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Impaired Recognition Memory in Patients With Lesions Limited to the Hippocampal Formation

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A recent literature survey of results from a widely used recognition memory test raised questions about the extent to which recognition memory impairment ordinarily occurs in human amnesia and, in particular, whether recognition memory is impaired at all after damage limited to the hippocampal region (J. P. Aggleton & C. Shaw, 1996). Experiment 1 examined the performance of 6 amnesic patients on 11 to 25 different recognition memory tests. Three patients had bilateral lesions limited primarily to the hippocampus (G.D.) or the hippocampal formation (W.H. and L.M.), as determined by postmortem, neurohistological analysis (N. Rempel-Clower, S. M. Zola, L. R. Squire, & D. G. Amaral, 1996). All 6 patients exhibited unequivocally impaired recognition memory. In Experiment 2, the 3 patients still available for study were each markedly impaired on a test of object recognition similar to the kind used to test recognition memory in nonhuman primates. Recognition memory impairment is a robust feature of human amnesia, even when damage is limited primarily to the hippocampus.

Recognition memory refers to the process by which a perceptual object is judged familiar. Recognition judgments are usually considered to express a form of declarative (explicit) memory whereby stimuli are consciously recollected as having been encountered previously (Schacter, Chiu, & Ochsner, 1993; Squire, Knowlton, & Musen, 1993; Tulving, 1983). Thus, recognition memory is dependent on the medial temporal lobe and diencephalic structures that are essential for declarative memory. An alternative idea is that recognition memory can be supported, at least in part, by a relatively automatic feeling of familiarity that is based on nondeclarative (implicit) memory. Specifically, it has been proposed that the phenomenon of priming (Tulving & Schacter, 1990) can serve as a basis for recognition memory (Jacoby, 1983; Johnston, Hawley, & Elliott, 1991; Mandler, 1980; Whittlesea, 1993). Accordingly, because priming is intact after damage to medial temporal lobe or diencephalic structures (Hamann, Squire, & Schacter, 1995; Schacter et al., 1993; Squire et al., 1993), such damage should to some extent spare recognition memory.

Recently, a literature survey of 112 amnesic patients, all of whom had completed a widely used recognition memory test based on words and faces (the Recognition Memory Test [RMT]; Warrington, 1984), suggested that patients with damage limited to the hippocampal region, the fornix, or the diencephalon exhibited only a mild recognition memory impairment and sometimes no impairment at all (Aggleton & Shaw, 1996). This conclusion was based on 7 patients who were judged to have suitably circumscribed lesions. In contrast to their relatively mild impairment in recognition memory, the overall severity of amnesia in these 7 patients was judged comparable to the overall severity of amnesia in the other groups of memory-impaired patients.

Studies of rodents (Mumby, Pinel, Kornecook, Shen, & Redila, 1995) and nonhuman primates (Alvarez, Zola-Morgan, & Squire, 1995) have found mild impairments in recognition memory after lesions limited to the hippocampus and subicular complex. In addition, two preliminary studies in monkeys found no impairment on a standard task of recognition memory, the delayed nonmatching to sample task, after ibotenate lesions intended for the hippocampal and amygdalar regions (Murray & Mishkin, 1996; O'Boyle, Murray, & Mishkin, 1993). Finally, a review of hippocampal function in rodents proposed that recognition memory, in contrast to associative, relational memory, might survive hippocampal damage (Eichenbaum, Otto, & Cohen, 1994). Together, these findings from rats, monkeys, and humans raise questions about the extent to which recognition memory impairment occurs in amnesia and, in particular, whether recognition memory impairment ordinarily occurs after damage limited to the hippocampal region.

Recently, an exhaustive neurohistological analysis was carried out with the brains of 3 amnesic patients whose memory impairment and other cognitive functions were well characterized during the years before their deaths (G.D., W.H., and L.M.; Rempel-Clower, Zola, Squire, & Amaral, 1996). Postmortem examination of the brains revealed bilateral lesions limited to the hippocampal formation (W.H.

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Table 1
Characteristics of Amnesic Patients

Patient	Year of birth	Education (in years)	WAIS–R IQ	WMS–R Attention	Verbal	Visual	General	Delay
G.D.	1940	13	92	109	86	88	85	60
W.H.	1922	16	113	88	72	82	67	<50
L.M.	1930	15	109	124	94	82	89	62
A.B.	1937	20	104	87	62	72	54	<50
P.H.	1922	19	120	117	67	83	70	57
L.J.	1937	12	98	105	83	69	69	<50

Note. G.D., W.H., and L.M. died in 1992, 1993, and 1990, respectively, and their brains have been examined in considerable detail (Rempel-Clower et al., 1996). A.B., P.H., and L.J. continue to participate in our studies. The Wechsler Adult Intelligence Scale—Revised (WAIS–R) and the Wechsler Memory Scale—Revised (WMS–R) yield a mean score of 100 in the normal population, with a standard deviation of 15.

and L.M.) and, in one case, limited primarily to the CA1 field of the hippocampus (G.D.). Of particular interest in the present context is that in addition to the RMT, which was the focus of the survey conducted by Aggleton and Shaw (1996), each of these 3 patients had been given from 11 to 19 different tests of recognition memory. In Experiment 1, we reexamined the full body of neuropsychological data for these 3 patients so as to better characterize the effects of circumscribed damage to the hippocampus and related structures on recognition memory.

We also present neuropsychological data for 3 other amnesic patients, whom we have been studying for many years. Two of these patients have radiologically confirmed damage to the hippocampal region (P.H. and L.J.), and one (A.B.), who is not eligible for magnetic resonance imaging scans because he wears a pacemaker, is suspected to have bilateral hippocampal pathology based on the etiology of his amnesia (anoxia). In the course of participating in our studies, these 3 patients have been given from 15 to 25 different tests of recognition memory (in addition to the RMT).

In Experiment 2, we present new findings from a test of object recognition memory that was administered to this second group of 3 amnesic patients. This test was designed to resemble the kind of recognition tests in standard use with nonhuman primates.

Experiment 1

Method

Participants. Two groups of well-characterized amnesic patients were studied (see Tables 1 and 2). These two groups represent all of the amnesic patients with circumscribed damage to the hippocampal formation that have been available to this laboratory since 1986 (we have excluded only patients W.I. and J.L., 2 severely amnesic patients who gradually worsened and then received a diagnosis of Alzheimer's disease after being studied by us for several years [Squire & Kritchevsky, 1996]). The first group consisted of 3 patients for whom postmortem neurohistological examinations of brain tissue had revealed bilateral lesions limited primarily to the hippocampus or the hippocampal formation (Rempel-Clower et al., 1996). G.D. became amnesic in 1983 after a period of hypotension that occurred during major surgery. He died in 1992. His lesion involved nearly all of the CA1 field of the hippocampus bilaterally, sparing a small portion of proximal CA1, and also included a small region of subiculum near the CA1 border. Patient W.H. became amnesic in 1986 during a period of about 3 days, but without antecedent head trauma, seizure, or a known episode of unconsciousness. He died in 1993. Neurohistological analysis revealed substantial bilateral cell loss in the CA fields, the dentate gyrus, and the subiculum. In addition, there was bilateral cell loss in Layers III, V, and VI of entorhinal cortex, with minimal cell loss in Layer II. Patient L.M. became amnesic in 1984 after a respiratory arrest that occurred during an epileptic seizure. He died in 1990. His lesion involved most of the CA1 field bilaterally, some damage to the CA2 field, and essentially complete loss of CA3 pyramidal cells bilaterally. In the dentate gyrus, there was extensive loss of cells in the polymorphic layer (the hilar region) and patchy loss of granular cells. There was also patchy loss of the most proximal portion of the subiculum and some cell loss in Layers II and III of entorhinal cortex. Finally, there was substantial cell loss in the medial septum.

The second group consisted of 3 additional amnesic patients who continue to be studied. Patients P.H. (Polich & Squire, 1993) and L.J. (unpublished observations) have bilateral hippocampal dam-

Table 2
Memory Test Performance

Patient	Diagram recall	Paired associates Trial 1	Trial 2	Trial 3	Word recall (%)
G.D.	7	2	1	2	40
W.H.	1	0	0	0	40
L.M.	6	1	1	3	47
A.B.	4	1	1	1	33
P.H.	3	0	0	1	27
L.J.	3	0	0	0	40
M	4.0	0.7	0.5	1.2	37.8
Control *M* (n = 8)	20.6	6.0	7.6	8.9	71.0

Note. The diagram recall score is based on the delayed (12-min) reproduction of the Rey–Osterrieth figure (Osterrieth, 1944; maximum score = 36). The average score of the amnesic patients for copying the figure was 30.6, a normal score (Kritchevsky, Squire, & Zouzounis, 1988). The paired-associates score is the number of word pairs recalled on three successive trials (maximum score = 10 per trial). The word recall score is the mean percentage of 15 words recalled across five successive study–test trials (Rey, 1964). The mean scores for control participants are from Squire and Shimamura (1986).

age identified by magnetic resonance imaging. P.H. had a 6-year history of 1- to 2-min "attacks" (with a possible epileptic basis) that were associated with gastric symptoms and transient memory impairment. In July 1989, he suffered from a series of brief episodes after which he had a marked and persistent memory loss. Patient L.J. became amnesic during a 6-month period that began in 1988 with no known precipitating event. Her memory impairment has remained stable since that time. Patient A.B., who is unable to participate in magnetic resonance imaging studies, became amnesic in 1976 after an anoxic episode following cardiopulmonary arrest and is presumed to have hippocampal damage on the basis of this etiology. Note that A.B. was included in this study because other patients with amnesia due to anoxia have, at histological examination, proven to have hippocampal formation damage (Cummings, Tomiyasu, Read, & Benson, 1984; Rempel-Clower et al., 1996).

For these 6 patients, immediate and delayed (12-min) recall of a short prose passage averaged 5.2 and 0 segments, respectively. They performed normally on the Boston Naming Test (Kaplan, Goodglass, & Weintraub, 1983), achieving a mean score of 56.3 (maximum = 60, range = 52–58). They also performed well on the Dementia Rating Scale (Mattis, 1976), losing points primarily on the Memory subportion. Their mean score was 133.8 (maximum = 144, range = 130–137), and they lost an average of 6.8 points on the Memory subportion. Scores for normal participants on these tests can be found elsewhere (Squire, Amaral, & Press, 1990). For each recognition memory test included in our survey, and for the Words test and the Faces test of the RMT, performance had also been assessed in groups of 6 to 20 volunteers matched to the amnesic patients with respect to age, education, and Wechsler Adult Intelligence Scale—Revised (WAIS–R; Wechsler, 1981) subtest scores.

Materials and procedure. In addition to the standard RMT that formed the basis for Aggleton and Shaw's (1996) survey, we identified 29 other recognition memory tests, reported in 21 publications from 1986 to 1995, in which 1 or more of the 6 amnesic patients had participated (see Table 3). This list of 29 tests comprised every recognition test completed by these patients from the time they became available for study through 1995. The tests involved both verbal material (e.g., words, names, sentences, stories, trivia facts, and letter strings; 13 tests) and nonverbal material (e.g., objects, photographs, line drawings, and dot patterns; 7 tests). Other tests assessed recognition memory for the equipment and procedures that had been used in the experiments (9 tests). Some of the 29 tests used the method of yes–no recognition (10 tests), and the others used the method of forced-choice recognition (19 tests) with two or more response alternatives.

Scores for amnesic patients on the 29 recognition tests were standardized (converted to z scores) on an experiment-by-experiment basis so that tests that used different performance measures could be compared with each other. To derive the patients' z scores, we subtracted the mean percentage correct score (or other performance measure) that was actually achieved by the control group in each experiment from the performance score obtained by each amnesic patient in the same experiment. We divided this difference by the standard deviation of the control group scores. This procedure resulted in a total of from 11 to 25 z scores for each of the 6 amnesic patients, thereby providing a common performance measure for all of the various recognition memory tests that had been administered. Each of the control groups used to derive the patients' z scores was taken to have a mean z score of zero. Finally, to evaluate statistically the recognition performance of the patients, we compared their z scores with a z score of zero using a one-sample t test.

The data for the standard RMT were considered separately. The RMT (Warrington, 1984) consists of two parts: a Words test and a Faces test. For the Words test, participants rated the pleasantness of 50 words that were presented visually one at a time for about 3 s each. Immediately after the presentation of the entire list, participants were presented with a test list of 50 target–foil pairs and were asked to choose the word from the study phase. The Faces test was identical except that the test material consisted of black-and-white photographs of adult male faces. We also considered, separately from the 29 recognition tests, the performance of all 6 patients on a variant of the RMT (Squire & Shimamura, 1986) in which different sets of 50 words and 50 faces were presented and recognition memory was tested after a 24-hr delay.

Results

The mean z scores of the 6 amnesic patients from the survey of 29 recognition memory tests are presented in Figure 1. As a group, the 6 patients were extremely impaired (relative to the mean control z score of zero), $t(5) = 7.06$, $p < .001$. For this comparison, an average z score was calculated for each patient. The difference between amnesic patients and controls was also significant when, instead of mean z scores, median z scores were analyzed in the same way, $t(5) = 7.10$, $p < .001$. In addition, each of the 6 individual patients exhibited impaired recognition memory performance, as determined by a one-sample t test comparing all of the z scores available for each patient with a z score of zero. The mean z scores of the patients ranged from -4.30 to -1.35, all $ts > 2.0$ and $ps < .05$.

The data were examined further by considering separately the performance on various subtypes of the recognition memory tests: (a) tests involving verbal material (13 tests), (b) tests involving nonverbal material (7 tests), (c) tests based on items presented at study and then in a recognition test (verbal plus nonverbal material, 20 tests), (d) tests based on questions about aspects of the experimental procedure (9 tests), (e) tests of yes–no recognition (10 tests), and (f) tests of forced-choice recognition (19 tests). Figure 2 shows that as a group, the 6 patients were impaired on each type of recognition test ($ts > 3.40$, $ps < .02$). Some patients received only a small number of tests of a particular subtype. However, in the 28 cases (out of a total of 29) in which five or more test scores were available for an individual patient, that patient exhibited significantly impaired recognition memory in 22 of the cases ($ts > 2.10$, $ps < .05$) and marginally significant recognition memory impairment in 2 additional cases, $ts(4) > 2.40$, $ps = .07$. The 4 remaining cases involved data sets for patient W.H. that included the same extremely negative z score (< -19), which reflected particularly impaired performance. When the extreme negative score was eliminated from these four data sets to reduce variability, these cases also revealed significant recognition memory impairment ($ts > 3.30$, $ps < .03$). Thus, when a sufficient amount of data is collected, and variability in the data set is not inflated by extremely impaired scores, significant memory impairment can be demonstrated in individual patients, whether the recognition test is based on verbal or nonverbal material, yes–no or forced-choice test methods, or questions about the experimental procedure.

Table 3
Sources of Data for Experiment 1

Source	Amnesic patient(s)	Recognition test description
Squire & Shimamura, 1986[a]	G.D., L.M., A.B.	Y/N for words
Shimamura & Squire, 1987, Exp. 1	G.D., L.M., A.B.	8-alt. FC for trivia facts
Shimamura & Squire, 1987, Exp. 2	G.D., L.M., A.B.	8-alt. FC for trivia facts
Squire et al., 1988, Exp. 1b	G.D., L.M., A.B.	2-alt. FC for objects
Janowsky et al., 1989, Exp. 1	G.D., W.H., L.M., A.B.	7-alt. FC for sentences
Benzing & Squire, 1989, Exp. 1	L.M., A.B.	4-alt. FC for test procedure
Benzing & Squire, 1989, Exp. 2	L.M., A.B.	4-alt. FC for test procedure
Squire & Frambach, 1990, Exp. 1	G.D., L.M., A.B.	5-alt. FC for test procedure
Shimamura et al., 1990, Exp. 1	G.D., W.H., L.M., A.B., L.J.	Y/N for words
Musen et al., 1990, Exp. 1	L.M.	3-alt. FC for story content
Musen et al., 1990, Exp. 2	L.M.	3-alt. FC for story content
Shimamura & Squire, 1991, Exp. 1	G.D., W.H., L.M., A.B.	8-alt. FC for trivia facts
Cave & Squire, 1991, Exp. 1	G.D., W.H., L.M., A.B., P.H.	8-alt. FC for objects
Musen & Squire, 1991, Exp. 1	L.M., P.H., L.J.	2-alt. FC for test procedure
Musen & Squire, 1991, Exp. 2	L.M., P.H., L.J.	2-alt. FC for test procedure
Squire & McKee, 1992, Exp. 1	L.M., A.B.	Y/N for names of persons
Cave & Squire, 1992, Exp. 1	L.M., A.B., P.H., L.J.	Y/N for line drawings
Cave & Squire, 1992, Exp. 2	A.B., P.H., L.J.	Y/N for line drawings
Knowlton et al., 1992	G.D., W.H., A.B., P.H., L.J.	Y/N for letter strings
Haist et al., 1992, Exp. 1	G.D., L.M., A.B.	2-alt. FC for word pairs
Musen & Squire, 1992	L.M., A.B., P.H.	4-alt. FC for line drawings
McKee & Squire, 1993, Exp. 2a	W.H., A.B., P.H., L.J.	Y/N for photographs of scenes
Squire & McKee, 1993	W.H., A.B., P.H., L.J.	Y/N for names of persons
Musen & Squire, 1993, Exp. 1	A.B., L.J.	3-alt. FC for test procedure
Knowlton & Squire, 1993	A.B., P.H., L.J.	Y/N for dot patterns
Knowlton et al., 1994, Exp. 1	W.H., A.B., P.H., L.J.	4-alt. FC for test procedure
Knowlton et al., 1994, Exp. 2	W.H., A.B., P.H., L.J.	4-alt. FC for test procedure
Knowlton et al., 1994, Exp. 3	W.H., A.B., P.H., L.J.	4-alt. FC for test procedure
Knowlton & Squire, 1995, Exp. 1	W.H., A.B., P.H., L.J.	Y/N for words and nonwords

Note. Y/N = yes–no recognition; Exp. = experiment; alt. = alternative; FC = forced-choice recognition (e.g., 8-alt. FC indicates that participants chose from among eight possible responses).
[a]Scores for W.H., P.H., and L.J. on the recognition portion of the Rey Auditory Verbal Learning Test were obtained subsequent to the cited publication and were included in the current data set.

Performance of the 6 amnesic patients and controls on the Words and Faces tests (both the immediate and the 24-hr delay tests) is shown in Figure 3. Recognition memory of the amnesic patients was impaired on the Words test, both at the immediate test, $t(17) = 4.08$, $p < .001$, and at the 24-hr delay $t(17) = 4.42$, $p < .002$. For the Faces test, recognition memory was marginally impaired when there was no delay, $t(11) = 1.89$, $p = .076$, and significantly impaired at the 24-hr delay, $t(10) = 3.44$, $p < .007$. Individual amnesic patients sometimes performed rather well on this test (patient L.J., Words test—no delay; patient L.M., Faces test—no delay; see General Discussion). Nevertheless, these results are consistent with the findings from our large multitest survey. Recognition memory is impaired in amnesic patients with lesions limited to the hippocampal formation.

Experiment 2

Important information about the role of medial temporal lobe structures in memory has come from cumulative studies of an animal model of human amnesia in the nonhuman primate (Mishkin & Murray, 1994; Squire & Zola-Morgan, 1991). The benchmark task for studies of recognition memory in monkeys has been the delayed nonmatching to sample task. In this task, the monkey is presented with a "junk object" and then, after some interval, is given a choice between the original object and a new one. The monkey obtains a reward by choosing the novel object. In one standard version of this task, the monkey is first presented with "lists" of up to 20 objects and is then tested with 20 pairs of objects (Mishkin, 1978). Each pair consists of one of the objects from the list and a new object, and the monkey is rewarded for choosing the new object.

Studies of human recognition memory have rarely used stimuli similar to the objects used in studies with monkeys (see Aggleton, Nicol, Huston, & Fairbairn, 1988; Squire, Zola-Morgan, & Chen, 1988). In Experiment 2, we assessed the recognition memory capacity of the 3 surviving amnesic patients (A.B., P.H., and L.J.) who participated in Experiment 1. Recognition memory was tested with a set of junk objects similar to those used with monkeys in the delayed nonmatching to sample task.

Method

Participants. Three of the amnesic patients described in Experiment 1 (A.B., P.H., and L.J.) and a group of 6 controls were tested.

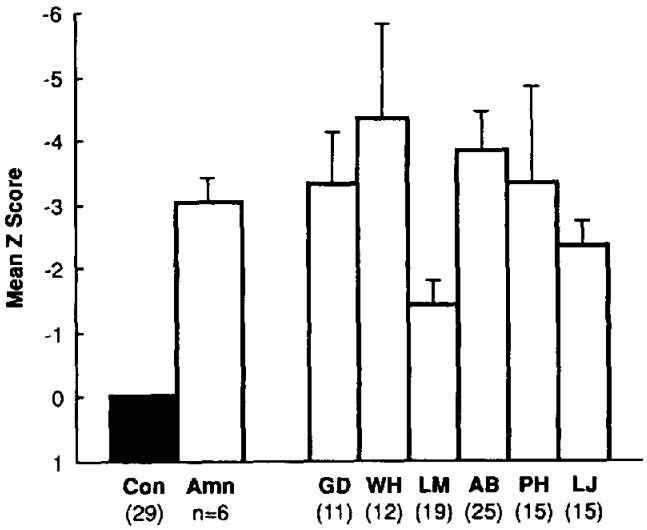

Figure 1. Performance of control (Con) participants (solid bar) and 6 amnesic (Amn) patients (as a group and individually; open bars) on tests of recognition memory. Each patient was tested on 11 to 25 different tests, and the raw performance scores from each test were converted to z scores based on the raw performance scores of concurrently tested control participants (see text). By this method, control participants were taken to have a mean z score of zero on each test. The z scores are negative because the values shown represent impaired performance. Higher bars represent greater impairment ($\pm SEM$). The numbers in parentheses indicate the number of recognition memory test scores that contributed to the mean z score.

Controls were volunteers and employees at the San Diego Veterans Affairs Medical Center who matched the amnesic patients with respect to age (M = 63.6 years vs. 64 years for the patients), education (M = 16.4 years vs. 17 years for the patients), and WAIS–R Information and Vocabulary subscale scores (Ms = 24.7 and 57.2, respectively, vs. 22.6 and 56 for the patients).

Materials and procedure. A set of 51 junk objects was created. The objects were constructed from broken, torn, and otherwise distorted pieces of colorful common objects, which served as raw materials (e.g., a plastic funnel, a bedroom slipper, and a change purse). Each unique junk object was small enough to fit in the palm of the hand and was composed of glued-together elements from 3 to 6 of the common objects. One object was used during the instruction phase of the experiment, and the remaining 50 were divided into two sets of 25 junk objects each. One set of 25 objects was used during the study phase, and items from the second set were used along with the first set during the test phase. The assignment of objects to the two sets was made such that both sets contained items that were similar in their ranges of sizes and colors and in the elements that composed them.

Participants were first informed that they would be seeing a series of objects composed of broken pieces of common items, and they were asked to rate each as either pleasant or unpleasant. After a practice trial with the sample object, participants were presented with each study item one at a time for about 3 s each. Presentation of the objects was followed by a 5-min conversation-filled interval and then by a test of recognition memory. For the test, participants were presented with two objects at a time, one from the study list and one new object, and they were instructed to indicate which was the "old" object. The left–right position of the new and old objects on each trial varied pseudorandomly across the 25 test trials.

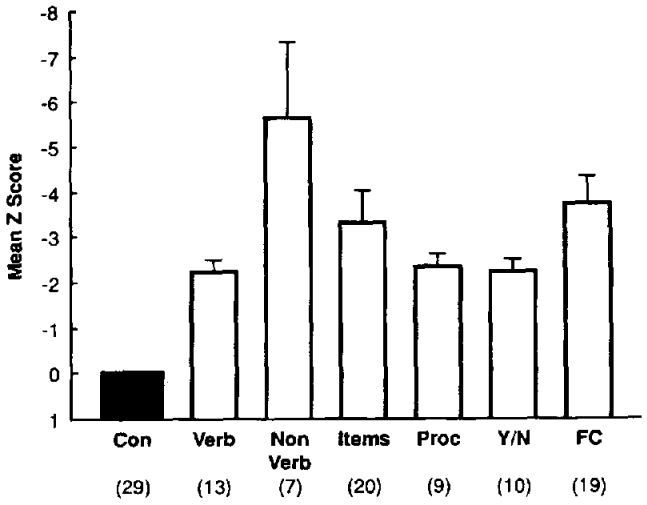

Figure 2. Mean z scores for control (Con) participants (solid bar) and the 6 amnesic patients (open bars) for six different categories of recognition test: (a) verbal material (Verb), (b) nonverbal material (Non Verb), (c) tests composed of study-list items and distractor items (Items), (d) tests asking about experimental equipment and procedures (Proc), (e) yes–no tests (Y/N), and (f) forced-choice tests (FC). The z scores are negative because the values shown represent impaired performance. Higher bars represent greater impairment ($\pm SEM$). The numbers in parentheses indicate the number of recognition memory tests that contributed to each score.

Results

Figure 4 shows the performance of amnesic patients and controls. The amnesic patients recognized significantly fewer objects ($M \pm SE$ = 68% ± 4.0%) than the controls ($M \pm SE$ = 95% ± 1.7%, range = 92% to 100%), $t(7) = 7.41, p < .0002$. Each patient scored outside the range of the

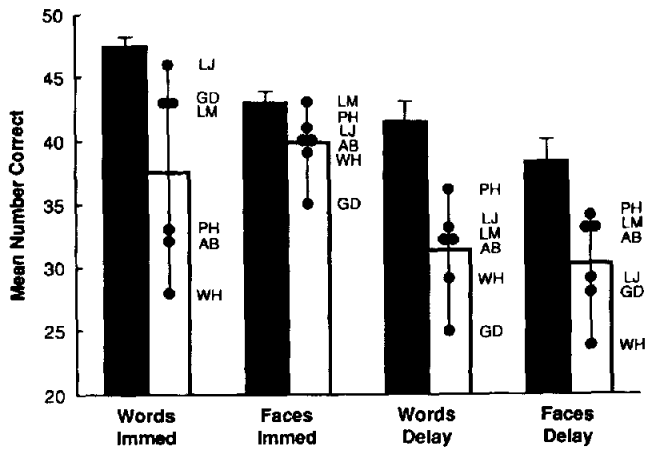

Figure 3. Performance of separate groups of control participants (solid bars; ns = 6 to 13) and amnesic patients (open bars; n = 6) on the Words and Faces tests (immediate testing [Immed] and testing after a 24-hr delay [Delay]). The mean number ($\pm SEM$) of correct responses (maximum = 50) for each group is represented by the bars, and individual scores for the amnesic patients are indicated by solid circles labeled with each patient's initials.

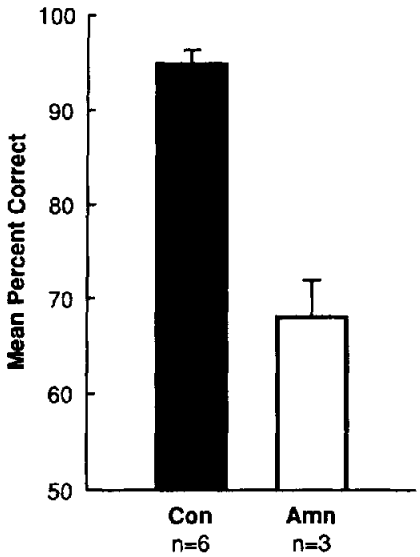

Figure 4. Mean (±*SEM*) scores for 6 control (Con) participants (solid bar) and 3 amnesic (Amn) patients (A.B., P.H., and L.J., open bar) on the recognition test involving 25 "junk objects."

controls (A.B., 64%, P.H., 64%, L.J., 76%). Thus, recognition memory was severely impaired when testing was done with stimuli similar to those used in studies of recognition memory in nonhuman primates.

General Discussion

Our findings contradict the position espoused by Aggleton and Shaw (1996), who suggested that recognition memory in amnesic patients is only mildly impaired or sometimes unimpaired when lesions are limited to the hippocampal region. It is important to note that their conclusion about the hippocampal region was based on data from only two recognition tests (i.e., the standard version of the Words test and the Faces test from the RMT) and from only 3 hippocampal patients (the patients whose data they used were our patients G.D., L.M., and A.B., who were part of the current study). Yet, when performance on a larger number of tests was evaluated, it became clear that each of these 3 patients exhibited an unequivocal impairment in recognition memory. We suppose that a single recognition memory test might fail to reveal a deficit when controls must exert considerable attentional effort at encoding. In this case, if controls do not try their best, they will not always outperform well-motivated patients with memory impairment. Indeed, we suggest that this circumstance may sometimes occur in the standard Faces test. In the case of other recognition memory tests, a deficit may fail to appear when the test consists of small numbers of items tested after short delays, so that a ceiling effect is present in the controls (e.g., Piercy & Huppert, 1972).

By examining performance on a large number of different tests administered on separate occasions, we obtained unambiguous evidence that amnesic patients with lesions limited to the hippocampal formation exhibit impaired recognition memory. The data from Experiment 2 provide further support for this conclusion and also show that lesions limited to the hippocampal formation impair recognition memory on a test similar to the kind used to assess recognition memory in nonhuman primates. Finally, recognition memory is impaired even when damage is limited primarily to the hippocampus proper. Both patient G.D. in the present study (Rempel-Clower et al., 1996) and patient R.B., reported previously (Zola-Morgan, Squire, & Amaral, 1986), demonstrated impaired recognition memory and had bilateral lesions limited to the CA1 fields of the hippocampus and to the CA1-subicular border zone. Unfortunately, R.B. could not be included in the current study. He completed only a small number of recognition memory tests and none of the tests that formed the basis of the current survey.

Another observation made by Aggleton and Shaw (1996) warrants comment. They compared the memory test performance of 5 amnesic patients with "limbic" lesions (3 patients with hippocampal region lesions and 2 patients with diencephalic lesions) with the performance of 14 patients with amnesia due to alcoholic Korsakoff's syndrome. Memory impairment was equivalent for the two groups, as assessed by the Wechsler Memory Scale—Revised (WMS–R; Wechsler, 1987), but the patients with Korsakoff's syndrome were more impaired than the other amnesic patients when recognition memory was assessed with the Words and Faces no-delay tests. On the basis of these data, Aggleton and Shaw proposed that "amnesics can have normal or near-normal RMT scores and yet show other memory losses that are as severe as those in other amnesics" (1996, p. 57). They also proposed that "certain patterns of pathology [as exist in patients with limbic lesions] disrupt processes involved in recall but largely spare those involved in performing the RMT" (Aggleton & Shaw, 1996, p. 57).

We examined this same issue by comparing performance on the WMS–R and on the Words and Faces tests (both the immediate and the 24-hr delay tests) for our 6 amnesic patients with hippocampal formation lesions and for 5 other amnesic patients with Korsakoff's syndrome (see Figure 5). The latter group of 5 patients (R.C., V.F., D.M., P.N., and J.W.) has been well characterized radiologically and neuropsychologically (Haist, Shimamura, & Squire, 1992). The Korsakoff patients generally obtained numerically lower scores than the other 6 patients and they performed significantly worse on the immediate Faces test ($p < .03$). However, there was no tendency for the Korsakoff patients to perform more poorly overall on recognition memory (the four RMT tests) while performing similarly on general memory ability (the WMS–R). Thus, in agreement with previous results from patients with hippocampal lesions (Haist et al., 1992; Hamann, Cahill, & Squire, 1997; Knowlton & Squire, 1995), and in contrast to the findings reported by Aggleton and Shaw (1996), we found no evidence to suggest that patients with hippocampal lesions exhibit disproportionate sparing of recognition memory ability in comparison with their general memory ability.

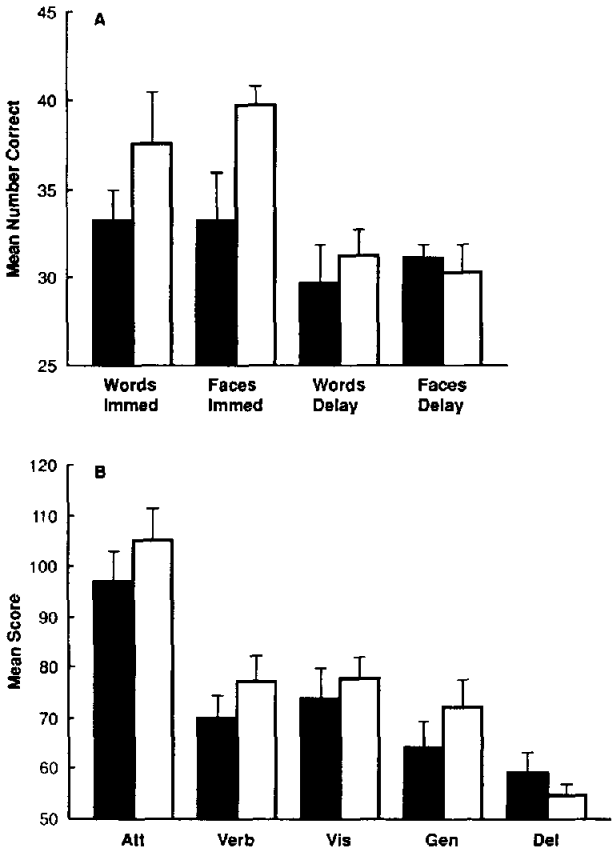

Figure 5. Performance (±*SEM*) on (A) the Words and Faces recognition tests and (B) the Wechsler Memory Scale—Revised (WMS–R) for 5 patients with Korsakoff's syndrome (solid bars) and 6 amnesic patients with damage to the hippocampal formation (open bars). Each Words and Faces test yields a maximum score of 50. Each WMS–R index yields a mean score of 100 in the normal population, with a standard deviation of 15. Immed = immediate testing; Delay = testing after a 24-hr delay; Att = Attention and Concentration; Verb = Verbal Memory; Vis = Visual Memory; Gen = General Memory; Del = Delayed Recall.

Finally, Aggleton and Shaw (1996) reported that recognition performance on the immediate Faces test (Warrington, 1984) was uncorrelated with WMS–R subtest scores ($r = .16$ for General Memory and $r = .36$ for Delayed Recall). Because the Faces test assesses recognition memory and the WMS–R assesses memory more broadly and includes recall tests, they took the low correlation as additional evidence that recognition memory scores are, to some extent, dissociable from other declarative memory processes. We obtained similar low correlations for our 6 patients between performance on the immediate Faces test and WMS–R subtest scores ($r = .31$ for General Memory and $r = .33$ for Delayed Recall). However, using the same method as Aggleton and Shaw (i.e., Spearman's rank-order technique), we also compared the WMS–R scores (General Memory and Delayed Recall) obtained for the 6 amnesic patients with their mean recognition test z scores in Figure 1. We obtained a high correlation in both cases ($r = .77$, $p < .08$, for General Memory and $r = .63$, $p < .18$, for Delayed Recall). Although the correlation coefficients were not statistically significant, they do show that high correlations between recognition memory and WMS–R scores can be obtained when a robust measure of recognition memory is used. More important, these high correlations provide no basis for supposing that recognition memory is different from other measures of declarative memory.

We agree with the suggestion of Aggleton and Shaw (1996) that a single administration of the RMT may not always record impaired recognition memory in a patient who is nevertheless amnesic as measured by many other tests (e.g., L.M., who performed adequately on the immediate Faces test despite being impaired on the other components of the RMT; see Figure 3). However, when the performance scores on many different recognition memory tests are considered together (e.g., 19 other tests in the case of L.M.; see Figure 1), recognition memory impairment emerges as a robust feature of amnesia. Thus, it would be incorrect to generalize from satisfactory performance on a single recognition memory test to the idea that recognition memory, as a category, is sometimes spared in amnesia.

We also agree with the suggestion (Aggleton & Shaw, 1996) that the standard delayed nonmatching to sample task, as usually given to monkeys, may not always be sensitive to recognition memory impairment. Here too, however, the data suggest that the difficulty lies with the task rather than with the nature of recognition memory capacity. In Experiment 2, amnesic patients with confirmed damage to the hippocampal formation were markedly impaired on a junk-object recognition task similar to the object recognition tasks used with monkeys. One important feature of the standard testing procedure for monkeys, a feature that could make the task easier and less sensitive to detecting impairment than when the task is given to humans, is that the rule of the task (e.g., the nonmatching rule) is first trained during several hundred trials. Thus, training on the rule provides the monkey with extended practice at holding novel objects in memory across short delays, which could then make it easier to hold novel objects in memory across the longer delays from which the performance scores for this test are derived.

Although recognition memory tasks such as delayed nonmatching to sample have been of enormous value in characterizing memory impairment after medial temporal lobe lesions in monkeys, other kinds of recognition tests will probably be needed as well to assess fully and reliably the memory impairment associated with restricted lesions to the hippocampal region. For example, the visual paired-comparison task, which requires no training and depends instead on the spontaneous looking preference of the animal, is a promising and sensitive test of recognition memory (Bachevalier, Brickson, & Hagger, 1993; Clark, Teng, Squire, & Zola, 1996, in press; McKee & Squire, 1993).

In summary, recognition memory impairment is a robust feature of human amnesia, even when damage is limited to the hippocampal formation or the hippocampus proper. Performance on recognition memory tests appears to provide a useful and accurate index of the overall severity of declarative memory impairment. For example, in the case of

patients with circumscribed damage to the hippocampal formation, moderately impaired scores on a group of recognition memory tests define a moderate level of overall memory impairment that can be demonstrated as well by other kinds of memory tests such as tests of cued recall or free recall.

References

Aggleton, J. P., Nicol, R. M., Huston, A. E., & Fairbairn, A. F. (1988). The performance of amnesic subjects on tests of experimental amnesia in animals: Delayed matching-to-sample and concurrent learning. *Neuropsychologia, 26,* 265–272.

Aggleton, J. P., & Shaw, C. (1996). Amnesia and recognition memory: A re-analysis of psychometric data. *Neuropsychologia, 34,* 51–62.

Alvarez, P., Zola-Morgan, S., & Squire, L. R. (1995). Damage limited to the hippocampal region produces long-lasting memory impairment in monkeys. *Journal of Neuroscience, 15,* 3796–3807.

Bachevalier, J., Brickson, M., & Hagger, C. (1993). Limbic-dependent recognition memory in monkeys develops early in infancy. *Neural Report, 4,* 77–80.

Benzing, W. C., & Squire, L. R. (1989). Preserved learning and memory in amnesia: Intact adaptation-level effects and learning of stereoscopic depth. *Behavioral Neuroscience, 103,* 538–547.

Cave, C. B., & Squire, L. R. (1991). Equivalent impairment of spatial and nonspatial memory following damage to the human hippocampus. *Hippocampus, 1,* 329–340.

Cave, C. B., & Squire, L. R. (1992). Intact and long-lasting repetition priming in amnesia. *Journal of Experimental Psychology: Learning, Memory, and Cognition, 18,* 509–520.

Clark, R. E., Teng, E., Squire, L. R., & Zola, S. (1996). The visual paired-comparison task and the medial temporal lobe memory system. *Society for Neuroscience Abstracts, 22,* 281.

Clark, R. E., Teng, E., Squire, L. R., & Zola, S. (in press). Perirhinal damage impairs memory on the visual paired-comparison task. *Society for Neuroscience Abstracts.*

Cummings, J. L., Tomiyasu, S., Read, S., & Benson, D. F. (1984). Amnesia with hippocampal lesions after cardiopulmonary arrest. *Neurology, 34,* 679–681.

Eichenbaum, H., Otto, T., & Cohen, N. J. (1994). Two functional components of the hippocampal memory system. *Behavioral and Brain Sciences, 17,* 449–518.

Haist, F., Shimamura, A. P., & Squire, L. R. (1992). On the relationship between recall and recognition memory. *Journal of Experimental Psychology: Learning, Memory, and Cognition, 18,* 691–702.

Hamann, S. B., Cahill, L., & Squire, L. R. (1997). Emotional perception and memory in amnesia. *Neuropsychology, 11,* 104–113.

Hamann, S. B., Squire, L. R., & Schacter, D. L. (1995). Perceptual thresholds and priming in amnesia. *Neuropsychology, 9,* 3–15.

Jacoby, L. L. (1983). Perceptual enhancement: Persistent effects of an experience. *Journal of Experimental Psychology: Learning, Memory, and Cognition, 9,* 21–38.

Janowsky, J. S., Shimamura, A. P., & Squire, L. R. (1989). Memory and metamemory: Comparisons between patients with frontal lobe lesions and amnesic patients. *Psychobiology, 17,* 3–11.

Johnston, W. A., Hawley, K. J., & Elliott, M. G. (1991). Contribution of perceptual fluency to recognition judgments. *Journal of Experimental Psychology: Learning, Memory, and Cognition, 17,* 210–223.

Kaplan, E. F., Goodglass, H., & Weintraub, S. (1983). *The Boston Naming Test.* Philadelphia: Lea & Febiger.

Knowlton, B. J., Ramus, S. J., & Squire, L. R. (1992). Intact artificial grammar learning in amnesia: Dissociation of classification learning and explicit memory for specific instances. *Psychological Science, 3,* 172–179.

Knowlton, B. J., & Squire, L. R. (1993). The learning of categories: Parallel memory systems for item memory and category knowledge. *Science, 262,* 1747–1749.

Knowlton, B. J., & Squire, L. R. (1995). Remembering and knowing: Two different expressions of declarative memory. *Journal of Experimental Psychology: Learning, Memory, and Cognition, 21,* 699–710.

Knowlton, B. J., Squire, L. R., & Gluck, M. (1994). Probabilistic classification learning in amnesia. *Learning and Memory, 1,* 106–120.

Kritchevsky, M., Squire, L. R., & Zouzounis, J. A. (1988). Transient global amnesia: Characterization of anterograde and retrograde amnesia. *Neurology, 38,* 213–219.

Mandler, G. (1980). Recognizing: The judgment of previous occurrence. *Psychological Review, 87,* 252–271.

Mattis, S. (1976). Dementia Rating Scale. In R. Bellack & B. Keraso (Eds.), *Geriatric psychiatry* (pp. 77–121). New York: Grune & Stratton.

McKee, R. D., & Squire, L. R. (1993). On the development of declarative memory. *Journal of Experimental Psychology: Learning, Memory, and Cognition, 19,* 397–404.

Mishkin, M. (1978). Memory in monkeys severely impaired by combined but not by separate removal of amygdala and hippocampus. *Nature, 273,* 297–298.

Mishkin, M., & Murray, E. A. (1994). Stimulus recognition. *Current Opinion in Neurobiology, 4,* 200–206.

Mumby, D. G., Pinel, J. P. J., Kornecook, T. J., Shen, M. J., & Redila, V. A. (1995). Memory deficits following lesions of hippocampus or amygdala in rat: Assessment by an object-memory test battery. *Psychobiology, 23,* 26–36.

Murray, E. A., & Mishkin, M. (1996). 40-minute visual recognition memory in rhesus monkeys with hippocampal lesions. *Society for Neuroscience Abstracts, 22,* 281.

Musen, G., Shimamura, A. P., & Squire, L. R. (1990). Intact text-specific reading skill in amnesia. *Journal of Experimental Psychology: Learning, Memory, and Cognition, 6,* 1068–1076.

Musen, G., & Squire, L. R. (1991). Normal acquisition of novel verbal information in amnesia. *Journal of Experimental Psychology: Learning, Memory, and Cognition, 17,* 1095–1104.

Musen, G., & Squire, L. R. (1992). Nonverbal priming in amnesia. *Memory & Cognition, 20,* 442–448.

Musen, G., & Squire, L. R. (1993). Implicit learning of color-word associations using a Stroop paradigm. *Journal of Experimental Psychology: Learning, Memory, and Cognition, 19,* 789–798.

O'Boyle, V. J., Murray, E. A., & Mishkin, M. (1993). Effects of excitotoxic amygdalo-hippocampal lesions on visual recognition in rhesus monkeys. *Society for Neuroscience Abstracts, 19,* 438.

Osterrieth, P. A. (1944). Le test de copie d'une figure complexe [The test of copying a complex figure]. *Archives de Psychologie, 30,* 206–356.

Piercy, M., & Huppert, F. A. (1972). Efficient recognition of pictures in organic amnesia. *Nature, 240,* 564.

Polich, J., & Squire, L. R. (1993). P300 from amnesic patients with bilateral hippocampal lesions. *EEG Clinical Neuropsychology, 86,* 408–417.

Rempel-Clower, N., Zola, S. M., Squire, L. R., & Amaral, D. G. (1996). Three cases of enduring memory impairment following bilateral damage limited to the hippocampal formation. *Journal of Neuroscience, 16,* 5233–5255.

Rey, A. (1964). *L'examen clinique psychologie* [The clinical exam in psychology]. Paris: Presses Universitaires de France.

Schacter, D. L., Chiu, C. Y. P., & Ochsner, K. N. (1993). Implicit memory: A selective review. *Annual Review of Neuroscience, 16,* 159–182.

Shimamura, A. P., Janowsky, J. S., & Squire, L. R. (1990). Memory for the temporal order of events in patients with frontal lobe lesions and amnesic patients. *Neuropsychologia, 28,* 803–814.

Shimamura, A. P., & Squire, L. R. (1987). A neuropsychological study of fact memory and source amnesia. *Journal of Experimental Psychology: Learning, Memory, and Cognition, 13,* 464–473.

Shimamura, A. P., & Squire, L. R. (1991). The relationship between fact and source memory: Findings from amnesic patients and normal subjects. *Psychobiology, 19,* 1–10.

Squire, L. R., Amaral, D. G., & Press, G. A. (1990). Magnetic resonance imaging of the hippocampal formation and mammillary nuclei distinguish medial temporal lobe and diencephalic amnesia. *Journal of Neuroscience, 10,* 3106–3117.

Squire, L. R., & Frambach, M. (1990). Cognitive skill learning in amnesia. *Psychobiology, 18,* 109–117.

Squire, L. R., Knowlton, B., & Musen, G. (1993). The structure and organization of memory. *Annual Review of Psychology, 44,* 453–495.

Squire, L. R., & Kritchevsky, M. (1996). Selective memory loss [Letter to the editor]. *Neurology, 47,* 853.

Squire, L. R., & McKee, R. D. (1992). Influences of prior events on cognitive judgments in amnesia. *Journal of Experimental Psychology: Learning, Memory, and Cognition, 18,* 106–115.

Squire, L. R., & McKee, R. D. (1993). Declarative and nondeclarative memory in opposition: When prior events influence amnesic patients more than normal subjects. *Memory & Cognition, 21,* 424–430.

Squire, L. R., & Shimamura, A. P. (1986). Characterizing amnesic patients for neurobehavioral study. *Behavioral Neuroscience, 100,* 866–877.

Squire, L. R., & Zola-Morgan, S. (1991). The medial temporal lobe memory system. *Science, 253,* 1380–1386.

Squire, L. R., Zola-Morgan, S., & Chen, K. (1988). Human amnesia and animal models of amnesia: Performance of amnesic patients on tests designed for the monkey. *Behavioral Neuroscience, 11,* 210–221.

Tulving, E. (1983). *Elements of episodic memory.* Cambridge, England: Oxford University Press.

Tulving, E., & Schacter, D. L. (1990). Priming and human memory systems. *Science, 247,* 301–306.

Warrington, E. K. (1984). *Recognition Memory Test.* Windsor, Ontario, Canada: FER-Nelson.

Wechsler, D. (1981). *The Wechsler Adult Intelligence Scale—Revised.* New York: Psychological Corporation.

Wechsler, D. (1987). *Wechsler Memory Scale—Revised.* New York: Psychological Corporation.

Whittlesea, B. W. A. (1993). Illusions of familiarity. *Journal of Experimental Psychology: Learning, Memory, and Cognition, 19,* 1235–1253.

Zola-Morgan, S., Squire, L. R., & Amaral, D. G. (1986). Human amnesia and the medial temporal region: Enduring memory impairment following lesion limited to field CA1 of the hippocampus. *Journal of Neuroscience, 6,* 2950–2967.

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