Behavioral Neuroscience
1999, Vol. 113, No. 2, 235–242

Intact Learning of Artificial Grammars and Intact Category Learning by Patients With Parkinson's Disease

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Patients with Parkinson's disease (PD) have been shown to be impaired on some nondeclarative memory tasks that require cognitive skill learning (perceptual-motor sequence learning, probabilistic classification). To determine what other skill-based tasks are impaired, 13 patients with PD were tested on artificial grammar learning, artificial grammar learning with transfer to novel lettersets, and prototype learning. Patients with PD performed similarly to controls on all 3 tests. The intact learning exhibited by PD patients on these tests suggests that nondeclarative cognitive skill learning is not a single entity supported by the neostriatum. If learning the regularities among visual stimuli is the principal feature of artificial grammar learning and prototype learning, then these forms of skill learning may be examples of perceptual learning, and they may occur in early visual cortical processing areas.

A number of cognitive skill learning tasks are known to depend on nondeclarative memory, that is, memory systems outside the medial temporal lobe memory system and diencephalic structures that are important for declarative memory (Squire, Knowlton, & Musen, 1993; Squire & Zola, 1996). These tasks include learning the regularities of artificial grammars, learning about categories from exemplars, and perceptual-motor sequence learning. Declarative memory is not required for learning these tasks. This conclusion is based on the finding that amnesic patients, who have impaired declarative memory, learn these tasks at a normal rate. For some tasks of nondeclarative memory, information is available to suggest which areas of the brain are important. For example, in the case of learning perceptual-motor sequences, findings from patients with Parkinson's disease (PD), patients with Huntington's disease (HD), and functional neuroimaging studies have implicated a cortico-striatal loop (for PD patients: Jackson, Jackson, Harrison, Henderson, & Kennard, 1995; Pascual-Leone et al., 1994; for HD patients: Knopman & Nissen, 1991; Willingham & Koroshetz, 1993; for neuroimaging: Grafton, Hazeltine, & Ivry, 1995, and Rauch et al., 1995).

Recently, patients with PD were also found to be impaired on a habit learning task that amnesic patients could acquire successfully (Knowlton, Mangels, & Squire, 1996). In this task, participants learn to classify a set of cues that are probabilistically related to two possible outcomes. The associations between the cues and the outcomes are learned during 50 trials of training. This type of learning, as well as the gradual learning of cue-outcome associations in experimental animals (Packard, Hirsch, & White, 1989), appears to depend on a neostriatal habit learning system. Thus, two of the best-studied nondeclarative skill learning tasks appear to depend on the integrity of the neostriatum. The question arises as to what other nondeclarative memory tasks are supported by this learning system.

In this study, we tested patients with PD on two additional skill learning tasks: artificial grammar learning and prototype learning. PD causes neuronal degeneration within the substantia nigra and a loss of a major input to the neostriatum. Thus, patients with PD provide a model of cognitive function in the context of a relatively selective deficit that includes dysfunction of the neostriatum. Both artificial grammar learning and prototype learning are acquired normally by amnesic patients (Knowlton, Ramus, & Squire, 1992; Knowlton & Squire, 1993, 1996; Squire & Knowlton, 1995). As discussed previously (Squire et al., 1993), these two tasks can be conceptualized as requiring that one learn an association between items or features and a category. In the case of artificial grammar learning, one learns to associate letter strings presented for training with the grammatical category. In the case of prototype learning, one learns to associate the exemplars with their prototype. This way of conceptualizing the two tasks emphasizes their formal similarity to habit learning and raises the possibility that the tasks could be impaired in patients with PD. However, another way to view the tasks is that they are exemplars of perceptual learning, whereby individuals gradually improve their ability to perceive features of visual stimuli. Perceptual learning is thought to depend on changes intrinsic to the visual cortex (Gilbert, 1998). If learning the

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This research was supported by the Medical Research Service of the Department of Veterans Affairs and by National Institute of Mental Health Grants MH24600 and F32 MH11150-01A1. We thank James Moore and Joyce Zouzounis for research assistance and Cliff Shults for referral of study patients.

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regularities among visual stimuli is the principal feature of artificial grammar learning and prototype learning, then these forms of skill learning may be examples of perceptual learning and should be intact in PD patients.

Previous work examined artificial grammar learning in patients with HD, a progressive condition also affecting the basal ganglia (Knowlton, Squire, Paulsen, Swerdlow, Swenson, & Butters, 1996). The patients with HD exhibited normal artificial grammar learning when given extended exposure to each study item (9-s exposure for both patients and controls rather than the usual 3-s exposure). Although the performance of patients with HD was similar to that of healthy controls in the extended exposure condition, the results could not be interpreted unambiguously. The increased exposure required by the patients with HD could indicate that the learning of the artificial grammar structure was slowed. Alternatively, it could indicate simply that these patients could not process the study stimuli as well as healthy controls.

In this study, the ability of patients with PD to learn artificial grammars was tested in both the standard condition and using the "letterset transfer" version of the task, in which knowledge of the grammar is tested using letters different from those used for training. The letterset transfer version of artificial grammar learning provides a way to assess whether individuals have acquired an abstract representation of the grammar (Reber, 1989). Although some authors have questioned whether the letterset transfer task requires truly abstract representations of the stimuli (e.g., Neal & Hesketh, 1997), this version of the task does require that grammatical knowledge cannot be bound to the surface features of the training stimuli, and thus this version requires some amount of abstraction above the surface form. The earlier study of patients with HD (Knowlton et al., 1996) did not include a test of letterset transfer. Thus, it remains possible that basal ganglia disease interferes with the acquisition of abstract information.

The ability of patients with PD to learn prototype information was tested by using the dot pattern categorization task introduced by Posner and Keele (1968), as modified by Knowlton and Squire (1993). The question of interest is whether the neostriatal habit learning system supports a broad range of nondeclarative skill learning tasks or whether this system supports only a particular kind of task.

Experiment 1

To assess whether the learning of artificial grammars depends on the intact function of the basal ganglia, patients with PD were tested on both the traditional artificial grammar learning paradigm and the letterset transfer version of the task. In each case, the performance of patients with PD was compared with the performance of matched controls. In these tests, participants are first shown a series of letter strings derived from a complex rule system (artificial grammar) and then are tested for their ability to discriminate between novel letter strings that are either grammatical or nongrammatical (nongrammatical strings are those that do not conform to the rule system). In addition, a separate group of controls was given the grammaticality test without any prior exposure to grammatical strings to provide an empirical estimate of "chance" performance on the grammaticality test. Any success by this group of controls would necessarily reflect grammar learning during the grammaticality test.

Method

Subjects

Patients. Thirteen patients with PD participated. The diagnosis of PD was confirmed by a senior staff neurologist at the University of California Medical Center, San Diego. The patients averaged 67.5 years of age (range = 55–79) and 16.1 years of education (range = 12–23 years). Their mean score on the Dementia Rating Scale was 138.2 (range = 133–143), indicating an absence of dementing illness (maximum score = 144; Mattis, 1976). The mean severity of Parkinsonian symptoms was stage 2.7 (range = 1–3) as rated by the Hoehn and Yahr Scale (1 = *least severe,* 5 = *most severe;* Hoehn & Yahr, 1967) and was 8.8 (range = 2–16) as rated by the Unified Parkinson's Disease Rating Scale, Hand and Foot subscale (0 = *normal,* 32 = *most severe;* Fahn & Elton, 1987). The mean score on the Beck Depression Inventory was 5.7 (range = 3–11; maximum possible score = 63), indicating an absence of clinical depression (Beck, Ward, Mendelson, Mock, & Erbaugh, 1961). At the time of testing, all patients were under the care of a neurologist and were optimally medicated. All the patients were receiving dopamine precursor treatments (Sinemet). In addition, 10 patients were taking a monoamine oxidase inhibitor (Eldepryl or Selegilene), 8 were taking a dopamine-enhancing drug (Parlodel, Permax, Amantadine, Bromocryptine, or Carbidopa), 2 were taking an anticholinergic drug (Artane), and 2 were taking an antidepressant (Amitriptilene).

Controls. The 13 controls were either employees or volunteers at the San Diego Veterans Affairs Medical Center or members of the retirement community of the University of California, San Diego. They were selected to match the PD patients with respect to age (M = 66.5 years, range = 47–80), education (M = 15.3 years, range = 12–18), and two subscales of the Wechsler Adult Intelligence Scale—Revised (WAIS–R; Wechsler, 1981): Information (M = 23.2, range = 19–28; for patients with PD, M = 24.5, range = 22–27) and Vocabulary (M = 58.4, range = 44–66; for patients with PD, M = 59.2, range = 50–63).

A separate group of 12 controls participated in the "imagine" condition (see below). These controls also matched the PD patients with respect to age (M = 67.0 years, range = 54–79), education (M = 15.7 years, range = 12–18), and two subscales of the WAIS–R (Wechsler, 1981): Information (M = 22.9, range = 19–27) and Vocabulary (M = 59.1, range = 46–66).

Materials

Grammatical letter strings were generated from two finite-state Markovian rule systems (Figure 1). The letter strings were formed by traversing the diagram from the *IN* arrow to the *OUT* arrow, adding a letter at each transition from one state to the next. Twenty-three training items and 23 test items, two to six letters in length, were generated from each rule system. Twenty-three nongrammatical test items were also generated from each rule system by introducing an error in each of 23 different grammatical items. Each letter string was presented on a 3 × 5 in. (7.6 × 12.7 cm) index card.

For the letterset transfer condition, different grammatical and nongrammatical letter strings were constructed by replacing the

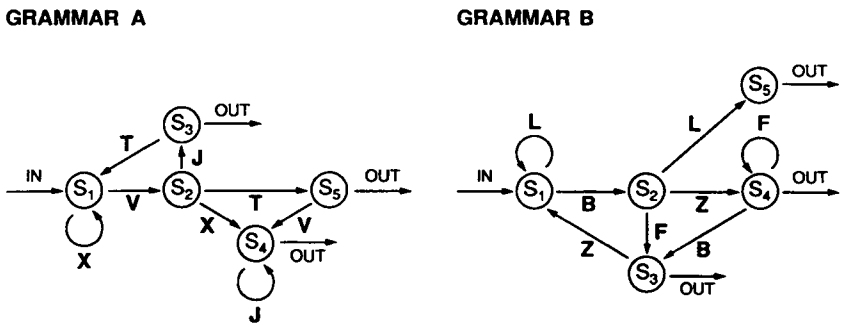

Figure 1. Artificial grammars used to generate stimuli in Experiment 1. S_1–S_5 indicate the five possible states that could occur during generation of grammatical letter strings. Each transition (arrow) is marked with a letter that is recorded when generating a grammatical letter string. Grammar A is from Abrams and Reber (1989). Grammar B is from Knowlton et al. (1992).

original letters with new letters. For the first two sessions, the lettersets JTVX or HNPS were used with grammar A and the lettersets BFLZ or DGKW were used with grammar B. For each participant, one grammar was used for the artificial grammar learning test, and the other grammar was used for the letterset transfer condition. The use of grammars across tests was counterbalanced. Thus, for the artificial grammar learning task, half the participants received grammar A, and half received grammar B. The lettersets seen at study and test were also counterbalanced. Thus, of those who saw grammar A, half saw study and test items constructed from the JTVX letterset, and half saw study and test items constructed from the HNPS letterset. Similarly, of those who saw grammar B, half saw study and test items constructed from the BFLZ letterset, and half saw study and test items constructed from the DGKW letterset. For the letterset transfer task, the lettersets were always different at training and test. For example, if the participant had seen study items based on grammar A and the JTVX letterset, the test items were also based on grammar A, but they were constructed from the HNPS letterset. To construct the letterset transfer tests, each letter in the list of 46 test items was replaced with a new letter. For example, to construct a letterset transfer test based on grammar A, after the grammar had been learned using the letters JTVX, each instance of *J* in each test item was replaced with *H,* each instance of *T* replaced with *N,* and so forth.

In the second two sessions, the same two grammars were used, but the lettersets JTVX and BFLZ were assigned to grammar B and the lettersets BFLZ and DGKW were assigned to grammar A. In addition, the letters DGKW were replaced by DMQR, because in the first two sessions we found that participants tended to confuse the letters in strings constructed from the letters DGKW during the study phase. Specifically, during the study phase, participants tended to rehearse the letter strings subvocally, leading to occasional confusion of the phonetically similar *D* and *G.* Participants also had some difficulty with the longer *W* sound. Although these difficulties did not lead to significantly poorer performance (nor any difference in performance between the groups), participants were frustrated by their occasional errors. Accordingly, the change in letterset was made to avoid introducing numerical differences in grammar difficulty across the tests.

Procedure

In each session, participants were first presented with 23 training items, one at a time, for 3 s. After each item was removed from view, the participant attempted to reproduce the item on a piece of paper. If the participant did not reproduce the item correctly, he or she was shown the same item again and was given a second chance to reproduce it. If the participant did not then reproduce the item correctly, the procedure was repeated a third time before moving on to the next item. The entire study procedure was then repeated a second time using the same 23 items.

Five minutes after the study phase, participants were informed that the items they had just seen had been generated by a complex set of rules. They were instructed that they would now see new letter strings that they should try to classify according to whether the item was or was not formed according to the same rules. Participants were told that the rules were very complex and that they should therefore base their judgments on their "gut feeling" as to whether a test item obeyed the rules. The 46 test items (23 grammatical and 23 nongrammatical items) were then displayed one at a time, and participants judged whether each item followed the rules by responding *yes* or *no.*

For sessions in which the letterset presented at test was different from the letters seen during study (letterset transfer task), participants were informed of this fact immediately before the test.

Overall testing procedure. Each participant completed four separate testing sessions (two sessions of artificial grammar learning and two sessions of the letterset transfer task), each of which consisted of a study phase and a grammaticality test. In the first two sessions, participants completed an artificial grammar learning task (grammar A or B, Figure 1) and a letterset transfer task, with a 1-week interval between the two sessions (order counterbalanced). The second two sessions were given an average of 167 days later (range = 136–210 days) and also consisted of both an artificial grammar learning task and a letterset transfer task (order counterbalanced). In each pair of sessions, each participant was given one test based on grammar A and one test based on grammar B. Also, in each pair of sessions, half of the participants in each group received artificial grammar learning first, and half received letterset transfer first.

Although reusing the grammars and lettersets in the second two sessions risked the possibility of interference from the first two sessions, the fact that the sessions were about 6 months apart and that the participants were retrained on the grammars in the second two sessions should have minimized interference effects. In addition, interference should have affected both the patients with PD and the controls similarly (or possibly adversely affected the patients with PD more strongly than the controls because of frontal dysfunction associated with PD).

"Imagine" control group. A separate group of controls (n = 12) was given the grammaticality test without any prior study. Half of the participants received a test based on grammar A (letterset

XVJT), and half received a test based on grammar B (letterset BFLZ). Any success this group achieved in making grammaticality judgments would necessarily reflect learning of the grammatical structure of the test items during the test. Prior to testing, participants were instructed to imagine that they had just seen a list of items that conformed to a complex set of rules. They were then asked to try to determine the grammaticality of the new items seen at test.

Results

Participants were quite accurate at reproducing the items during the study phases of each test. Controls correctly completed 89.5% of the items on the first attempt and 97.6% of the items in three attempts. Patients with PD correctly completed 82.8% of the items on the first attempt and 95.8% of the items in three attempts.

The Imagine control group correctly identified grammatical strings 48.7% (±3.1 *SEM*) of the time. Their performance was not different from chance and therefore provided no evidence for learning of the grammatical structure of the test items during the grammaticality test.

Average percentage correct (±*SEM*) for making grammaticality judgments for the patients with PD was 67.2% (±2.4) and 61.4% (±2.5) across the two sessions and 57.9% (±3.2) and 61.7% (±2.7) for the letterset transfer condition across the two sessions. Controls obtained 66.0% (±2.7) and 68.9% (±2.3) correct for grammaticality judgments across the two sessions and 61.5% (±2.2) and 63.0% (±1.9) for the letterset transfer condition. For each test type, a 2 × 2 analysis of variance (ANOVA) examining the effect of session and group on performance was performed. Neither grammaticality judgments nor letterset transfer test performance were sensitive to the effect of session (Fs < 1.0) or group (Fs < 1.6, ps > .20). For the grammaticality test, there was a marginal interaction between group and session, $F(1, 25) = 3.32, p < .10$, reflecting the fact that the patients did numerically worse on the second session and the controls did numerically better.

Because the overall performance on both the standard artificial grammar test and the letterset transfer version of the test was similar across the two testing sessions in which each of these tests was given, ts(24) < 1.15, results from the two sessions were combined to yield one score for artificial grammar learning. In addition, results from the other two sessions were combined to yield one score for the letterset transfer condition. Performance of the patients with PD and the controls on the grammaticality test and the letterset transfer test is shown in Figure 2. A 2 × 2 ANOVA (evaluating the effect of test type within-group and contrasting the two groups) revealed a significant effect of test type, $F(1, 25) = 10.67, p < .01$, reflecting the fact that performance on the grammaticality test was better than on the letterset transfer test. There was no effect of group, $F(1, 25) = 1.74, p > .15$, nor an interaction between group and test type $F(1, 25) = 0.55$. The 95% confidence interval for the difference in performance between the two groups was −2.0% to 8.4% for the artificial grammar task and −3.1% to 8.0% for the letterset transfer task, reflecting the similar performance of the groups on both tasks. In addition, both groups performed significantly better than chance (50%), ts > 4.38, ps < .001, and better than the Imagine group, ts > 2.91, ps < .01.

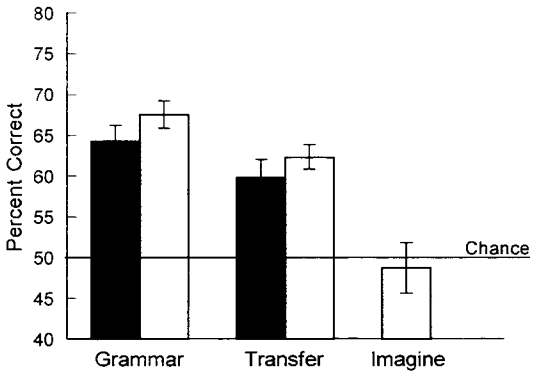

Figure 2. Percentage correct scores for the grammatical classification task of Experiment 1. Chance = 50% correct. Shaded bars indicate the performance of patients with Parkinson's disease (n = 13); open bars indicate the performance of the controls (n = 13). The two bars at the left show performance on the standard grammaticality tasks when the letter strings at test were composed of the same letters as in the training items. The two bars in the middle show performance on the letterset transfer task when the test items were composed of different letters from those in the training items. The open bar at the far right indicates performance by controls (n = 12) when no study items were presented prior to the grammaticality test. These controls provide an empirical estimate of chance performance. Error bars indicate the standard error of the mean.

Discussion

Patients with PD exhibited normal learning of artificial grammars and were also able to transfer this knowledge across a change in letterset as well as the controls did. The performance of the Imagine group indicates that for both the patients and the controls, performance on the grammaticality and letterset tests reflects grammatical knowledge acquired during the study phase. Learning of artificial grammars does not appear to depend on the integrity of the neostriatum. In addition, the neostriatum does not appear essential for the ability to develop and apply more abstract representations of the grammatical structure as required by the letterset transfer version of the artificial grammar learning task.

Experiment 2

The successful artificial grammar learning exhibited by patients with PD in Experiment 1 indicates that the neostriatum is not essential for all instances of nondeclarative cognitive skill learning. However, reports of impaired learning exhibited by PD patients in some nondeclarative learning tasks, such as perceptual-motor skill learning (Jackson et al., 1995; Pascual-Leone et al., 1994) and habit learning (Knowlton & Squire, 1996), indicate that some types of nondeclarative memory are impaired in PD. In Experiment 2, we asked whether the learning of category-level knowledge is impaired in patients with PD. The task

used here is one used in previous studies (Knowlton & Squire, 1993; Squire & Knowlton, 1995), which showed that amnesic patients exhibit normal category learning. The stimuli were patterns of nine white dots on a black background (Figure 3). During the study phase, participants saw 40 different dot patterns that were derived from an underlying prototype. In a subsequent test phase, participants were shown novel patterns and asked to judge whether or not they belonged to the training category.

There have been several reports suggesting that there is visuospatial dysfunction in PD (e.g., Boller et al., 1984; Bondi, Kaszniak, Bayles, & Vance, 1993; Bowen, Hoehn, & Yahr, 1972; Hovestadt, De Jong, & Meerwaldt, 1987; Postle, Jonides, Smith, Corkin, & Growdon, 1997). However, tests of visuospatial skills may often be confounded by the high cognitive demand of these tasks and in particular by the demands these tasks place on frontal executive function (Bondi et al., 1993; Dubois & Pillon, 1997). To assess the ability of patients with PD to perform cognitive tasks based on the same visuospatial stimuli used in the category learning tasks, the patients were given a perceptual test and a recognition memory test based on similar stimuli.

Method

Subjects

Patients. The same 13 patients with PD that participated in Experiment 1 also participated in this experiment.

Controls. The 13 controls (different from those in Experiment 1) were either employees or volunteers at the San Diego Veterans Affairs Medical Center or members of the retirement community of the University of California, San Diego. They were selected to match the patients with PD with respect to age (M = 67.6, range = 56–79), education (M = 16.1, range = 12–21), and two subscales of the WAIS–R (Wechsler, 1981): Information (M = 24.8, range = 19–27) and Vocabulary (M = 57.3, range = 38–67).

Procedure

Categorization. Examples of study and test items appear in Figure 3. The study items were constructed from a prototype dot pattern following the method of Posner, Goldsmith, and Welton (1967). First, a prototype pattern was constructed by placing nine dots within a 12- × 12-cm area of a computer screen. The study items were "high" distortions of this prototype, constructed by displacing each dot in a random direction for a distance determined probabilistically. For training, 40 study items (40 different high distortions of the prototype) were presented for 5 s each, and participants were instructed to point to the dot closest to the center of the pattern. Five minutes later, participants were instructed that the patterns had all belonged to a single category of patterns in the same sense that, if a series of different dogs had been presented, they would all belong to the category *dog*. Testing then proceeded with 84 new patterns, and for each pattern participants judged (*yes* or *no*) whether it belonged to the same category as the training patterns. The test items consisted of four repetitions of the prototype, 20 new high distortions of the prototype, 20 "low" distortions of the prototype (in which each dot was displaced with a lower probability than in the case of high distortions), and 40 random dot patterns that were high distortions of new prototypes. No more than three test items of the same type occurred consecutively. This classification test was given on two different occasions (with different materials), with a 1-week delay between sessions.

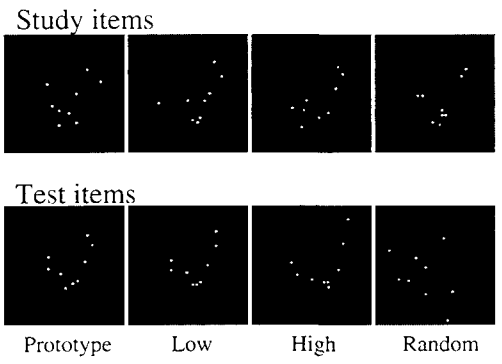

Figure 3. Examples of study items and test items from the dot pattern categorization task of Experiment 2. The study items were high distortions of a prototype dot pattern. The test items were presentations of the training prototype, low and high distortions of the training prototype, and random dot patterns.

Recognition. Two recognition tests were given in a single session an average of 19 days (range = 6–110 days) after the two category learning sessions. The study phase consisted of five different prototype dot patterns, each presented eight times (40 total study items). Each item was presented on the computer screen for 5 s, and participants were instructed to point to the dot closest to the center of the pattern. Five minutes later, participants were given a 10-item recognition memory test consisting of the 5 targets and 5 foils. The use of two recognition tests provides a more stable estimate of recognition performance than could be obtained in a single recognition test with twice the number of study items.

Perceptual task. Between the two recognition tests, participants were also given a visuospatial comparison test based on dot pattern stimuli. Two dot patterns were presented together on the computer screen with a vertical white bar dividing the screen into halves. Participants were allowed 4 s to make a *same* or *different* judgment for the two patterns. The 40 trials of the test consisted of 20 *same* trials in which the dot patterns were identical and 20 *different* trials in which four of the dots in one of the patterns had been moved 9.4 mm to create a slightly different pattern.

Results

The performance of the patients with PD and the controls for the category learning task, the recognition memory test, and the visuospatial comparison test is shown in Figure 4 (Panels A–D). Endorsement rates on the category judgment task for the patients and controls was compared with a 4 × 2 ANOVA (comparing the four stimulus types within group and contrasting the two groups). There was an overall linear effect across stimulus type, $F(1, 25) = 36.72$, $p < .001$, reflecting the fact that the endorsement rates increased as a function of how closely the test item resembled the prototype (Figure 4A). There was no effect of group nor any interaction between group and stimulus type (Fs < 1.0). For the prototype and the low and high distortion items, a *yes* response is correct; for the random items, a *yes* response is incorrect. Overall percentage correct also did not differ between the two groups, $t(25) = 0.40$ (Figure 4B). The 95% confidence interval for the difference in overall performance between the two groups was −6.4% to 8.9%.

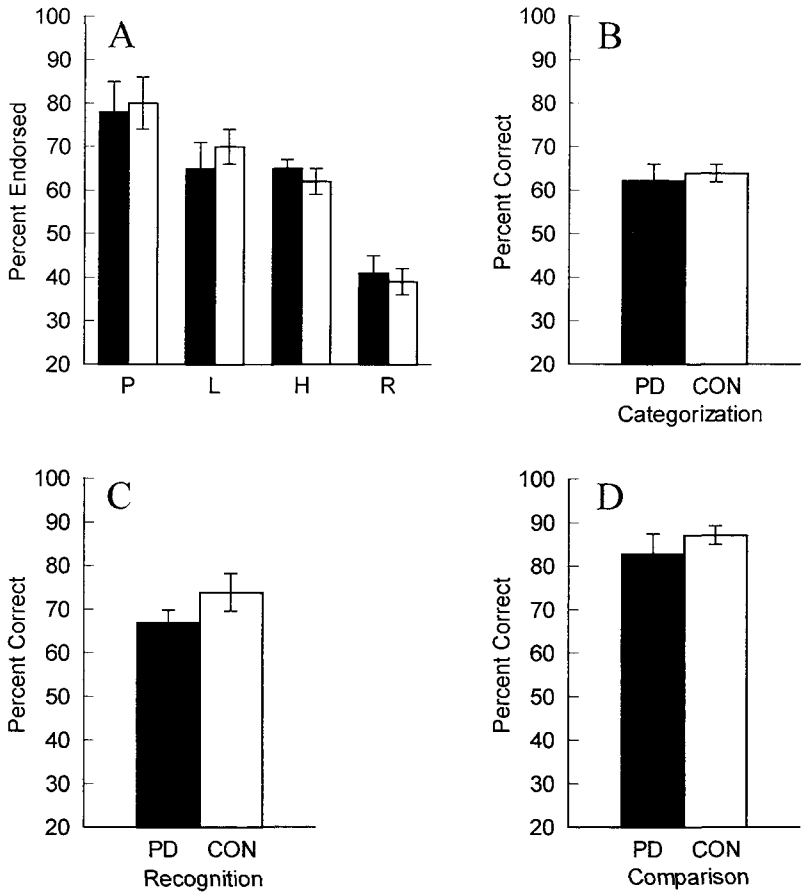

Figure 4. Performance on the dot pattern categorization task (A and B), recognition task (C), and the perceptual task (D) in Experiment 2. In each panel, performance of the patients with Parkinson's disease (PD) is shown in shaded bars, and performance of controls (CON) is shown in open bars. Error bars indicate the standard error of the mean. (A) Performance varied similarly for each group as a function of how closely the test items resembled the study items. (B) Overall percentage correct on the categorization task (chance = 50%). (C) Overall percentage correct performance on the recognition task (chance = 50%). (D) Overall percentage correct performance on the comparison test (chance = 50%). P = prototype pattern; L = low distortion of prototype; H = high distortion of prototype; R = random dot pattern.

Performance on the recognition test (Figure 4C) was 66.9% correct (±2.9) for the patients with PD and 73.9% correct (±4.3) for the controls. Recognition memory performance did not differ between the two groups, $t(25) = 1.33$, $p > .15$. Performance on the perceptual test (Figure 4D) was 82.8% correct (±4.6) for the patients with PD and 87.1% correct (±2.1) for the controls. The ability to compare dot patterns did not differ between the two groups, $t(25) = 0.86$.

Discussion

Patients with PD exhibited normal learning of category information. The PD patients also did not exhibit any evidence of visuospatial difficulties with the dot patterns as assessed by either recognition memory performance or by performance on a dot pattern comparison task. The categorization, recognition, and perceptual tasks used here do not appear to depend on the integrity of the neostriatum.

The largest difference in performance between the PD patients and controls, albeit not significant, was on the recognition test for the dot patterns. Impaired recognition memory in PD patients has been reported previously (e.g., Koivisto, Portin, & Rinne, 1996) but has not been consistently found (e.g., Gabrieli, Singh, Stebbins, & Goetz, 1996). Impaired performance might be observed most readily in conditions under which strategic use of memory is important to performance (Gabrieli et al., 1996).

General Discussion

Patients with Parkinson's disease exhibited normal learning of artificial grammars both in the traditional form of the grammaticality test and in the letterset transfer condition. Although this conclusion rests on accepting the null hypothesis that the groups do not differ, it should be noted that in all cases the groups performed quite similarly to each other and

significantly above chance. The intact learning exhibited by patients with PD suggests that acquiring abstract information about a complex rule system does not depend on the intact function of the neostriatum. Patients with PD also exhibited normal learning of prototypical dot patterns, suggesting that the neostriatum is also not essential for learning abstract, visuospatial categories. In addition, it should be noted that these results indicate that the frontal dysfunction typically associated with PD (Dubois & Pillon, 1997) also does not appear to interfere with the cognitive abilities assessed here.

Thus far, neuropsychological studies of artificial grammar learning and prototype learning have not identified the areas of the brain that support these kinds of nondeclarative learning. The results reported here, together with the previous findings of intact learning by amnesic patients (Knowlton et al., 1992; Knowlton & Squire, 1993; Squire & Knowlton, 1995), indicate that neither the neostriatum nor medial temporal lobe–diencephalic structures are essential for these tasks. A clue about the neural basis of prototype learning has recently become available from functional neuroimaging studies (Reber, Stark, & Squire, 1998a; 1998b). Posterior cortical areas exhibited differential activity for categorical and noncategorical dot pattern stimuli after a category of dot patterns had been learned. During classification judgments, processing of the categorical stimuli evoked less activity than did processing of noncategorical stimuli. This result suggests that learning the category to which the exemplar dot patterns belonged resulted in a reorganization of early cortical visual processing areas. As a result, subsequent processing of categorical stimuli was faster and required less effort than did the processing of noncategorical stimuli. Thus, an important aspect of learning about dot patterns and extracting categorical information may occur in early visual processing areas. In this respect, learning a visual prototype may be a form of perceptual learning, which is also thought to occur in early cortical visual areas (Gilbert, 1998). We suggest that learning the regularities of artificial grammars may similarly involve perceptual learning. However, transfer to new lettersets also occurs in artificial grammar learning, and this kind of learning is difficult to understand as perceptual learning. Functional neuroimaging studies of artificial grammar learning including the letterset transfer condition should be informative in identifying which cortical areas participate in this more abstract form of artificial grammar learning.

Although the integrity of the neostriatum is not essential for learning artificial grammars or for learning about prototypes, the neostriatum has been implicated in two other nondeclarative, cognitive skill learning tasks: perceptual-motor sequence learning (Jackson et al., 1995; Pascual-Leone et al., 1994) and probabilistic classification (Knowlton, Mangels, & Squire, 1996). These tasks can be conceptualized as tasks of habit learning. In both cases, individuals make decisions and immediately receive feedback about the correctness of the decisions. This information must be integrated across many trials. In perceptual-motor sequence learning (e.g., the serial reaction time task), individuals receive immediate feedback about the correctness of their keypresses. In probabilistic classification learning, feedback about each choice is provided, and individuals must associate each outcome with their choice. In contrast, in artificial grammar learning and prototype learning, individuals are simply exposed to a large number of stimuli (or patterns), all of which conform to an underlying structure. Later, individuals make judgments about new stimuli. In both tasks, each stimulus contains relevant task information in either a visual array of letters (artificial grammar) or a visuospatial array of dots. There is no feedback and the order of training stimuli is irrelevant. Instead, individuals are encouraged simply to perceive the stimuli and later to make judgments about their regularities.

Type of feedback has been shown to be an important factor determining whether patients with PD exhibit normal learning. Vriezen and Moscovitch (1990) reported that patients with PD were impaired at learning conditional associations when they were told only whether their guess on each trial was correct or incorrect (trial-and-error learning). However, performance was normal when the correct answers were provided prior to learning and the correct answer was also provided during learning each time an error was made. The type of learning being expressed is also an important factor. Dominey, Ventre-Dominey, Broussolle, and Jeannerod (1997) reported normal explicit sequence learning in PD patients when error feedback was provided. One possibility is that the neostriatum is only crucial to skill learning for nondeclarative memory tasks that require making use of feedback to guide learning.

If feedback is a critical variable determining whether the neostriatum is important for nondeclarative learning, the artificial grammar learning and categorization tasks might be modified so as to depend on the intact function of the neostriatum. For example, if the tasks were altered such that both correct and incorrect stimuli were presented during training, with feedback provided for each choice, then the tasks would clearly require feedback for learning and the neostriatal habit learning system might be required. It would also be important that the task continue to depend on nondeclarative memory, such that intact individuals could not benefit materially by memorizing the outcomes of each trial (cf. Dominey et al., 1997).

The finding that PD patients exhibit intact learning of both artificial grammars and dot pattern prototypes but are impaired at habit learning (Knowlton, Mangels, & Squire, 1996) shows that skill learning is not a single entity. This point depends on our comparing findings across different studies. A comparison of the same patients in the same study would provide an even stronger dissociation between forms of nondeclarative memory. The present findings reinforce the idea that nondeclarative memory is a collection of phenomena supported by distinct brain areas (Squire & Knowlton, 1995). Studies in humans and experimental animals suggest that the neostriatum has a specific role in habit learning (Knowlton, Mangels, & Squire, 1996; Packard et al., 1989) and that other forms of nondeclarative memory depend on other brain systems. Artificial grammar learning and prototype learning, as studied here, depend on brain regions outside both the neostriatum and the medial temporal

lobe. We suggest that these forms of nondeclarative memory depend on changes intrinsic to neocortical visual areas.

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Received June 18, 1998
Revision received September 23, 1998
Accepted October 1, 1998 ■