Probabilistic Classification Learning in Amnesia

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Abstract

Amnesic patients and control subjects participated in a study of probabilistic classification learning. In each of three tasks, four different cues were each probabilistically associated with one of two outcomes. On each trial, the cues could appear alone or in combination with other cues and subjects selected the outcome they thought was correct. Feedback was provided after each trial. In each task, the amnesic patients learned gradually to associate the cues with the appropriate outcome at the same rate as control subjects, improving from 50% correct to ~65% correct. Presumably because the cue-outcome associations were probabilistic, declarative memory for the outcomes of specific trials was not as useful for performance as the information gradually accrued across trials. Nevertheless, declarative memory does appear to make a contribution to performance when training is extended beyond ~50 trials, because with further training control subjects eventually outperformed the amnesic patients. It was also demonstrated that performance on the probabilistic classification task was not the result of holding knowledge of cue-outcome associations in short-term memory, because both control subjects and amnesic patients demonstrated significant

savings when testing was interrupted by a 5-min delay (experiment 2). Probabilistic classification learning appears to provide an analog in human subjects for the habit learning tasks that can be acquired normally by animals with hippocampal lesions.

Introduction

In recent years there has emerged a great deal of evidence for the existence of multiple memory systems that depend on different brain regions (Tulving 1991; Schacter et al. 1993; Squire et al. 1993). Some of the best evidence for this idea has come from the study of amnesic patients, who have sustained damage to the medial temporal lobe or diencephalic regions. Despite their severe impairment in memory for facts and events, amnesic patients are capable of normal learning of some kinds of information (Squire 1987; Mayes 1988). The kind of memory that is impaired, described as declarative (or explicit), is available to conscious recollection. The kind that is spared, described as nondeclarative (or implicit), does not describe a single memory system but, rather, a collection of different memory abilities that are expressed through performance without any necessary access to conscious memory content.

Tasks of nondeclarative memory include simple classical conditioning, motor skill learning, and priming. One striking finding is that the tasks that can be acquired in amnesia are not limited to tasks that depend primarily on sensory or motor abilities. Tasks such as text-specific speeded reading,

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artificial grammar learning, and prototype abstraction can also be acquired normally by amnesic patients (Musen et al. 1990; Knowlton et al. 1992; Knowlton and Squire 1993, 1994).

Work with experimental animals has also demonstrated dissociations between different kinds of learning and memory abilities (Squire 1992). The important finding is that rats and monkeys with lesions of the hippocampus or related structures fail some memory tasks, but they exhibit fully intact performance on other tasks, independently of the sensory and motor abilities needed to perform. For example, rats with fornix lesions are able to learn normally which arms of a radial arm maze are consistently baited (Packard et al. 1989). In addition, monkeys with medial temporal lobe lesions are able to learn normally a difficult pattern discrimination task (Zola-Morgan and Squire 1984) and to learn nearly as well as normal animals a concurrent object discrimination task in which only one trial is given each day (Malamut et al. 1984). These preserved learning abilities have been described collectively as habit learning because animals can be said to acquire predispositions to respond in a particular way to stimuli (Mishkin et al. 1984). Stimuli become connected to responses by reinforcement. This process has also been described as dispositional learning (Thomas 1984). One important characteristic of habit learning is that information is acquired gradually across many trials. In contrast, the type of associative learning that is impaired after lesions of the hippocampal region is specialized for rapid acquisition, often in a single trial.

Does habit learning also describe a class of nondeclarative learning abilities in human subjects? Can humans learn associations between stimuli and responses independently of the medial temporal lobe and diencephalic brain regions? In the case of habit learning, it has been unclear how close a parallel can be drawn between humans and experimental animals. The difficulty is that human subjects can apparently depend on declarative memory even when they are given the same tasks that are used to test habit learning in animals. For example, human amnesic patients were impaired at the same 24-hr concurrent discrimination task that monkeys with large medial temporal lobe lesions readily learn (Squire et al. 1988). This difference probably resulted because humans and animals approach the task differently. Monkeys learn the discriminations gradually as habits, because the 24-hr interval between trials is too long for

them to bridge easily using declarative memory. In contrast, human subjects attempt to remember explicitly which objects have been rewarded from trial to trial, with the result that normal subjects perform better than amnesic patients. The idea is that declarative memory is dominant in humans, and humans may engage their declarative memory in a wider range of situations than do other animals.

To determine whether human subjects can accomplish habit learning independently of declarative memory, amnesic patients should be given a task that is difficult to approach with a declarative learning strategy. One possible way to discourage the use of declarative memory would be to test concurrent discrimination learning using an intertrial interval longer than 1 day. Another possibility would be to make the associations to be learned less obvious, that is, less memorizable. In this study we have taken the latter approach by asking subjects to learn probabilistic associations. Because the associations between stimuli and responses are probabilistic, information from a single trial is not reliable and therefore not as relevant as information accrued across many trials. If probabilistic classification learning in humans is analogous to habit learning in experimental animals, then one would expect that amnesic patients should perform normally.

Probabilistic learning has been studied extensively in humans and animals since the 1950s (Estes 1972, 1991). In a typical probabilistic learning task, stimuli are associated with responses with fixed probabilities. An indication that subjects have learned the probabilities is that they will often “probability match”, that is, they will make a particular response with the same probability that it is reinforced (Estes et al. 1957; Gluck and Bower 1990). That is, a stimulus that is reinforced 80% of the time will come to be selected 80% of the time, whereas a second alternative, which is reinforced 20% of the time, comes to be selected 20% of the time. Note that probability matching produces less than an optimal level of reinforcement. In the example just given, a subject who probability matches will be reinforced $(.8)(.8) + (.2)(.2) = .68$ of the time, but a subject who always chooses the first alternative will be reinforced 80% of the time. Probability matching occurs in a wide variety of species (Weitzman 1967; Shimp 1966). Thus, fundamental mechanisms may exist for accumulating information about the probabilistic structure of the environment.

The present study attempted to demonstrate a parallel between animal and human learning systems. We adopted a paradigm that has been used previously with normal human subjects to study probabilistic classification learning (Gluck and Bower 1988a). Three tasks were developed that had a different surface appearance but the same underlying probabilistic structure. In each case, to test declarative memory for the training episode, subjects were asked to answer factual questions about the training sessions. In experiment 1, the three tasks were administered to amnesic patients and control subjects, in two cases for 350 training trials (tasks 1 and 2), and in one case for 50 training trials (task 3). In experiment 2, task 3 was readministered for 90 trials but with 5-min delays interposed after trials 1–50 and after trials 51–70. The delays served to evaluate whether the ability of amnesic patients to perform these tasks could extend beyond immediate memory, which is intact in amnesia.

Experiment 1

Materials and Methods

SUBJECTS

AMNESIC PATIENTS

Eight amnesic patients (six men and two women) participated in this study. Two of the pa-

tients (R.C. and J.W.) have Korsakoff's syndrome. Both patients had participated in quantitative magnetic resonance imaging (MRI) studies that demonstrated marked volume reductions in the volume of the mammillary nuclei (Squire et al. 1990). Patient M.G. sustained a bilateral medial thalamic infarction, which was confirmed by MRI (L.R. Squire, D.G. Amaral, and G.A. Press, unpubl.). Of the other five patients, three have bilateral damage to the hippocampal formation, as confirmed by MRI [for J.L. and W.H. (Squire et al. 1990); for P.H. (Polich and Squire 1993)]. A fourth patient, A.B., is unable to participate in MRI studies, but the etiology of his amnesia (anoxia) is consistent with hippocampal damage. Finally, patient L.J. became amnesic during a 6-month period in 1988 with no known precipitating event. Her impairment has remained stable since that time. All eight patients are well characterized neuropsychologically (Tables 1 and 2).

The patients averaged 63.4 years of age at the time of the study and had 14.6 years of education. Immediate and delayed (12 min) recall of a short prose passage averaged 4.8 and 0 segments, respectively [maximum number of segments, 21 (Gilbert et al. 1968)]. Scores on other memory tests appear in Tables 1 and 2. The mean score on the Dementia Rating Scale was 132.5 [maximum possible score, 144 (Mattis 1976)]. Most of the points that were lost were on the memory subportion of the test (mean points lost = 7.0). The mean score for the Boston Naming test was 55.6 [maxi-

Table 1: Characteristics of amnesic patients

Patients	Lesion	Age (years)	WAIS-R IQ	WMS-R				
				attention	verbal	visual	general	delay
R.C.	Dien	75	106	115	76	97	80	72
J.W.	Dien	55	98	104	65	70	57	57
M.G.	Dien	59	111	113	89	84	86	63
A.B.	HF ^a	54	104	87	62	72	54	<50
P.H.	HF	69	115	117	67	83	70	57
W.H.	HF	69	113	88	72	82	67	<50
J.L.	HF	72	116	122	73	83	74	58
L.J.	unknown	54	98	105	83	60	69	<50
Mean		63.4	107.6	106.4	73.4	78.9	69.6	57.1

(WAIS-R) Wechsler Adult Intelligence Scale-Revised; (WMS-R) Wechsler Memory Scale-Revised. (HF) Hippocampal formation, (Dien) diencephalon. The WAIS-R and the WMS-R indices yield a mean score of 100 in the normal population with a standard deviation of 15. The WMS-R does not provide scores for subjects who score below 50. Therefore, the three scores below 50 were scored as 50 for calculating a group mean.

^aThe lesion site has not been confirmed radiologically but is strongly supported by the etiology of amnesia (see text).

Table 2: Memory test performance

Patients	Diagram recall		Paired associates		Word recall (%)	Word recognition (%)	Words (50)	Faces (50)
R.C.	3	0	0	0	19	85	37	30
J.W.	4	0	0	2	29	90	29	34
M.G.	0	0	0	2	33	71	30	34
A.B.	4	1	1	2	33	83	32	33
P.H.	3	0	0	1	27	84	36	34
W.H.	1	0	0	0	40	84	29	24
J.L.	1	0	0	0	40	93	31	20
L.J.	3	0	0	0	40	93	33	29
Mean	2.4	0.13	0.13	0.88	32.6	85.4	32.1	29.8
Control means ($n = 8$)								
	20.6	6.0	7.6	8.9	71.0	97.0	41.1	38.1

The diagram recall score is based on delayed (12-min) reproduction of the Rey-Osterrieth figure (Osterrieth 1944; maximum score = 36). The average score for the amnesic patients for copying the figure was 27.5, a normal score (Kritchevsky et al. 1988). The paired associate scores are the number of word pairs recalled on three successive trials (maximum score = 10/trial). The word recall score is the percentage of words identified correctly on five successive study-test trials (Rey 1964). The word recognition score is the percentage of words identified correctly by yes/no recognition across five successive study-test trials. The score for words and faces is based on a 24-hr recognition test of 50 words or 50 faces (modified from Warrington 1984; maximum score = 50, chance = 25). The mean scores for healthy control subjects shown for these tests are from Squire and Shimamura (1986).

num score = 60 (Kaplan et al. 1983)]. Scores for normal subjects on these tests can be found elsewhere (Janowsky et al. 1989; Squire et al. 1990). All of the patients participated in three different tasks, described below, except J.L., who was available only for the first two tests. An average interval of 16 months intervened between task 1 and task 2 (minimum 8 months), and an average interval of 5 months intervened between task 2 and task 3 (minimum 2 weeks).

CONTROL SUBJECTS

The control subjects were either employees or volunteers at the San Diego Veterans Affairs Medical Center or were recruited from the retirement community of the University of California, San Diego. The control group consisted of 37 subjects (17 men and 20 women), matched to the amnesic patients with respect to the mean and range of their ages, years of education, and scores on the Information and Vocabulary subtests of the Wechsler Adult Intelligence Scale-Revised (WAIS-R). They averaged 63.8 years of age (range, 53–76), 14.7 years of education (amnesic pa-

tients = 14.6), and 21.7 and 55.2 on the Information and Vocabulary subtests, respectively (amnesic patients = 20.8 and 57.3). Immediate and delayed recall of the short prose passage averaged 6.1 and 5.7 segments, respectively. The 37 subjects participated in one of three tasks, as described below (task 1, $n = 10$; task 2, $n = 15$; task 3, $n = 12$). Each group of control subjects was matched separately to the amnesic patients.

MATERIALS

Three different tasks of probabilistic classification learning were administered on a computer screen. Each task required subjects to learn which of two outcomes was predicted by combinations of one, two, three, or four different cues (Fig. 1). Each cue was independently associated to each outcome with a fixed probability, and the two outcomes occurred equally often. Table 3 shows the probability of outcome 1 given each possible combination of cues and the frequency with which each pattern was presented. In the first task, one, two, three, or four cues could appear on each trial (15 possible patterns). For the other two tasks, the

Figure 1: The four cues used for each of the three tasks.

pattern with all four cues present (pattern 15) was not used, resulting in 14 possible patterns. For each subject on each test, the sequence of cue patterns across trials was randomized with the constraint that the cue patterns appeared with the frequencies listed in Table 3 and the same cue pattern never appeared on two successive trials.

In the first task, subjects decided on each trial which of two fictitious diseases (nermitis or cal-dosis) an imaginary patient had on the basis of a pattern of one, two, three, or four symptoms (modified from Gluck and Bower 1988a). For the second and third tasks, subjects decided on each trial whether sunshine or rain would occur on the

Table 3: Probability structure of the three tasks

Pattern	Cue				<i>P</i> (cue combination)		
	1	2	3	4	task 1	tasks 2, 3	<i>P</i> (outcome)
1.	0	0	0	1	0.137	0.140	0.15
2.	0	0	1	0	0.083	0.084	0.38
3.	0	0	1	1	0.086	0.087	0.10
4.	0	1	0	0	0.083	0.084	0.62
5.	0	1	0	1	0.063	0.064	0.18
6.	0	1	1	0	0.046	0.047	0.50
7.	0	1	1	1	0.040	0.041	0.21
8.	1	0	0	0	0.137	0.140	0.85
9.	1	0	0	1	0.057	0.058	0.50
10.	1	0	1	0	0.063	0.064	0.82
11.	1	0	1	1	0.031	0.032	0.43
12.	1	1	0	0	0.086	0.087	0.90
13.	1	1	0	1	0.031	0.032	0.57
14.	1	1	1	0	0.040	0.041	0.79
15.	1	1	1	1	0.017	0.000	0.50

On any trial, 1 of 15 possible combinations of four cues could appear with the probability indicated above [*P* (cue combination)]. Each combination of cues predicted outcome 1 with the probability *P* (outcome) shown above and predicted outcome 2 with a probability of 1 – *P* (outcome).

basis of a set of one, two, or three cues (out of four possible cues). There were four possible cue outcome association strengths: A given cue could be associated either 75%, 57%, 43%, or 25% (approximately) with outcome 1. These probabilities were obtained by calculating the probability of outcome 1 given each particular cue. Specifically, the conditional probabilities were computed by calculating the probability that outcome 1 and a particular cue would occur together and then dividing by the total probability that the cue would occur, regardless of the outcome. For example, as one can calculate from Table 3, in the case of cue 1, the probability that cue 1 would be present and that outcome 1 could occur [$P(\text{cue combination}) \times P(\text{outcome 1})$] is calculated by summing across patterns 8–15 (.345 for task 1 and .337 for tasks 2 and 3); the total probability that cue 1 would occur regardless of the outcome equals the sum of the $P(\text{cue combination})$ for patterns 8–15 (.462 for task 1 and .445 for tasks 2 and 3). Thus, the association strength with outcome 1 was .345/.462, or 74.7%, for task 1 and .337/.445, or 75.7%, for tasks 2 and 3. The association strength of cue 2 can be calculated similarly by computing the sum of $P(\text{cue combination}) \times P(\text{outcome 1})$ across the patterns in which cue 2 appears and dividing by the sum of $P(\text{cue combination})$ for these patterns. This value is .229/.406, or 56.4%, for task 1 and .225/.389, or 57.8%, for tasks 2 and 3. Across subjects, each cue was equally likely to be assigned one of the four association strengths. There were 4! or 24 different ways in which the cues could be assigned their association strengths.

PROCEDURE

TASK 1 (MEDICAL DIAGNOSIS TASK)

Subjects were instructed that they would be seeing one, two, three, or four symptoms on each trial and that they should decide whether an imaginary patient that exhibited these symptoms would have either nermatitis (fictitious disease number 1) or caldosis (fictitious disease number 2). Subjects were told that at first they would feel as if they were just guessing but that they would gradually improve their performance. On each trial, subjects pressed one key on the computer keyboard to indicate disease 1 or a second key to indicate disease 2. To begin a trial, a list of one to four symptoms appeared in a column at the left of

the screen for 5 sec, during which time the subject was asked to respond. If the subject did not respond within 2 sec, a message appeared at the bottom of the screen asking them to “please respond now.” The names of diseases 1 and 2 were at the right of the screen throughout the training. If the subject’s response was correct, a high-pitched tone was sounded and the words “right answer” appeared on the screen. If the subject’s response was incorrect, a low tone was sounded and the words “wrong answer” appeared. This feedback remained on the screen for 2 sec and was followed by a 1-sec intertrial interval.

Each subject was tested for 350 trials, with a pause (no more than 1 min) scheduled after each block of 50 trials. The break was terminated whenever the subject wished to continue (usually after ~10 sec). Immediately after completing the task, the subjects answered 11 four-alternative multiple-choice questions about the training session that asked about the names of the diseases, the layout of the screen, the number of trials in the task, and what appeared on the screen to provide feedback after each trial.

TASK 2 (WEATHER PREDICTION WITH CARDS)

Task 2 was the same as task 1 except that subjects were instructed that they would be seeing one, two, or three cues with geometric symbols on each trial and that they should decide whether the cards predicted sunshine or rain. The intertrial interval was shortened to 0.5 sec. Also, instead of providing feedback with the words “right answer” or “wrong answer,” a smiling face appeared on the screen if the subject was correct and a frowning face appeared if the subject was incorrect. Finally, a vertical scale bar at the right of the screen, set initially at 600, increased by 1 unit for each correct response and decreased by 1 unit for each incorrect response. When 350 trials had been completed, the subjects were asked 11 four-alternative multiple-choice questions about the test session. These questions asked about the number of trials in the task, the nature of the cues, the layout of the screen, what appeared on the screen to provide feedback after each trial, and where this information appeared.

TASK 3 (WEATHER PREDICTION WITH PICTURES)

The procedure was exactly the same as for task 2 except that only 50 training trials were

given. Also, only 7 multiple-choice questions were given instead of 11.

DATA ANALYSIS

A subject was considered to have made a correct response on a particular trial if the subject selected the outcome that was most associated with the cue pattern. Thus, subjects could have been scored as making a correct response (because they selected the most likely outcome) even though on that particular trial the feedback they received told them that their response was incorrect. In this way the percent correct score reflected how well subjects learned the probabilistic associations between the cues and the two outcomes. Because the two outcomes occurred equally often, chance performance was 50%. Cue patterns for which both outcomes were equally likely (patterns 6, 9, and 15; see Table 3) were not included in the analysis, because a subject's choice on trials that involved these patterns provided no information about classification learning. Percent correct scores were analyzed in blocks of 10 trials for the first 50 trials and in blocks of 50 trials for the remaining trials.

Results

Figure 2 shows learning curves for both groups on the three tasks. The results are described below in terms of early learning (trials 1–50) and later learning (trials 51–350).

EARLY LEARNING

For the first 50 trials of all three tasks, control subjects and amnesic patients performed similarly. In all three tasks both groups performed near chance on the first block of 10 trials (all $t_s < 1.3$, $P > 0.1$) and exhibited a similar degree of learning during the first 50 trials. Separate two-way analyses of variance (ANOVAs) for each task, performed on the scores obtained by the two groups across five blocks of 10 trials, revealed no group effects ($F_s < 1$), an effect of trial block [for tasks 1 and 2, $F_s > 2.96$, $P_s < 0.05$; for task 3, $F(4,68) = 1.99$, $P < 0.11$], and no interaction of group and trial block ($F_s < 1.4$, $P_s > 0.2$). In addition, with one exception (task 3, amnesic patients), all of the

Figure 2: Percent correct performance for the control subjects (●) and the amnesic patients (○) on the three tasks. For tasks 1 and 2, 350 trials were given in one session. Performance for the first 50 trials is shown in blocks of 10 trials; performance for trials 51–350 is shown in blocks of 50 trials. Only 50 trials were given in task 3.

groups performed above chance levels on the final block of 10 trials, that is, on trials 41–50 (all $t_s > 2.24$, $P < 0.05$), and there were no differences between groups on the final block for any of the tasks ($t_s < 0.9$, $P > 0.1$). On task 3 the score ob-

tained by the amnesic patients on the final block of 10 trials ($58.5\% \pm 10.0\%$) was not above chance [$t(6) = 0.84$, $P > 0.1$]. Finally, across all 50 trials of tasks 1 and 3, the amnesic patients obtained scores of $58.8\% \pm 3.0\%$ and $61.0\% \pm 3.8\%$, respectively, which were significantly above chance ($P_s < 0.05$). For the first 50 trials of Task 2, the amnesic patients scored $59.2\% \pm 4.2\%$, which was marginally above chance ($P = 0.07$). There were no differences between the groups on this measure for any task ($t_s < 1.0$, $P_s > 0.1$).

Figure 3 shows the average performance of the eight amnesic patients across all three tasks (patient J.L.'s score was based on only two tasks) and the average score obtained by control subjects (i.e., a simple average of the three learning curves obtained by the three different groups of control subjects). The amnesic patients scored near chance on the first block of 10 trials ($53.1\% \pm 3.0\%$ correct, $P > 0.1$) and then improved to an above-chance score of $64.0\% \pm 4.7\%$ for trials 41–50 [$t(7) = 2.98$, $P < 0.05$]. This score was similar to the average score obtained by the three groups of control subjects [68.2% , $t(7) = 0.89$, $P > 1.0$]. For the amnesic patients, performance on trials 41–50 was marginally better than performance on trials 1–10 [$t(7) = 2.16$, $P < 0.07$].

A three-way ANOVA (group $\times$ task $\times$ trial block) was performed on the combined data for the first 50 trials. Although this analysis treats the amnesic patients as separate groups for each task,

Figure 3: The mean percent correct scores for the amnesic patients on all three tasks are shown by the broken line. The average of the three learning curves for the three groups of control subjects for the three tasks is shown by the solid line.

Figure 4: Performance of the control subjects (CON) and amnesic patients (AMN) on the debriefing questionnaire. Brackets show S.E.M.

it provides a more sensitive way to detect differences between the groups than does the separate analysis of the data from each task. There was a main effect of trial block [$F(4,216) = 5.48$, $MS_e = 671.0$, $P < 0.01$], no main effect of either group or task ($F_s < 1$), and no interactions ($F_s < 1$).

LATER LEARNING

When training was extended past 50 trials for tasks 1 and 2, differences emerged between the groups (Fig. 2). For both tasks the two groups performed significantly above chance on trials 51–350 (all $t_s > 3.1$, $P_s < 0.05$). Two-way ANOVAs (2 groups $\times$ 6 blocks of 50 trials) indicated a marginal effect of group for task 1 [$F(1,16) = 3.36$, $MS_e = 605.7$, $P = 0.09$] and a significant effect for task 2 [$F(1,21) = 5.39$, $MS_e = 445.0$, $P < 0.05$]. The interaction of group and trial block was not significant for either task ($F_s < 1.0$). For the final block of 50 trials in both tasks, the control subjects performed significantly better than the amnesic patients [for task 1, control subjects = $72.9\% \pm 2.0\%$, amnesic patients = $60.8\% \pm 5.7\%$, $t(16) = 2.19$, $P < 0.05$; for task 2, control subjects = $73.5\% \pm 3.2\%$, amnesic patients = $60.7\% \pm 3.4\%$, $t(21) = 2.54$, $P < 0.05$].

DEBRIEFING QUESTIONS

For all three tasks, the amnesic patients performed more poorly than the control subjects on the debriefing questionnaire (Fig. 4; $t_s > 4.9$, $P_s < 0.01$).

Discussion

In three different probabilistic classification tasks, amnesic patients performed like control subjects (trials 1–50), as performance improved from ~50% correct to ~65% correct. However, performance of the control subjects eventually surpassed that of the amnesic patients (tasks 1 and 2, trials 51–350). The lack of a group difference early in training was not the result of the lack of statistical power; no differences between the groups emerged even when the data from all three tasks were combined. For the combined data of the amnesic patients (Fig. 3), the range of standard errors for the first five blocks of 10 trials was 3.0–5.2, which was similar to the range of standard errors for blocks of 50 trials later in training (2.4–5.7). Because group differences could be detected later in training, it should also have been possible to detect a group difference early in training, if one was present. The finding that amnesic patients performed normally during initial training suggests that declarative knowledge does not contribute to the early acquisition of classification learning. Accordingly, probabilistic classification learning appears to resemble habit learning in experimental animals. In the case of habit learning in rats and monkeys (Packard et al. 1989; Wang et al. 1990), as in humans, the learning is independent of the hippocampus and related structures.

In an earlier study of cognitive skill learning (Squire and Frambach 1990), the subject's objective was to achieve a target level of sugar production at a fictitious factory by deciding on each trial how many workers should be hired (Berry and Broadbent 1984). Sugar production on each trial was a function of the sugar production achieved in the previous trial and the number of workers hired in the present trial. Subjects were not told about the relationship between these variables. Early in training the amnesic patients performed as well as control subjects. However, in a later training session, normal subjects were able to outperform the amnesic patients and also to demonstrate better declarative knowledge about the strategy that they were acquiring. A similar situation may have occurred in the present study. That is, as training progressed, the control subjects may have been able to gain more declarative knowledge of the task, which enabled them eventually to outperform the amnesic patients.

The amnesic patients performed more poorly than the control subjects on the debriefing ques-

tionnaire that was administered after each of the three tasks. Thus, the amnesic patients did not remember facts about the training episode as well as control subjects did, even when the questionnaire was given at a time when the amnesic patients were performing as well as the control subjects on the classification task (e.g., after task 3).

The normal performance of the amnesic patients early in training strongly suggests that declarative memory does not make an important contribution to performance during the early stages of probabilistic classification learning. However, because amnesic patients have intact immediate (short-term) memory, as measured by tasks such as digit span (Baddeley and Warrington 1970; Cave and Squire 1992), the possibility should be considered that the patients were retaining knowledge of the cue outcome associations in immediate memory by rehearsing them during the early part of training. This possibility is addressed in experiment 2.

Experiment 2

In experiment 1 the amnesic patients performed as well as the normal subjects on three different tasks during the first 50 trials of training. Experiment 2 was designed to determine whether this gradual improvement in classification ability might depend on immediate memory, which is intact in amnesia. To address this issue we administered 50 additional trials of task 3 to control subjects and amnesic patients. (It was not expected that there would be significant savings from the 50 training trials given as part of experiment 1, because at least 6 months intervened between experiment 1 and experiment 2, except for one amnesic patient who was retested after 1 month.) After the 50 training trials, there was a 5-min delay followed by an additional 20 training trials. Then, there was a second 5-min delay and a second set of 20 trials. The question of interest was whether the learning that occurred during the first 50 trials was retained across the delays.

Materials and Methods

SUBJECTS

The same seven amnesic patients and the same 12 control subjects that participated in task

3 of experiment 1 also participated in experiment 2.

MATERIALS AND PROCEDURE

The procedure was identical to that of task 3 (experiment 1), except that 20 additional trials were given after a 5-min delay, followed by a second 5-min delay, the administration of the debriefing questionnaire, and then a final block of 20 trials. The subject and experimenter engaged in conversation during the delays. Each subject was assigned the same cue outcome associations that he or she had received during testing in task 3 (experiment 1). The questionnaire was identical to the one used for task 3, except that it began with four questions asking subjects to estimate how often they thought each of the pictures, when presented alone, predicted each of the two outcomes. These four questions were phrased, "When only the (boat, butterfly, candle, telephone) was present, what percent of the time was the outcome sunshine and what percent of the time was the outcome rain?" Subjects were instructed that their two estimates should add to 100%. Note that this method for obtaining estimates differs from the method used by Gluck and Bower (1988a). Gluck and Bower asked subjects to estimate how often each outcome occurred when a particular cue was present regardless of which other cues were also present.

Results

As was the case in experiment 1, there were no differences between the groups in the first 50 trials (Fig. 5). Both groups performed at chance levels during the first block of 10 training trials ($t_s < 0.09$). Thus, as expected, neither group demonstrated any savings from the 50 training trials that had been given several months earlier. A two-way ANOVA (2 groups $\times$ 5 blocks of 10 trials) revealed no effect of group and no interaction between group and trial block ($F_s < 1$) but a marginally significant effect of trial block [$F(4,68) = 2.48$, $MS_e = 630.1$, $P = 0.052$].

Both groups also exhibited savings across the two delays. The control subjects averaged 70.3% correct on the final two blocks of 20 trials [cf. their 49.4% score on the first 10 trials of the session, $t(11) = 4.48$, $P < 0.01$]. The amnesic patients

Figure 5: Classification performance by control subjects (●) and amnesic patients (○). The data are for 50 training trials and for two additional blocks of 20 trials, each separated by a 5-min delay.

scored 64.5% correct on the final two blocks of 20 trials [and they also scored 49.4% correct on the first 10 trials, $t(6) = 2.39$, $P = 0.054$]. The scores of the two groups were similar during the final two blocks of 20 trials [$t(17) = 0.7$, $P > 0.1$]. It is also worth mentioning that for both groups, savings were apparent even during the first 10 trials after each delay (all $t_s > 2.54$, $P_s < 0.05$).

ESTIMATIONS OF THE ASSOCIATIVE STRENGTHS OF THE CUES

A two-way ANOVA (2 groups $\times$ 4 cues) was performed on the estimates given by subjects of the probability with which each cue predicted the outcome sunshine (Table 4). There was a main effect of cue, indicating that subjects discriminated among the cues with respect to how much they were associated with the outcome sunshine [$F(3,51) = 4.37$, $MS_e = 2621.6$, $P < 0.01$]. There was no effect of group [$F(1,17) = 1.07$, $MS_e = 673.1$, $P > 0.1$] and no interaction between group and cue ($F < 1$). Despite the absence of an interaction, separate one-way ANOVAs on the scores of each group suggested that the control subjects were able to discriminate among the cues, whereas the amnesic patients were not. For control subjects there was an effect of cue on the pattern of estimations [$F(3,33) = 4.85$, $P < 0.01$]. Pairwise comparisons with Bonferroni correction indicated that control subjects estimated that cue 1 was more associated with the outcome "sunshine"

Table 4: Estimates of the associative strength of each cue

Cue	Control subjects (%)	Amnesic patients (%)
1	73.5 ± 6.1	60.7 ± 12.7
2	53.9 ± 6.1	46.0 ± 11.8
3	40.4 ± 6.6	39.3 ± 7.7
4	44.4 ± 7.9	41.6 ± 7.4

The values are the estimates (means ± S.E.M.) by subjects of the percent of time that each cue predicted outcome 1 when it appeared alone. The actual values were 85%, 62%, 38%, and 15% for cues 1, 2, 3, and 4, respectively.

than was cue 3 or cue 4 [$t(11) > 2.7$, $P < 0.05$]. For the amnesic patients, the effect of cue did not approach significance ($F < 1$) and none of the pairwise comparisons involving the four estimates was significant [$t(6) < 1.4$, $P > 0.2$]. Thus, although the amnesic patients performed as well as control subjects on the classification task itself (Fig. 5), they differed from control subjects in being unable to discriminate among the associative strengths of the cues.

DEBRIEFING QUESTIONS

The amnesic patients were impaired relative to the control subjects on the questions that asked about the nature of the task [$71.4\% \pm 4.4\%$ vs. $85.7\% \pm 3.0\%$, $t(17) = 2.74$, $P < 0.05$].

Discussion

Just as was observed in experiment 1, the amnesic patients performed as well as control subjects on the classification learning task. The key finding in experiment 2 was that the two groups exhibited equivalent savings across the 5-min delays. Because amnesic patients were able to retain knowledge of the associations between the cues and the outcomes across an interval of 5-min, they were not relying on immediate memory of previous trials to perform the task. Rather, it appears that information relevant for classification performance is acquired gradually within long-term memory. This learning occurs independently of the brain structures damaged in amnesia.

The estimation task used in the present exper-

iment was designed to measure whether in the course of the training trials subjects acquired any knowledge about the cue outcome associations. Neither group was particularly accurate when asked to estimate how often each of the two outcomes was associated with each cue. Responses were highly variable for both groups, and this variability may be one reason that no significant group differences emerged. Nevertheless, there is a suggestion in the data that the control subjects estimated the relationships between the cues and the outcomes better than the amnesic patients did. This conclusion must remain tentative in view of the fact that there was not an overall significant difference between the groups and no interaction of group $\times$ cue. Nevertheless, only the control subjects were able to discriminate between the cues in terms of how often each cue was associated with each outcome. The amnesic patients did not estimate that any of the cues were more associated with one outcome than the other outcome.

General Discussion

In experiments 1 and 2, amnesic patients exhibited normal learning of the probabilistic relationship between the cues and the outcomes, at least during the first 50 training trials. Because the performance of the amnesic patients could not be explained by reliance on short-term memory (experiment 2), it appears that performance is dependent on long-term, nondeclarative memory. At the same time, it appears that some declarative knowledge does develop about the cue-outcome associations after more extended training, because the control subjects were eventually able to outperform the amnesic patients. Experiment 2 showed that the amnesic patients had more difficulty than the control subjects in estimating verbally how often each cue was followed by each outcome, and in both experiments the amnesic patients were significantly impaired at recollecting facts about the testing sessions. These results support the idea that at least two kinds of knowledge can be acquired in the probabilistic classification tasks: On the one hand, subjects acquired nondeclarative knowledge early in training about the relationship between the cues and the outcomes; on the other hand, they also acquired declarative knowledge about the task, including information about the cue-outcome relationships, which gradually became robust enough to enhance classification per-

formance. Because the associations between the cues and outcomes were probabilistic, subjects needed to store a sufficient number of trials in declarative memory before they could have explicit knowledge of cue-outcome associations. Thus, the contribution of the hippocampal system could only become apparent later in training.

The probabilistic classification task appears to involve a kind of category learning. Implicit learning about categories has been demonstrated in other tasks in which explicit knowledge does not exert a strong influence on performance. For example, amnesic patients exhibited normal learning of categories defined by the rules of an artificial grammar (Knowlton et al. 1992; Knowlton and Squire 1994). Amnesic patients also exhibited normal learning in a classification task in which the categories were defined by the resemblance of items to a prototype (Knowlton and Squire 1993). Category learning appears to involve some of the same principles as conditioning (Gluck and Bower 1988a, 1988b). The Rescorla–Wagner rule (Rescorla and Wagner 1972), which describes the increment in the strength of the association between a CS and a US in classical conditioning, can also describe the increment in associative strength between a cue and an outcome in a category-learning experiment. In both cases, various cues (or CSs) compete for associative strength such that if one cue is highly associated with a particular outcome (or US), other possible associations between cues and that outcome are learned less well (Rescorla and Wagner 1972; Gluck and Bower 1988a). This cue competition, as embodied by the Rescorla–Wagner rule, results in phenomena such as blocking and overshadowing, which can be observed in conditioning paradigms. These phenomena also occur in category learning paradigms similar to the ones used in this study (see also Estes et al. 1989; Markman 1989; Shanks 1991). Conditioning and category learning undoubtedly have different neural substrates: Conditioning of discrete skeletal muscle responses depends on the cerebellum and associated brain stem circuitry (Thompson 1990), and conditioning of emotional responses depends on circuitry that includes the amygdala (LeDoux 1987). The neural substrates of category learning probably involve neither of these structures. However, it is an interesting possibility that different nondeclarative learning tasks share similar formal properties.

The probabilistic classification task is analogous to habit learning tasks studied in animals in

that subjects are learning a set of associations between stimuli, independently of declarative memory. The normal performance of amnesic patients on this task emphasizes that nondeclarative memory abilities are not solely perceptual or motor but include cognitive abilities as well (also Squire and Frambach 1990). The demonstration of nondeclarative habit learning in human subjects strengthens the idea that there are similarities among mammalian species with respect to the organization of memory, and it underscores the usefulness of animal models for the study of human nondeclarative memory.

In experimental animals, performance on habit learning tasks is disrupted by lesions of the caudate nucleus (Packard et al. 1989; Wang et al. 1990). The neostriatum has also been implicated in some kinds of nondeclarative learning tasks in humans. Patients with Huntington's disease, who sustain prominent damage in the caudate nucleus, exhibit deficits in nondeclarative tasks in which a motor program must be acquired (Heindel et al. 1988; Heindel et al. 1991; Knopman and Nissen 1991). In addition, these patients may be impaired at learning cognitive skills that can be learned rather well by amnesic patients (Saint-Cyr et al. 1988). Perhaps the striatum is also the locus of habit learning in human subjects. If so, patients with Huntington's disease should have difficulty with the probabilistic category learning task. Alternatively, in humans the highly developed cerebral cortex may be capable of forming the gradual connections between stimuli and responses that support habit learning.

One final point concerns the finding that late in training the control subjects performed better than the amnesic patients. A similar finding was reported in an earlier study of cognitive skill learning (Squire and Frambach 1990). One interpretation of this late training advantage is suggested by a recent computational theory of corticohippocampal processing (Gluck and Myers 1993). The theory distinguishes between two distinct but interacting memory processes. A representational process, assumed to be hippocampal-dependent, forms new stimulus representations, and an associational process, assumed to be hippocampal-independent, learns to map from these representations to expected future outcomes. These future outcomes would be category labels (e.g., rain and sunshine) in probabilistic classification learning or the unconditioned stimuli in studies of conditioning.

The key idea behind the proposed hippocampal-dependent processing is that it requires recognition of stimulus–stimulus relationships in the environment. An efficient representation is characterized both by compression of redundant, co-occurring cues and by differentiation of cues that predict different future events. Hippocampal lesions eliminate this representational processing but leave intact the simpler associational process. According to the theory, stimulus–stimulus regularities in the training environment can be represented only after the subject has experienced a sufficient subset of the environment. Until this occurs, learning should depend virtually entirely on associational processes. The impact of new hippocampal-dependent representations should, however, become evident later in training, once these representations have had time to develop. This idea implies that early in training, amnesic patients and control subjects should behave similarly. Later in training, however, control subjects will develop new stimulus representations and the performance of the two groups should diverge. (For a review of similar data from animals with hippocampal lesions, see Gluck and Myers 1993).

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