in learning comes from studies of patients with Parkinson's disease. In Parkinson's disease, dopamine-containing neurons in the substantia nigra pars compacta degenerate, causing a decrease in striatal dopamine and disrupting basal ganglia function (Agid, Javoy-Agid, & Ruberg, 1987; Robertson & Robertson, 1988). Thus, patients with Parkinson's disease provide a good opportunity for studying the role of the basal ganglia in cognition.

Indeed, humans with Parkinson's disease are impaired on a variety of cognitive tasks. Early studies of cognitive deficits in Parkinson's disease focused on tasks sensitive to frontal lobe function, such as working memory (Lange & Robbins, 1992; Owen, Beksinska, et al., 1993, Owen, Iddon, Hodges, Summers, &

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Robins, 1997) and set-shifting (Downes et al., 1989; Owen, Roberts, et al., 1993), presumably impaired in Parkinson's disease as a result of disruption of striatofrontal loops (e.g., Gotham, Brown, & Marsden, 1988; Owen et al., 1992; Taylor, Saint-Cyr, & Lang, 1986). More recent studies have shown that Parkinson's patients are impaired at implicit, procedural learning tasks that are not considered to be "frontal" tasks. Further, these impairments are not correlated with patients' performance on typical measures of frontal function (Knowlton et al., 1996). For example, Parkinson's patients were found to be impaired at visuomotor sequence learning (Jackson et al., 1995; Pascuale-Leone et al., 1993), verbal serial reaction (Westwater, McDowall, Siegert, Mossman, & Abernathy, 1998), conditional association (Myers et al., 2003; Vriezen & Moskovitch, 1990), and probabilistic category learning (Knowlton et al., 1996). The probabilistic category learning task, in particular, has been considered a good example of the role of the basal ganglia in learning, because functional magnetic resonance imaging (fMRI) reveals basal ganglia activity in healthy controls engaged in learning this task (Poldrack et al., 2001; Poldrack, Prabhakaran, Seger, & Gabrieli, 1999).

Nonetheless, a precise understanding of the role of the basal ganglia in learning remains elusive. Studies have shown that basal ganglia damage does not impair all kinds of nondeclarative, implicit learning (Bondi & Kaszniak, 1991; Harrington, Haaland, Yeo, & Marder, 1990; Heindel, Salmon, Shults, Walicke, & Butters, 1989; Koivisto, Portin, & Rinne, 1996; Reber & Squire, 1999; Smith, Siegert, & McDowall, 2001). Further, some studies have reported impaired learning in Parkinson's patients on other tasks that are not considered to rely on implicit, procedural learning, such as impaired recognition memory (Owen, Beksinska, et al., 1993; Whittington, Podd, & Kan, 2000), impaired recall memory (Bondi & Kaszniak, 1991; Breen, 1993), impaired explicit visuospatial memory (Pillon et al., 1996), and impaired delayed match-to-sample (Owen, Beksinska, et al., 1993).

One reason for the lack of a precise understanding of the role of basal ganglia in learning may be that most behavioral studies have focused on "bottom-line" performance, demonstrating that basal ganglia damage leads to impaired performance compared with that of control participants in some cases, but not in others. However, such findings can be interpreted in more than one way. For example, individuals with basal ganglia dysfunction may be impaired on a learning task because they are slower to learn in general. This explanation would be consistent with the general motor and cognitive slowness that are typical of the disease (Cooper, Sagar, Tidswell, & Jordan, 1994; Kolb & Whishaw, 1995). Alternatively, the basal ganglia may play a critical role in supporting particular types of cognitive processing, so that damage to the basal ganglia forces learning to rely on other strategies and brain systems. This view would be consistent with electrophysiological and anatomical studies implicating a role for the basal ganglia in specific types of learning (Middleton & Strick, 1994; Schultz, 1998) and in specific types of motor behavior (e.g., Graybiel, 1995). If this is the case, one might expect to find that individuals with basal ganglia damage would engage in different learning strategies compared with healthy controls.

To examine these possibilities, we directly compared performance of individuals with Parkinson's disease and matched controls on a learning task previously shown to be particularly sensitive to basal ganglia function (Knowlton et al., 1996; Poldrack et al., 1999, 2001), and used mathematical models to assess learning strategies in each individual.

The task, known as the "weather prediction" category learning task (Gluck, Shohamy, & Myers, 2002; Knowlton et al., 1996; Knowlton, Squire, & Gluck, 1994), requires participants to learn to predict a weather outcome (rain or sunshine) on the basis of the appearance of four cues (tarot cards with geometric shapes; see Figure 1). In this task, the relation between the cues and outcomes is probabilistic. For example, one card might predict sunshine with 80% accuracy, but predict rain on the remaining 20% of trials; the most likely outcome on any given trial depends on the combination of cards that appear (see Figure 2).

Because of the probabilistic nature of the weather prediction task, in which no individual trial can provide accurate information about the cue–outcome associations, it has generally been assumed that participants learn this task by incrementally acquiring associations between all four cues and each outcome (Gluck & Bower, 1988; Knowlton et al., 1994, 1996). This *multicue* strategy is the optimal way to learn the task. However, given the structure of the task, there are also suboptimal single-cue strategies that can lead to reasonable performance. For example, an individual could focus on one cue, such as the card with the square shape, and learn how to predict the outcome on the basis of the presence or absence of that card alone, ignoring the other cards (a "one-cue" strategy; see Figure 3a). Another suboptimal strategy would be to learn the correct answer to only those patterns on which a single card appears, but to respond randomly on those trials in which two or more cards appear (a "singleton" strategy; see Figure 3b). Each of these suboptimal strategies can lead to performance that is significantly above chance. In a recent experiment with young healthy controls, we found that these three classes of strategies—multicue, one-cue, and singleton—provided a good description of the performance (over 200 training trials) of over 98% of participants, and that less than 25% of those participants tested appeared to use an optimal multicue strategy (Gluck et al., 2002).

One question is therefore: Do Parkinson's patients use the same range of strategies as controls? We hypothesized that if Parkinson's patients use the same kinds of learning strategies as controls, but simply acquire them more slowly, this would suggest that the basal ganglia may be particularly important in modulating learning

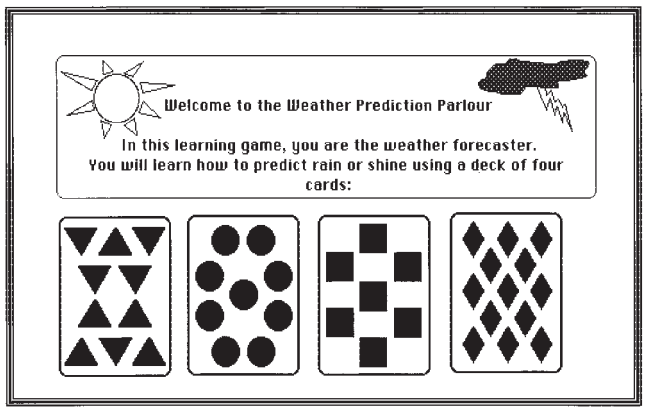

Figure 1. Example of stimuli used in the weather prediction classification task. Reprinted with permission from Knowlton, B. J., Mangels, J. A., & Squire, L. R. (1996, September 6). A neostriatal habit learning system in humans. *Science, 273,* 1399–1402. Copyright 1996 AAAS.

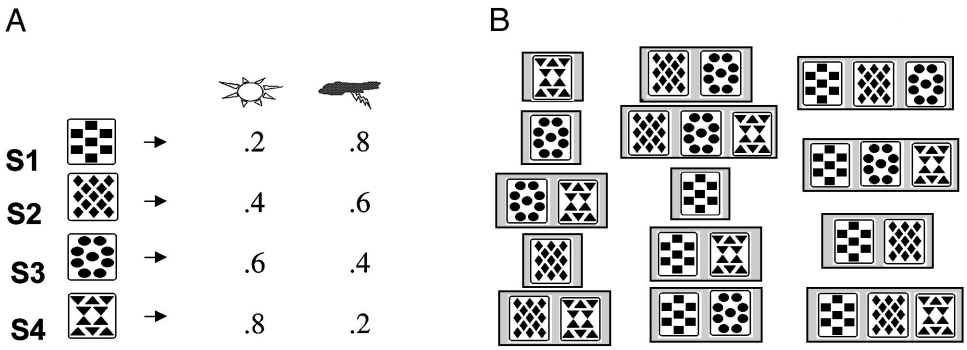

Figure 2. A: Each card (S1–S4) was associated with each possible outcome (rain vs. sunshine) with a fixed probability. B: On each trial, one of these 14 patterns of cue combinations was presented.

rate. In contrast, if patients with Parkinson's disease use different kinds of learning strategies, this may suggest a more specific role for the basal ganglia in particular types of learning. To address these questions, we administered the weather prediction task to a group of Parkinson's patients and matched healthy controls. Given the possibility of particularly slow learning among the Parkinson's patients, we also extended training over 3 consecutive days to examine whether Parkinson's patients would eventually reach levels of performance comparable to those of healthy controls.

Method

Participants

Participants included 12 individuals with a diagnosis of idiopathic Parkinson's disease (8 men and 4 women) and 14 age-matched healthy controls (8 men and 6 women). All patients were in the mild-to-moderate stages of the disease, with scores on the Hoehn–Yahr scale of motor function (Hoehn & Yahr, 1967) that ranged from 2 to 3. All Parkinson's patients were nondemented, as indicated by scores greater than 24 on the Mini-Mental State Exam (MMSE; Folstein, Folstein, & McHugh, 1975). Parkinson's patients were also screened for clinical depression, as indicated by scores below 15 on the Beck Depression Inventory (Beck, Steer, & Brown, 1996). All patients were being treated with L-dopa and were tested while on medication. Patient and control information is presented in Table 1.

Controls were not significantly different from the Parkinson's patients in age, education, or MMSE scores (independent samples t test, $p > .10$). Controls were screened for the presence of any neurological disorder or history of psychiatric illness including depression.

All participants signed statements of informed consent before participating in behavioral testing. All studies conformed to research guidelines established by Rutgers University and the federal government.

Apparatus and Stimuli

The experimental task was programmed with SuperCard software (Allegiant Technologies, San Diego, CA) and was presented on an Apple Macintosh 1400c or equivalent laptop computer with a color screen. Testing took place in a quiet room. Responses were recorded on a standard Macintosh keyboard, masked except for two keys, labeled *sun* and *rain*, which the participant used to enter responses.

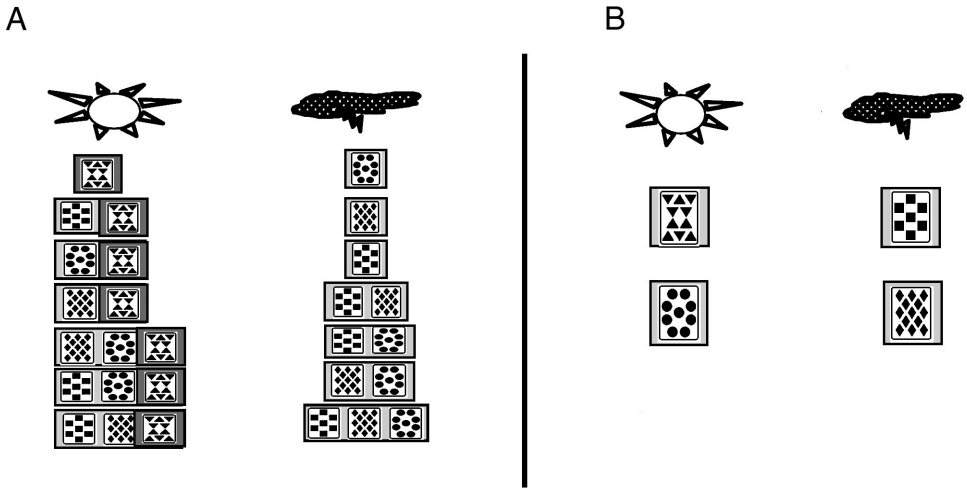

Figure 3. Examples of different kinds of strategies a participant could use to learn the weather prediction task. A: One-cue strategy: All patterns with a particular cue (here the triangles card) present are mapped to sun; the remainder are mapped to rain. B: Singleton strategy: Those patterns with a single card present (singleton patterns) are learned; the subject guesses on the remaining patterns.

Table 1
Participant Information for Parkinson's Patients and Controls

Group	Age	Education	MMSE	Hoehn-Yahr	Disease duration
Parkinson's	59.5 ± 3.3	16.4 ± 1.4	29.0 ± 0.7	2.5 ± 0.2	9.8 ± 5.2
Controls	65.1 ± 2.8	16.3 ± 2.1	29.0 ± 0.7		

Note. Age, education, and disease duration are shown in years. Hoehn-Yahr is a rating of motor function. MMSE = Mini-Mental State Examination.

The stimuli consisted of four tarot cards, each with a different geometric shape (circle, square, triangle, diamond), presented in black and white. On each trial, between one and three cards were presented in the center of the screen. A vertical score bar was presented at the right of the screen.

Participants were required to learn which of two outcomes was predicted by each combination of cards (Figure 1). Each card was independently associated with each outcome with a fixed probability, and the two outcomes occurred equally often. Table 2 shows the probability of Outcome 1 (sun) given each possible combination of cards and the frequency with which each combination was presented within one block of 200 trials. The probability with which each card predicts each outcome is obtained by calculating the probability of that outcome given that the card is present, P(outcome|card), divided by the total probability that the card would occur regardless of the outcome, P(card). For example, as one can calculate from Table 2, Card 1 is present in seven patterns (H–N). Because Patterns H–N occur on 100 trials, 20 of which are associated with sun, P(sun|card 1) = 20 ÷ 100 = 0.2. Similarly, Cards 2–4 are associated with sun with probabilities of 0.4, 0.6, and 0.8, respectively. Note that the two outcomes occur with equal probability throughout the block of 200 trials, and that each individual card is likewise present on exactly half of all trials.

Procedure

The participant was seated at a comfortable viewing distance from the computer screen. Instructions appeared on the computer screen, as previously described (e.g., Knowlton et al., 1994, Experiment 1). Briefly, the instructions stated that the participant was to learn to predict the weather (sun or rain) on the basis of the tarot cards; for each day, between one and three cards would be dealt, and the participant should enter a prediction by pressing the keyboard key labeled *sun* or *rain*. Participants were told that at first they would have to guess but that they would gradually improve their performance. Participants were not given any explicit information about the probabilistic nature of the stimulus–outcome relations.

At the start of each trial, cards appeared at the center of the screen and the participant was requested to respond. The computer recorded the participant's response. The actual weather was then revealed by a sun or rain cloud icon that appeared above the cards. If the participant's response matched the weather, a "smiley face" icon appeared and the score bar increased; if the participant's response did not match the weather, or if no response had been made, a "frown face" icon appeared and the score bar decreased. In addition, there was auditory feedback in the form of a high tone on match trials and a low tone on nonmatch trials. If the subject did not respond within 2 s, an "Answer Now!" prompt appeared. If the subject did not respond within the next 3 s, the trial was terminated and the weather was shown.

Each training session consisted of 200 trials. Testing took place in three 200-trial sessions, on 3 consecutive days. After testing on the last day was completed, participants were debriefed.

Data Analysis

On each trial, the computer recorded the pattern, the participant's response, and the actual weather.

In a probabilistic categorization task, the optimal response is one in which the participant responds to each combination of cues by predicting the outcome that is, on average, most often associated with that combination. For example, because Pattern A occurs on 19 trials, 17 times associated with sun and 2 times associated with rain (Table 2), the optimal

Table 2
Probability Structure of the Weather Prediction Task

	Cue						
Pattern	1	2	3	4	P(pattern)	Frequency (no. per 200 trials)	P(outcome)
A	0	0	0	1	0.095	19	0.89
B	0	0	1	0	0.045	9	0.78
C	0	0	1	1	0.130	26	0.92
D	0	1	0	0	0.045	9	0.22
E	0	1	0	1	0.060	12	0.83
F	0	1	1	0	0.030	6	0.50
G	0	1	1	1	0.095	19	0.89
H	1	0	0	0	0.095	19	0.11
I	1	0	0	1	0.030	6	0.50
J	1	0	1	0	0.060	12	0.17
K	1	0	1	1	0.045	9	0.55
L	1	1	0	0	0.130	26	0.08
M	1	1	0	1	0.045	9	0.44
N	1	1	1	0	0.095	19	0.11

Note. On any trial, 1 of 14 possible combinations of four cues could appear with the probability indicated: P(pattern). Each combination of cues predicted one outcome with the probability P(outcome) shown above and predicted the other outcome with a probability of 1 − P(outcome).

response to Pattern A is "sun," even though on a few trials, the actual outcome will be rain. Following earlier studies by Knowlton et al. (1994) and others, we accordingly defined a correct response as one that obeyed this optimal response rule, regardless of the actual outcome (i.e., whether the participant accurately predicted the weather). Note that there is no optimal response defined for Patterns F and I, which are equally often associated with each outcome. Percent correct scores were analyzed by 200-trial blocks across the 3 days of testing; following Knowlton et al. (1994), we also analyzed performance in blocks of 10 trials each for the first 50 trials of Day 1.

Strategy Analysis

To investigate response strategies, for each session of 200 training trials, we generated model response profiles based on how "ideal" participants would respond on each trial if they had been following each strategy: multicue, one-cue, or singleton. For each participant, we then calculated the degree to which each "ideal" mathematical model fit the participant's data, using a least mean square measure, with 0.0 indicating a perfect fit. Comparing across all strategies examined, the model that most closely approximated a participant's individual response profile was defined as the *best fit model* for that participant. Because some participants may not be well fit by any predefined model, we excluded strategy analysis data from any participant who was not fit by any model within a tolerance of 0.1. Full details and mathematical equations can be found in Gluck et al. (2002).

As described above, we considered the following three classes of learning strategies:

1. *Multicue strategy*: Under this strategy, a participant should respond to each pattern of cues with the outcome most often associated with that pattern. This involves attending to the entire pattern (i.e., all cues) present on each trial. A participant reliably following this strategy would be scored as making 100% correct responses over the course of the experiment.

2. *One-cue strategy*: Using this strategy, a participant should respond to each pattern on the basis of the presence or absence of a single card, disregarding the other cards. For example, a participant might respond "rain" whenever Card 1 is present and "sun" otherwise, regardless of what other cards are present. A participant reliably following this strategy should generate 90% correct responses. (Card 4, which predicts sun with high accuracy, could also be used to generate 90% correct responses. Cards 2 or 3, which are associated less reliably with the two outcomes, could each be used to generate 67% correct responses.)

3. *Singleton strategy*: In this strategy, a participant should learn the outcomes associated with those patterns in which only a single card appears. For example, a participant would learn that Cards 1 and 2 each reliably predict rain, whereas Cards 3 and 4 reliably predict sun. Because Patterns A, B, D, and H occur with such high frequency during the experiment (accounting for 28% of all trials), a participant responding correctly to these patterns and randomly to the remaining patterns could achieve up to 64% correct over the course of the experiment.

To determine whether the distribution of best fit strategies differed between control and Parkinson's groups, and whether best fit strategies changed across days, we conducted a 2 × 3 × 3 log–linear chi-square analysis for three variables (Group × Day × Strategy).

Results

Overall Classification Performance

Figure 4 shows classification performance for Parkinson's patients and controls, over 3 days of testing (200 trials per day). A repeated measures analysis of variance (ANOVA; Day × Group) revealed that both groups improved significantly across the 3 days of testing, as evidenced by a significant main effect of days, $F(2, 48) = 125.8$, $p < .01$; however, the Parkinson's patients were consistently impaired compared with the controls, as confirmed by a significant main effect of group, $F(1, 24) = 4.9$, $p < .05$. There was no significant interaction between group and day, $F(2, 48) = 1.3$, $p = .20$. In addition, to test our a priori hypothesis that Parkinson's patients might improve with extensive training over 3 days, we conducted a separate repeated measures ANOVA on the Parkinson's data alone, revealing significant learning among the Parkinson's patient group over 3 days, $F(2, 22) = 5.4$, $p < .01$.

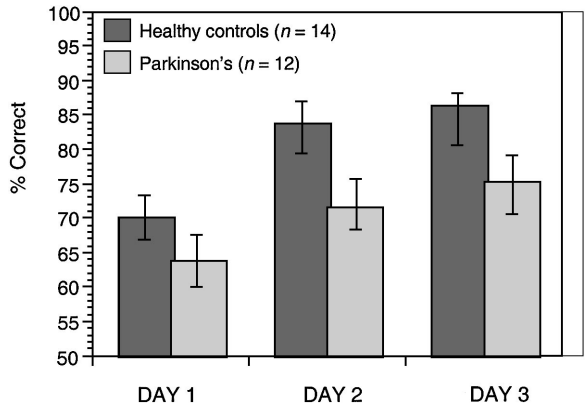

Figure 4. Classification performance over 3 days of training. Error bars indicate *SEM*.

Post hoc Tukey's analyses revealed that the Parkinson's deficit was related mainly to significant differences between the groups later in training, on Day 2 and Day 3 (both ps $< .05$), but not on Day 1 ($p > .50$). In addition, because previous reports have found group differences during the first 50 trials of Day 1, we performed a separate analysis of that period. In contrast to previous reports (Knowlton et al., 1996), we found no significant differences between the groups in the first 50 trials of Day 1: a repeated measures ANOVA (Block × Group) found no significant effect of block, $F(4, 96) = 1.7$, $p = .10$; no main effect of group, $F(1, 24) = 0.7$, $p = .40$, nor any Group × Block interaction, $F(4, 96) = 0.4$, $p = .80$.

Learning Strategies

Over all 3 days, 97% of the control data and 94% of the Parkinson's data were best fit within defined tolerance by one of the three strategies described above: multicue, one-cue, or singleton. Those data that did not fit within defined tolerance were excluded from further analysis (1 healthy control on Day 1, 1 Parkinson's patient on Day 1, and 1 Parkinson's patient on Day 2). Figure 5 shows the distribution of strategy models providing a best fit to data from the control and Parkinson's groups, across the 3 days of testing.

Among controls, the singleton strategy (learning responses to single-card patterns) provided a best fit model for the majority of participants on Day 1. By Day 3, a large majority of control participants were best fit by an optimal multicue strategy, reliably responding to each pattern on the basis of the association of each of the four cues with its most probable outcome.

By contrast, although the Parkinson's group showed a generally similar strategy distribution on Day 1, with most participants' data best fit by a singleton strategy, there was relatively less evidence

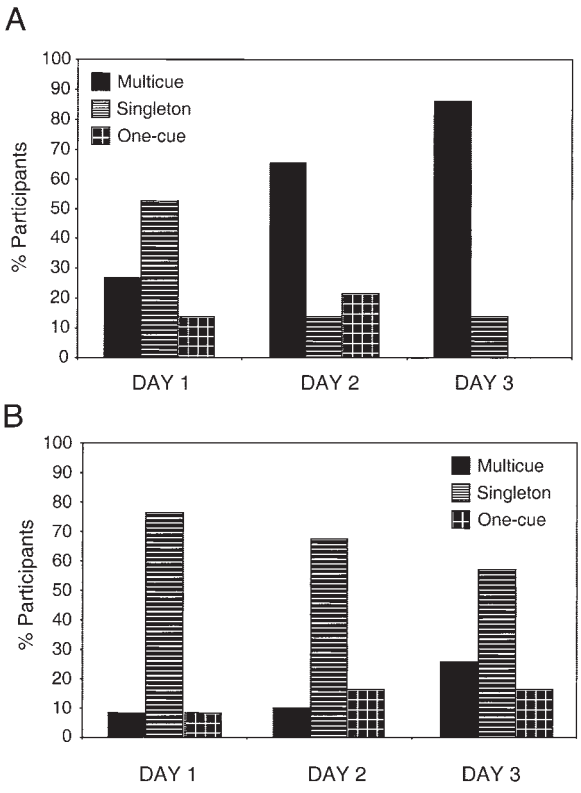

Figure 5. Learning strategies by day. A: Control data. B: Parkinson's data.

of a shift away from that strategy on Days 2 and 3, compared with controls. The majority of Parkinson's data was still best fit by a singleton strategy model on Days 2 and 3.

A chi-square three-way comparison of strategies by group across the 3 days (log-linear analysis for three variables, Strategy × Day × Group) revealed a significant interaction between these three variables, $\chi^2(12, N = 75) = 32.70$, $p < .01$. Pairwise contrasts with alpha corrected to .025 for multiple analyses confirmed that this interaction was due to a significant change in strategies among control participants across the 3 days: Day × Strategy chi-square comparison in the control group, $\chi^2(4, N = 41) = 11.35$, $p < .03$, whereas there was no such shift among the Parkinson's disease group, $\chi^2(4, N = 34) = 2.15$, $p = .70$.

A comparison of performance by strategy for the last day of testing (Day 3) is shown in Figure 6. As shown, within each group, those following a multicue strategy performed better than those following a singleton strategy. An ANOVA on Performance × Group × Strategy revealed a significant main effect of strategy, $F(1, 19) = 60.7$, $p < .01$, but there was no main effect of group nor a Group × Strategy interaction (all ps $> .10$). A very similar pattern of results was found for performance on Days 1 and 2, as well: Those participants following a multicue strategy significantly outperformed those following a singleton strategy, regardless of group: main effect of strategy, Day 1, $F(1, 18) = 11.8$, $p < .01$; Day 2, $F(1, 18) = 17.0$, $p < .01$; no main effect of group nor a Group × Strategy interaction (all ps $> .10$). We conducted a separate analysis for those participants best fit by the singleton strategy, demonstrating that, as expected, their performance did not differ significantly from 64% correct, which is the theoretical maximum for that strategy: Parkinson's, $t(6) = 0.74$, $p > .10$; controls, $t(1) = 0.05$, $p > .10$ (although note that some subgroups in these analyses, e.g., control singleton on Day 3, consist of a small number of subjects).

To further explore the effect of trial type on learning, we examined performance of Parkinson's and controls separately for singleton trials versus multicue trials. An ANOVA examining performance by group (Parkinson's vs. controls) and trial type (singleton trial vs. multicue trial) revealed a significant main effect of group, $F(1, 44) = 13.2$, $p < .01$, and of trial type, $F(1, 44) = 18.7$, $p < .01$, as well as a significant Group × Trial Type interaction, $F(1, 44) = 5.6$, $p < .05$. In confirmation of the results of the model-based strategy analyses, post hoc Tukey's analyses found that this interaction was due to significantly better performance among controls than among Parkinson's patients on the multicue trials ($p < .01$), whereas there was no significant difference in performance between controls and Parkinson's patients on the singleton trials ($p = .80$).

There were no obvious demographic differences (e.g., age, education, gender, or MMSE) in either group between those that did shift to the optimal multicue strategy and those that did not, nor were there any significant differences among the Parkinson's patients in terms of Hoehn–Yahr scores or disease duration and overall performance or strategy use (independent sample t tests, all ps $> .50$).

Discussion

The purpose of the present study was to gain a deeper understanding of the nature of the learning and memory impairments in Parkinson's disease by focusing on how individuals with Parkinson's disease learn, rather than just examining overall learning levels. Specifically, we sought to determine whether Parkinson's patients use learning strategies that are the same as those used by controls, or whether they use different kinds of learning strategies than controls, presumably because the strategies used by controls rely on basal ganglia function, which is disrupted in Parkinson's disease.

We found that Parkinson's patients were impaired at acquiring the multiple-cue–outcome associations that are required for learning this task in an optimal way. Most Parkinson's patients did not

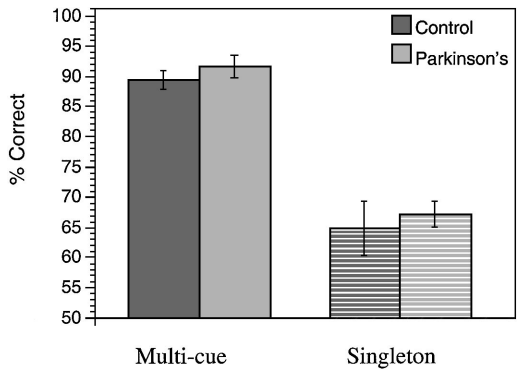

Figure 6. Performance by strategy on Day 3.

learn to respond to each multicue stimulus according to the most usual outcome for that stimulus. Instead, Parkinson's patients used learning strategies that focus on single cues. These single-cue associations are also used by control participants early in training; however, whereas most control participants shifted to using the optimal multicue strategy later in training, most Parkinson's patients did not. It is important to note that those (few) Parkinson's patients who did shift to a multicue strategy were as accurate as controls (and, conversely, accuracy levels were similar among Parkinson's patients and those few controls who remained best fit by the singleton strategy). This suggests that when Parkinson's patients are able to learn the multicue–outcome associations, they are as accurate as controls in using that strategy; however, most Parkinson's patients do not shift to the optimal multicue–outcome strategy.

These findings are also reflected in the overall performance of the two groups. We found no difference between the control and the Parkinson's groups on the 1st day of testing, but we found that controls outperformed the patients on the 2nd and 3rd days. The finding that Parkinson's patient performance improved throughout training suggests that although they rely on singleton associations, they are nevertheless able to show significant learning within those constraints.

Clearly, the strategy analyses reported here provide only a preliminary assessment of participants' behavior and do not provide an exhaustive examination of all possible strategies used by each participant during learning. Similarly, changes in strategy fit do not necessarily reflect a conscious decision on the part of the participant; a previous study found that healthy controls are generally unable to verbalize their strategies well, or to declare exactly when they shift strategies (Gluck et al., 2002). This shifting most likely occurs gradually over several trials as a participant learns to perform better on different kinds of trials, allowing a gradual shift toward using singleton information in the multicue patterns. Nonetheless, the different patterns of strategy fit between Parkinson's patients and controls suggest important differences in how Parkinson's and controls learn this task.

The Basal Ganglia and Learning About Multicue Stimuli

The finding that individuals with Parkinson's disease show little evidence of learning the multicue strategy suggests that this type of learning requires a cognitive function normally subserved by the basal ganglia–frontal loops that are impaired in Parkinson's disease.

One possible explanation of this finding is that Parkinson's patients have a deficit in learning to integrate responding across multiple stimulus–response associations. The singleton strategy is defined as learning cue–outcome associations for each of the four cues in the simplest cases, in which a single cue is presented and is associated with an outcome. The multicue strategy can be viewed as learning cue–outcome associations for each of the four singletons, but integrating the cue–outcome associations in order to respond in cases where the cues appear together. Thus, to the extent that controls learn to respond to multicue stimuli by integrating responses from single-cue stimuli, this would suggest that Parkinson's patients may be impaired at such integration.

This idea is consistent with the functional anatomy of the basal ganglia and its disruption in Parkinson's disease: The neostriatum receives highly convergent input from many cortical areas (Alexander et al., 1986; Wise, Murray, & Gerfen, 1996), suggesting a role in compressing or integrating information across multiple cues. The striatum is also modulated by dopamine input representing important stimulus-specific information (Horvitz, 2000; Schultz, 1998, 2002) that may be critical in modifying behavior during learning. Given the loss of these dopamine projections and the disruption of striatal function that occur in Parkinson's disease, it seems plausible that patients with Parkinson's disease may be specifically impaired on learning tasks that require feedback-based acquisition of associations between multiple cues and outcomes.

An alternative view of multicue learning could be that this strategy involves learning about multiple, separate patterns of cues (14), each processed as an individual configural pattern, as opposed to learning about 4 cues. If so, the impaired performance of the Parkinson's patients may reflect a working memory impairment (14 cues would involve heavier memory load than 4 cues), or an impairment in attending to or processing multiple cues. This would be consistent with the frontal disruption and related attentional and working memory deficits in Parkinson's disease (Kolb & Whishaw, 1995; Owen et al., 1997; Owen, Beksinska, et al., 1993; Owen, Roberts, et al., 1993; Taylor et al., 1986). However, recent evidence suggests that although Parkinson's patients are impaired at selective attention (attending to a single dimension), they are less impaired at attentional integration, which would presumably be necessary if subjects were indeed treating each of the 14 stimulus patterns as configural cues (Ashby, Noble, Filoteo, Waldron, & Ell, 2003). Furthermore, this kind of configural learning is more often associated with the hippocampal-region structures that are impaired in medial temporal amnesia but spared in Parkinson's disease (e.g., Rudy & Sutherland, 1989). Therefore, this explanation seems less consistent with the cognitive deficits and the neuropathology of Parkinson's disease.

Learning Versus Shifting

An alternate explanation of the present findings is that Parkinson's patients are not specifically impaired at learning the multicue strategy, but are selectively impaired at shifting from one strategy to another. Thus, to the extent that the change in strategies in control participants reflects abandonment of one strategy in favor of a (more successful) new strategy, the present findings may be explained by a selective impairment in shifting strategies among the Parkinson's patients. This idea is consistent with other evidence of shifting deficits in Parkinson's disease. A number of studies suggest that Parkinson's patients are impaired at adjusting performance to reflect altered task demands (Owen, Beksinska, et al., 1993; Ravizza & Ivry, 2001; Taylor et al., 1986). Although in the weather prediction task there is no explicit shift in task demands that requires shifting attention between rules or between stimuli, the nature of the task is such that the category structure cannot be deduced until a large number of trials are experienced. Thus, to the extent that control participants shift between possible strategies on the basis of trial-by-trial feedback, in an attempt to improve their performance, it is possible that some form of a shifting deficit may also account for, or contribute to, the Parkinson's patients' impaired performance on this task.

Early Versus Late Training Deficit

In general, the finding that Parkinson's patients are impaired on this task is consistent with previous findings (Knowlton et al., 1996). However, that study concluded that Parkinson's patients were impaired early in training (first 50 trials) but not later in training (Trials 50–150). The pattern of impairment we found appears to be the opposite: Parkinson's patients performed similar to controls in the first 50 trials, and in the entire first session (200 trials), and the Parkinson's-related deficit was revealed in the 2nd and 3rd day (Trials 201–600). However, because the patients in the Knowlton et al. (1996) study were only tested for a single session, the main difference between their results and the present results lies in the impaired early learning in the Knowlton et al. (1996) study, as opposed to the relatively spared early learning in the present study.

One possible reason for this discrepancy is that Knowlton et al. (1996) found the learning deficit to be most pronounced in patients with advanced Parkinson's disease, whereas the patients in the present study were all diagnosed with mild-to-moderate Parkinson's disease. Therefore, it may be that probabilistic category learning is only mildly disrupted early in the disease, but devastated later in the course of the disease. This would account for the fact that the patients in Knowlton et al.'s (1996) study were impaired overall during the single training session (although they did improve within that session), whereas the patients in the present study showed no significant impairment during the first training session.

This distinction may be important given that the disease course progressively affects different brain circuits and cognitive function (Agid et al., 1993; Kish, Shannak, & Hornykiewicz, 1988; Owen, Beksinksa, et al., 1993; Owen et al., 1992, 1997). In the early stages of the disease, approximately 80% of dopaminergic cells projecting to the striatum, mostly in projections to the dorsal striatum, are already devastated when a patient first begins to show motor deficits (Agid et al., 1987; Damier, Hirsch, Agid, & Graybiel, 1999; Pakkenberg, Moller, Gundersen, Mouritzen, & Pakkenberg, 1991). Therefore, patients with mild versus advanced Parkinson's disease both have extensive dopamine depletion in these regions. However, as the disease progresses, there are changes in the degree and topography of dopamine cell loss: Later in the disease, damage progresses from the putamen and the dorsal caudate nucleus to more ventral parts of the striatum, and beyond the basal ganglia to the mesocorticolimbic dopamine system (Agid et al., 1993; Damier et al., 1999). This raises the possibility that the differences in performance between our patients and Knowlton et al.'s (1996) more advanced patients may be attributed to the difference in the extent of dopamine depletion in particular striatofrontal circuits, or in mesocorticolimbic dopamine projections. Future studies directly comparing mild versus advanced Parkinson's patients on the probabilistic classification task will be instrumental in clarifying whether disease progression does in fact account for the disparity between these studies.

The present findings are also generally consistent with data and models emerging from the work of Ashby, Filoteo, Maddox, and colleagues emphasizing the role of the striatum in particular aspects of categorization (Ashby, Alfonso-Reese, Turken, & Waldron, 1998; Ashby et al., 2003; Filoteo & Maddox, 1999; Filoteo, Maddox, & Davis, 2001; Maddox & Filoteo, 2001). For example, these studies found that Parkinson's patients are particularly impaired at learning and applying nonlinear (as opposed to linear) categorization rules (Maddox & Filoteo, 2001). To the extent that nonlinear rule learning involves integration of stimulus dimensions, this finding is consistent with the present findings of a deficit among Parkinson's patients in learning to integrate multiple cues. A more recent study, however, found that Parkinson's patients were impaired relative to controls on a test where optimal performance required the use of a single stimulus cue, whereas they were intact on a test requiring responding to stimuli for which the rule was based on integration of multiple stimulus components (Ashby et al., 2003). Although this finding may appear to be inconsistent with the present findings regarding the role of the basal ganglia in integrating responses across multiple cues, it is important to emphasize that there may be critical differences in the kind of integration required in the different experiments. The experiment used in the Ashby et al. (2003) study requires perceptual/attentional integration of multiple stimulus dimensions, in which a subject cannot respond correctly on the basis of only a single dimension, and in which the dimensions are not easily separable at the perceptual level. Thus, the Ashby et al. results suggest that Parkinson's patients show intact attentional integration. By contrast, in the present study, the different stimulus cues appeared as discrete and separate stimuli (cards with geometric shapes), such that participants could (and in fact did) learn to associate a distinct response to each of these separate components. Optimal performance required participants to integrate these stimulus–response associations when the multiple cues appeared together. Thus, it is this form of response integration, not stimulus integration, that the present study suggests may be impaired in Parkinson's patients. Future studies are necessary to further elucidate the selective contribution of the basal ganglia to attentional–perceptual aspects of cognition versus mapping of stimulus–response associations.

The Weather Prediction Task: Limitations and Future Directions

It has generally been assumed, because of the probabilistic nature of the weather prediction task, that learning about this task involves incremental acquisition of associations between the four cues and the outcomes. Indeed, because the optimal response to any combination of cards can only be known by observation across several trials, incremental learning would be the most effective way to master this task. On the basis of this assumption, degraded performance on this task has often been taken as evidence for a specific deficit in procedural learning.

The current results suggest that different individuals may approach this task by using a variety of strategies, and that significant learning can be achieved even by individuals who appear to be following a less than optimal strategy. In healthy individuals, multiple brain regions are presumably involved in learning this task, and various strategies may rely differentially on specific brain regions. For example, to the extent that incremental learning of associations between cues and outcomes relies on the type of processes that take place in the basal ganglia, basal ganglia activity would be expected to underlie learning the multicue strategy in this task. By contrast, to the extent that learning singleton and one-cue strategies depends on rule-based learning, and to the extent that

this type of learning is dependent on the medial temporal lobe, one would expect that medial temporal lobe activity might be critical to learning these types of strategies. In fact, recent neuroimaging (fMRI) evidence has shown that, in healthy controls, learning the weather prediction task involves interacting activity in both the basal ganglia and the medial temporal lobe (Poldrack et al., 2001). One possible interpretation of these results is that the medial temporal lobes are involved early in learning (when participants might be investigating simple, easily verbalizable strategies), whereas basal ganglia involvement increases later in training (as subjects move to more optimal, less verbalizable strategies). This is consistent with current findings of a Parkinson's-related deficit later in training. It is interesting to note that the most easily verbalizable and highest payoff strategy is the one-cue strategy. We found little evidence of subjects engaging in the one-cue strategy in either group.

However, it is important to note that although certain strategies may appear to be more verbalizable than others, each strategy could, in fact, be learned through either implicit or explicit memory. For example, although the one-cue strategy could be learned by memorizing a rule ("press *sun* every time you see a square"), it could also be learned by incremental acquisition of associations between the cue and the outcomes. Similarly, although the complex multicue strategy may be more amenable to incremental, implicit learning, it is potentially possible that a participant would instead memorize the outcome associated with each pattern. Therefore, the present data remain noncommittal as to whether a particular strategy relies on implicit or explicit learning systems.

Future studies comparing learning strategies among other groups of brain-damaged populations will allow further insight into the extent to which a particular strategy may rely on particular brain regions. For example, data from individuals with amnesia caused by hypoxia-induced hippocampal atrophy suggest that although such individuals are impaired at learning this task, they show a different pattern of impairment compared to individuals with Parkinson's disease (Hopkins, Myers, Shohamy, Grossman, & Gluck, 2004). Future studies with other brain-damaged populations will also be critical to examine whether the tendency to rely on the singleton strategy is unique to Parkinson's patients, or is also seen in patients with other kinds of brain damage. In addition, imaging studies will be most useful for exploring the brain regions involved during different learning strategies among healthy controls.

It is worth noting that the present findings suggest the possibility that with even further extended training, individuals with Parkinson's disease might eventually show a shift toward using the optimal multicue strategy. Clearly, this possibility is difficult to test with patients, and remains to be explored with computational models or animal studies, which can be run more freely for longer training sessions.

Finally, Parkinson's disease is treated with L-dopa, which increases brain levels of dopamine and alleviates many of the motor symptoms. The effect of L-dopa on cognition is not well known, and studies have led to inconsistent results, with L-dopa sometimes helping cognitive function, sometimes having no effect, and sometimes impairing cognitive function. In the present study, all Parkinson's patients were tested while taking dopaminergic medication (L-dopa). Future studies are necessary to determine the extent to which L-dopa may affect probabilistic category learning in Parkinson's patients.

Conclusions

There has been a recent surge of evidence documenting the role of the basal ganglia in learning and memory. These studies have generally focused on whether patients are impaired or spared at learning, usually by measuring learning speed or by measuring performance levels after a fixed number of trials. A fundamental question here is whether the basal ganglia are themselves specifically responsible for particular forms of cognitive processing, as opposed to merely modulating cognitive processes elsewhere. This question has been posed in the realm of motor function (for discussion of this debate in the context of motor behavior, see Graybiel & Kimura, 1994). In the present study, we attempted to address this question in the cognitive domain by focusing on how patients with Parkinson's disease learn. We found that a previously documented learning deficit on a probabilistic category learning task is associated with Parkinson's patients' failure to learn the optimal learning strategy for this task. An open question remains as to whether this impairment is due to a learning deficit per se, or whether it is due to a shifting deficit.

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