Characterizing Amnesic Patients for Neurobehavioral Study

Larry R. Squire and Arthur P. Shimamura
Veterans Administration Medical Center, San Diego
and Department of Psychiatry
University of California, San Diego

During the past 100 years, neuropsychological testing of amnesic patients has provided a valuable method for learning about the structure and organization of normal memory. One complicating feature of this work is the fact that amnesic patients differ in terms of the pattern of their lesions and in terms of what damage is present in addition to the lesions that cause amnesia. Accordingly, as the questions asked of amnesic patients have become more sophisticated, it has become increasingly important in every group of study patients to obtain information about both the severity and the selectiveness of memory impairment. The present article considers the suitability of several memory tests and other cognitive tests for the purpose of characterizing amnesic patients. Data from these tests are presented for 10 amnesic patients (6 with Korsakoff's syndrome, 3 with amnesia owing to anoxia or ischemia, and case N.A.), who constitute our standing population of study patients, and for two control groups. Data from most of the tests are also presented for patients who were amnesic following bilateral electroconvulsive therapy. Neuropsychological descriptions of patients, which appear in the Subjects section of experimental articles, need to be expanded and standardized if published findings from one laboratory are to provide a foundation for work in other laboratories with different study patients.

In the earliest collections of human amnestic cases (Ribot, 1881; Winslow, 1861), it was recognized that clinical cases are valuable for understanding normal memory. During the past 100 years, neuropsychological studies of human amnesia have provided an important source of information about the structure of memory and its neurological foundations (Baddeley, 1982; Barbizet, 1970; Butters & Cermak, 1980; Claparède, 1911; Mayes & Meudell, 1983; Milner, 1972; Rapaport, 1942; Schacter, 1984; Squire, in press; Talland, 1965; Warrington & Weiskrantz, 1982). In recent years, this work has become more rigorous and cumulative. Standing populations of patients are available in several locations for continuous study, and a variety of quantitative methods are available to assess the status of memory functions (Brooks & Lincoln, 1984; Erickson & Scott, 1977; Lezak, 1983; Mayes, 1986; Squire, 1986). Typically, however, when amnesic patients are the subjects of individual research studies, only one or two tests are used to characterize the memory deficit, and different investigators favor different tests. As a result, questions have arisen regarding similarities and differences between patient groups tested in different laboratories (Butters & Cermak, 1974; Warrington, 1982; Weiskrantz, 1985), and it is often difficult to determine from published data the relative severity of amnesia in two different study populations.

The research in this article was supported by the Medical Research Service of the Veterans Administration and by National Institutes of Mental Health Grant PHS MH24600.

We thank Kim Rivero-Frink, Deborah Rosenthal, and Joyce Zouzounis for research assistance and Stuart Zola-Morgan for many helpful comments.

Correspondence concerning this article should be addressed to Larry R. Squire, Department of Psychiatry, Veterans Administration Hospital, 3350 La Jolla Village Drive, San Diego, California 92161.

The Wechsler Memory Scale (WMS; Wechsler, 1945) is commonly used, and it does provide one index of the severity of memory impairment. However, the WMS has been frequently criticized (Mair, Warrington, & Weiskrantz, 1979; Prigatano, 1978; Russell, 1975; Squire, 1986), because much of the test measures functions (e.g., immediate memory, orientation) that are unaffected in human amnesia. Other tests such as delayed prose recall and paired-associate learning are helpful in detecting the presence of amnesia. However, many patients score near zero on these tests, so that discrimination among patient groups is often not possible. Clinical observers are well aware of the difference between the patient who scores zero for delayed recall (and who also denies having been presented any material recently) and the patient who scores zero (but who remembers hearing a story and produces some material semantically related to the story).

It would be more satisfactory to develop a set of simple tests, including ones free of floor and ceiling effects, which could come into regular use in studies of human amnesia. Whatever the objective of any particular experimental study, it is important to characterize the study population independently of the hypothesis being tested. This is true both in the case of stable, chronic amnesic patients (for example, patients with alcoholic Korsakoff's syndrome) as well as in the case of patients with gradually changing conditions (for example, patients with Alzheimer's disease). Only when the population under study is adequately characterized is it possible to evaluate published work and to extend it in other laboratories with different patient populations.

Amnesic patients differ not only with respect to the severity of memory impairment but also with respect to the selectiveness of the impairment. Amnesia can occur as one of many intellectual deficits, as in dementia, or it can occur in the absence of any other detectable impairment. In Korsakoff's
syndrome, amnesia occurs together with certain specific deficits, for example, impaired metamemory abilities (Shimamura & Squire, 1986a) and failure to release from proactive interference (Moscovitch, 1982; Squire, 1982). Whereas these deficits are common in patients with Korsakoff’s syndrome, they are absent in other amnesic patients, even when the memory impairment is just as severe. The importance of identifying deficits that are dissociable from amnesia is widely recognized (Moscovitch, 1982; Weiskrantz, 1985; Weiskrantz & Warrington, 1975; Zola-Morgan & Squire, 1985). It follows from this idea that amnesic patients should be evaluated with tests of general intellectual function, and with other tests, to assess the selectivity of the memory impairment.

The purpose of this article is to examine the utility of a group of tests for characterizing the severity and the selectiveness of memory impairment in amnesic patients. All the tests are either commercially available or extremely simple to construct. We included the WMS because it is commonly used in studies of memory. We included tests of both recall and recognition, in order to sample performance over a wide range of ability. Aside from the WMS we used six tests of memory, a standard IQ test, and two tests of cognitive ability: a dementia rating scale and a test of object naming. Tests were given to 10 amnesic patients who constitute our study population, to patients who were amnesic following prescribed bilateral electroconvulsive therapy, and to groups of control subjects.

Method

Subjects

Patients with Korsakoff’s syndrome. The group of patients with Korsakoff’s syndrome consisted of 4 men and 2 women living in supervised facilities in San Diego County. These patients have been studied in our laboratory for several years, and their memory impairment is well documented (Shimamura & Squire, 1986b; Squire, 1982). The 6 patients averaged 52.0 years of age, had 11.8 years of education, and had an average Weschler Adult Intelligence scale (WAIS) score of 102.8 (see Table 1 for individual values). Their average Weschler Memory Scale (WMS) score was 86.0, and the average WAIS-WMS difference was 22.8.

Four amnesic cases. We tested four cases of amnesia with etiologies other than Korsakoff’s syndrome: (a) Patient AB became amnesic in 1976 after an anoxic episode during cardiac arrest; (b) Patient LM became amnesic in 1984 as the result of a respiratory arrest that occurred during an epileptic seizure; (c) Patient GD became amnesic in 1983 following a period of hypotension that occurred during major surgery; and (d) Patient N.A. has been amnesic for verbal material since 1960 when he sustained a penetrating brain injury from a miniature fencing foil. CT scans revealed a lucency in the left dorsomedial thalamus (Squire & Moore, 1979). His memory impairment has been documented in previous studies (Kaushall, Zetin, & Squire, 1981; Squire & Slater, 1978; Teuber, Milner, & Vaughan, 1968). As a group, these 4 amnesic patients averaged 48.8 years of age, had 15.2 years of education, and had an average WAIS score of 118.2 (see Table 1). They averaged 93.5 on the WMS, and their average WAIS-WMS difference was 24.7.

Patients prescribed bilateral ECT. We tested a total of 23 patients who were receiving bilateral ECT for relief of depressive illness. All were inpatients at one of five hospitals in San Diego County. Memory impairment is a prominent side effect of treatment (Price, 1982; Squire, 1984; Squire, 1986); it is most severe during the hours after treatment, diminishes to some extent during the interval between treatments, and accumulates across individual treatments. Sixteen of the 23 patients were treated with a Medcraft B-24 device, and the other 7 patients were treated with a MECTA device. In all cases, electrode placement was bitemporal. Treatments were given in the mornings three times a week. Four of the patients had received a prior course of ECT, but none had received ECT during the preceding year. The 23 patients participated in one of two test protocols (see the Procedure section).

Alcoholic control subjects. We tested 8 alcoholic control subjects (5 men and 3 women) who were current or former enrollees in alcohol treatment programs in San Diego County. The subjects were matched to the Korsakoff patients with respect to age, education, and intelligence test (Information and Vocabulary) subscores. They had an average drinking history of 11.8 years, but had abstained from alcohol for an average of 2.3 years prior to participating in the experiment. They averaged 53.3 years of age, had 12.7 years of education, and had Weschler Adult Intelligence Scale-Revised (WAIS-R) subscores of 18.9 for Information (18.5 for Korsakoff patients) and 42.5 for Vocabulary (43.2 for Korsakoff patients). The alcoholic subjects had

<table>
<thead>
<tr>
<th>Patient</th>
<th>Diagnosis</th>
<th>Age</th>
<th>Education</th>
<th>IQ</th>
<th>WMS</th>
<th>IQ-WMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>K1</td>
<td>Korsakoff</td>
<td>42</td>
<td>12</td>
<td>102</td>
<td>86</td>
<td>16</td>
</tr>
<tr>
<td>K2</td>
<td>Korsakoff</td>
<td>65</td>
<td>10</td>
<td>114</td>
<td>93</td>
<td>21</td>
</tr>
<tr>
<td>K3</td>
<td>Korsakoff</td>
<td>47</td>
<td>12</td>
<td>91</td>
<td>69</td>
<td>22</td>
</tr>
<tr>
<td>K4</td>
<td>Korsakoff</td>
<td>51</td>
<td>12</td>
<td>111</td>
<td>73</td>
<td>38</td>
</tr>
<tr>
<td>K5</td>
<td>Korsakoff</td>
<td>58</td>
<td>11</td>
<td>96</td>
<td>76</td>
<td>20</td>
</tr>
<tr>
<td>K6</td>
<td>Korsakoff</td>
<td>49</td>
<td>14</td>
<td>103</td>
<td>83</td>
<td>20</td>
</tr>
<tr>
<td>AB</td>
<td>Anoxia</td>
<td>48</td>
<td>20</td>
<td>122</td>
<td>91</td>
<td>31</td>
</tr>
<tr>
<td>LM</td>
<td>Anoxia</td>
<td>55</td>
<td>15</td>
<td>123</td>
<td>105</td>
<td>18</td>
</tr>
<tr>
<td>GD</td>
<td>Ischemia</td>
<td>45</td>
<td>13</td>
<td>104</td>
<td>81</td>
<td>23</td>
</tr>
<tr>
<td>NA</td>
<td>Injury</td>
<td>47</td>
<td>13</td>
<td>124</td>
<td>97</td>
<td>27</td>
</tr>
<tr>
<td>ECT</td>
<td></td>
<td>37.2</td>
<td>14.7</td>
<td>100.5</td>
<td>78.2</td>
<td>22.3</td>
</tr>
</tbody>
</table>

Note. For the amnesic patients, IQ was based on the Weschler Adult Intelligence Scale (WAIS). For the ECT patients, n = 6. IQ was based on the WAIS (N = 3) or an alternate form, the Weschler-Bellevue (W-B, N = 3). In normal subjects, the WMS is equivalent to the WAIS. ECT patients were tested beginning 6 to 8 hr after the fifth treatment of the series. IQ = Intelligence Quotient; WMS = Weschler Memory Scale; ECT = bilateral electroconvulsive therapy.
an average WMS score of 114.3 (range = 105–129). None had a prior history of head injury. One patient had a period of unconsciousness lasting longer than 5 min.

Healthy control subjects. We tested 8 healthy control subjects (3 men and 5 women) who were volunteers or employees of the San Diego Veterans Administration Medical Center. They were matched to the four individual amnesic cases with respect to age, education, and intelligence test subcores. They averaged 50.9 years of age, had 14.8 years of education, and had WAIS-R subtest scores of 21.9 for Information (21.5 for the four amnesic cases) and 51.8 for Vocabulary (56.2 for the four amnesic cases). They had an average WMS score of 117.6 (range = 104–143).

Memory Tests

1. Prose Recall. Subjects were read a short prose passage containing 21 segments. Recall was tested immediately and 12 min after presentation (Squire & Chace, 1975).

2. Paired-Associate Learning. Subjects were presented 10 noun–noun word pairs on each of three study trials. After each study trial, subjects were shown the first word of each pair and asked to recall the second word (Jones, 1974).

3. Recall of Complex Design. Subjects copied the Rey-Osterreith figure (Osterreith, 1944) and were asked to reproduce it from memory after a 12-min delay.

4. Word List Recall and Yes/No Recognition (Rey Auditory Verbal Learning Test: Rey, 1964; Lezak, 1983). To test recall memory, subjects were presented a list of 15 words and asked to recall as many words as possible immediately after presentation. Five successive study–test learning trials were presented using the same words but each time in a different order. To test recognition memory, a different list of 15 words was presented. Immediately after presentation, subjects were shown 30 words one at a time (the 15 study words intermixed with 15 new words), and they were asked to determine whether or not a word had been presented during the study phase. Five successive study–test trials were presented using the same study words, each time in a different order. Different distractor words were used on each test trial. Recognition scores were based on the percentage correct, including both hits and correct rejections.

5. Two-choice Recognition Memory for Words and Faces (Warrington, 1984). In the study phase, subjects were shown 50 words after providing the following instructions:

   "This is a test of memory for words. I am going to show you this pack of words, one at a time, and for each word I want you to say yes if your associations with it are pleasant and no if your associations with the word are not so pleasant. There is no right or wrong answer but I do want to make a judgment about each word."

   Immediately following the study phase, subjects were given a two-alternative forced-choice recognition test for all 50 study words.

   The same procedure was then used to test recognition memory for 50 black and white (3½ × 4½ in.; 8.25 × 10.80 cm) photographs of unfamiliar faces. In addition, we constructed a second version of the same test using different words and faces. We used this second version to test word and face recognition memory after a 24-hr retention interval.

6. Continuous Recognition Test of Verbal and Nonverbal Stimuli (Kimura, 1963; Teuber et al., 1968). In the verbal test, subjects were shown a total of 144 stimuli—48 words, 48 nonwords, and 48 numbers. Each stimulus was presented for 3 s, and subjects were asked to determine whether or not the stimulus was previously presented. The first 24 stimuli were new. Thereafter, 12 of these 24 stimuli were repeated five times each for a total of 60 repeated items. These repeated stimuli were intermixed with 60 new ones. Scores were based on the number of correct yes responses (i.e., hits) minus the number of false alarms (perfect score = 60). The nonverbal test was similar but used geometric or nonsense figures as stimuli. A total of 160 stimuli were presented—80 geometric drawings and 80 nonsense shapes. The first 20 figures were new. Thereafter, 8 of the 20 figures were repeated seven times each for a total of 56 repeated items. The repeated items were intermixed with 84 new ones. A perfect score on the nonverbal test was 56.

Other Cognitive Tests

1. Dementia Rating Scale (Coblenz et al., 1973). The scale assesses a spectrum of cognitive functions, which includes memory, attention, initiation and perseveration, construction, and conceptualization. A perfect score is 144 points.

2. Boston Naming Test (Kaplan, Goodglass, & Weintraub, 1983). This test assesses the ability to name 60 drawings of different objects ranging from easy items (e.g., helicopter, camel) to more difficult ones (e.g., trellis, yoke). Our test was based on an 85-item, earlier version of the same test. It eliminated the easiest items and consisted of 72 drawings.

Procedure

All subject groups except the ECT patients were given all six memory tests, as well as the WMS. Two of the alcoholic subjects and 1 normal control subject were not available for the 24-hr delay version of the recognition test for the words and faces. The two cognitive tests—the DRS and the Boston Naming Test—were administered to the Korsakoff patients and the four individual amnesic cases. We also administered the DRS to all 8 alcoholic subjects. Testing occurred during several test sessions in an 8-month period.

It was not possible to administer all tests to a single group of ECT patients. Therefore, two groups of ECT patients received different test protocols. One group of 14 ECT patients (6 men and 8 women; age = 38.5 years; education = 13.0 years) was given tests of paired-associate learning, story recall (10–12-min delay), and diagram recall (10–12-min delay) on the day before the first ECT treatment and again 1–2 hr after the fourth, fifth, sixth, or seventh ECT treatment (mean = 4.6 treatments). For each of the three tests, we used two different but equivalent forms—one form was given before ECT and the other form was given after ECT.

A second group of 9 patients prescribed bilateral ECT (1 man and 8 women; age = 43.6 years; education = 15.4 years) was given the Rey Auditory Verbal Learning Test (Rey, 1964; Lezak, 1983) and the Recognition Memory Test for Words and Faces (immediate test only) beginning 2 hr after the fourth or fifth ECT treatments. To assess IQ and WMS in ECT patients, 6 of the patients from this same group were also given the WMS and two versions of the IQ test (Wais and Weschler-Bellevue Test [W-B]). The WMS and one of the IQ tests were given 6 to 10 hr after the fifth treatment (Table 1). The second IQ test was given beginning 2 hr after the sixth treatment. For half of the patients, the Wais was given first and the W-B was given second, and for the other patients, the order of the IQ tests was reversed.
Results

IQ and WMS

The difference between the IQ and the WMS score provides one index of the severity of memory impairment (Table 1). In normal subjects the WMS score is equivalent to the IQ, and the standard deviation for both scores is 15. Each memory-impaired patient had an IQ in the normal or above-normal range, and each patient had a WMS score at least 16 points below his or her IQ. The WMS score for each patient type (the 6 with Korsakoff's syndrome, the ECT patients, the 3 with amnesia due to anoxia or ischemia, and patient N.A.) averaged about 1.5 standard deviations below normal.

We used the WAIS to measure IQ because the WMS was designed to be used in conjunction with the WAIS. In 1981 a revised version of the WAIS became available (WAIS-R), and it was also given to the 10 amnesic patients listed in Table 1. An interval of at least 4 months separated the administration of the two tests. The mean score on the WAIS-R was 101.6 (range = 88–120), 8.4 points lower than the mean score on the WAIS. This difference is exactly what would be expected, on the basis of normative data available for the two tests (Wechsler, 1981).

The IQ and WMS data presented in Table 1 for patients prescribed ECT were obtained on the average 6.4 hr after the fifth bilateral treatment. At that time, IQ scores averaged 100.5, and WMS scores averaged 78.2. To understand better the effects of ECT on IQ and WMS, we also tested the same patients with the alternate form of the IQ test (WAIS or W-B) beginning 2 hr after the sixth treatment of the series. The average IQ score at that time was 102.2. In addition, we administered the WMS to a separate group of 8 patients (2 men and 6 women; mean age = 47.4 years; mean education = 13.9 years) at 2 hr after the fifth bilateral treatment. The WMS score for this group was 78.5.

These data suggest that the cognitive effects of ECT are rather stable between 2 and 8 hr after the fifth treatment. The impaired WMS scores (78.5 at 2 hr after the fifth treatment; 78.2 at 6–10 hr after the fifth treatment) can be attributed to ECT and not to the depressive illness for which ECT was prescribed. Six depressed psychiatric inpatients at the same hospitals, who were not receiving ECT, (2 men and 4 women; mean age = 40.5 years; mean education = 13.1 years) obtained an average WMS score of 106.0.

-- Paired-Associate Learning, Story Recall, and Diagram Recall

Figure 1 shows the results for three tests of memory frequently used to assess anterograde amnesia. All patient groups were severely impaired on all tests. Whereas the WMS yielded a score of 1.5 standard deviations below normal (see Table 1), every patient group on each of these three tests scored more than two standard deviations below the score of the corresponding control group.

The score for the paired-associate test was the total number of pairs correct after three trials (maximum score = 30). The patients with Korsakoff's syndrome averaged 1.7 ± 0.4 pairs correct (M ± SE), the patients with amnesia due to anoxia or ischemia (A-I) averaged 4.0 ± 0.6 correct, and ECT patients averaged 5.8 ± 2.0 correct. The scores for the control groups were 21.9 ± 2.3, 22.5 ± 2.7, and 17.4 ± 2.3 for the alcoholics, healthy controls, and depressed patients, respectively. On the story recall test, every Korsakoff and A-I patient obtained a zero score. The ECT patients recalled an average of 1.3 ± 0.5
would be expected, all subjects performed better on recognition tests than on recall tests. On the recognition test, the amnesic patients performed better than 85% after five trials. However, the control subjects exhibited ceiling effects after the second learning trial, so that even a score as high as 85% signified impairment.

Because performance on these two tests gradually improved across the five learning trials, it was possible with these tests to discriminate among groups of amnesic patients (Korsakoff, A-I, and ECT). Although all groups were impaired, an analysis of the recall data for the three amnesic groups (3 groups × 5 trials) revealed a significant effect of group, F(2, 15) = 10.2, p < .01. Further comparisons indicated that the Korsakoff patients were more impaired than the ECT patients (t = 2.4, p < .05). The group of anoxic and ischemic patients exhibited intermediate levels of recall, and their performance was not significantly different from either of the other two patient groups. Similarly, the recognition data showed that ECT and A-I patients exhibited similar levels of recognition performance, whereas the patients with Korsakoff’s syndrome exhibited somewhat poorer performance. On the recognition test, however, these differences were not statistically significant. Thus, whereas difficult tests of paired-associated learning or delayed recall suggested that memory impairment was similarly severe across groups (see Figure 1), tests more sensitive to impaired levels of performance permitted some differences to emerge (see Figure 2).

N.A. was also given the Rey Verbal Learning Test. His scores for five recall trials were 67%, 40%, 53%, 47%, and 40%. His scores for five recognition trials were 77%, 93%, 97%, 100%, and 100%. N.A.’s high intelligence probably accounts for his surprisingly good performance on the first trial of the recall test. However, he was not able to improve beyond that level of performance and even regressed to some extent on subsequent trials. On the recognition test, N.A. did benefit from repeated learning trials. His performance was impaired on the first two trials but then reached the maximum level on the last two trials.

Recognition Memory: Words and Faces

Figures 3 and 4 show the results for the words and faces test (see Table 2 for individual scores). Subjects were first tested on the original version developed by Warrington (1984), in which recognition memory was assessed immediately after presentation of 50 items. Later, subjects were tested after a 1-day retention interval, with a similar version developed in our laboratory as an equivalent form. The comparability of these two forms was assessed directly by giving all four tests to 6 healthy subjects in counterbalanced fashion and testing retention immediately after presentation of each set of 50 items. The scores were similar. Warrington’s words 48.7, our words 49.0; Warrington’s faces 44.2, our faces 45.0.

We first subjected the word data (Figure 3) to a two-way ANOVA involving four groups (Korsakoff, A-I, alcoholics, and controls) and two delays (immediate and 1 day). The effects of group, F(3, 18) = 16.2, p < .01, and delay, F(1, 18) = 71, p < .01, were highly significant. Additional comparisons

Figure 2. Performance by amnesic patients and control subjects on the Rey Auditory Verbal Learning Test. (Left panel shows recall scores for 15 words during five study–test trials. Right panel shows yes–no recognition for 15 study words and 15 distractor words during five study–test trials. KOR = 6 patients with Korsakoff’s syndrome; A-I = 3 patients with amnesia due to anoxia or ischemia; ECT = 9 patients prescribed bilateral electroconvulsive therapy. Testing began two hours after the fourth or fifth treatment. ALC = alcoholic control subjects; CON = healthy control subjects.)
showed that each amnesic group was impaired relative to the corresponding control group for both immediate testing ($p < .01$) and for 1-day testing ($p < .01$). For immediate testing, the alcoholic control group averaged $47.1 \pm 1.1$ (range = 42–50). For 1-day testing, this group averaged $36.2 \pm 2.2$ (range = 30–43). For immediate testing, the healthy control group averaged $48.4 \pm 0.8$ (range = 44–50). For 1-day testing, this group averaged $41.1 \pm 1.9$ (range = 33–45). N.A.'s scores were compared with those obtained by the healthy control group. His score of 40 correct on the immediate test was outside the range of any control subject. His score on the delayed test (33 correct) was equal to the lowest score obtained by a control subject.

The data for 9 patients prescribed bilateral ECT (see Table 1) were analyzed separately because they were not tested in the delay condition. Material was presented at 2 hr after the fourth or fifth treatment, and retention was tested immediately afterwards (Figures 3 and 4). Word recognition by the ECT patients was significantly lower than the performance of either control group, $t(15) > 3.3, p < .01$.

Performance on the faces test (Figure 4) was not so clear cut, mainly because performance was quite variable. For example, the scores of the alcoholic control subjects averaged $40.8 \pm 2.0$ on the immediate test (range = 30–48) and $36.2 \pm 2.0$ on the 1-day test (range = 33–41). The scores of the healthy normal control subjects ranged from 30 to 49 correct in the immediate test ($M = 41.9 \pm 2.2$) and 33 to 45 in the 1-day test ($M = 38.1 \pm 1.4$). Table 2 shows that performance of the amnesic patients was also variable. As a result, the two-
Table 2
Performance on Memory Tests

<table>
<thead>
<tr>
<th>Patient</th>
<th>Rec.</th>
<th>No delay</th>
<th>1 Day</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Recall</td>
<td>Recognition</td>
<td>Words</td>
</tr>
<tr>
<td>K1</td>
<td>23%</td>
<td>71%</td>
<td>44</td>
</tr>
<tr>
<td>K2</td>
<td>27%</td>
<td>91%</td>
<td>38</td>
</tr>
<tr>
<td>K3</td>
<td>28%</td>
<td>88%</td>
<td>35</td>
</tr>
<tr>
<td>K4</td>
<td>32%</td>
<td>56%</td>
<td>29</td>
</tr>
<tr>
<td>K5</td>
<td>29%</td>
<td>83%</td>
<td>32</td>
</tr>
<tr>
<td>K6</td>
<td>29%</td>
<td>89%</td>
<td>30</td>
</tr>
<tr>
<td>AB</td>
<td>33%</td>
<td>83%</td>
<td>32</td>
</tr>
<tr>
<td>LM</td>
<td>44%</td>
<td>98%</td>
<td>46</td>
</tr>
<tr>
<td>GD</td>
<td>36%</td>
<td>79%</td>
<td>43</td>
</tr>
<tr>
<td>NA</td>
<td>49%</td>
<td>93%</td>
<td>40</td>
</tr>
<tr>
<td>ALC</td>
<td>61%</td>
<td>96%</td>
<td>47.1</td>
</tr>
<tr>
<td>CON</td>
<td>71%</td>
<td>97%</td>
<td>48.4</td>
</tr>
</tbody>
</table>

Note. The score for the Rey Test is the average score for two trials. For the words and faces test, chance = 25 and the maximum score = 50. For the continuous recognition test, the maximum scores are 60 for the verbal portion and 56 for the nonverbal portion. The bottom two rows show scores for two control groups. Recog. = Recognition; ALC = alcoholic control subjects, N = 8; CON = healthy control subjects, N = 8.

way ANOVA involving four groups (Korsakoff, A-I, alcoholics, and controls) and two delays (immediate and 1 day) did not reveal a group effect $F(3, 18) = 1.6, p = .2$. Performance was, however, affected by the delay $F(1, 18) = 6.2, p < .05$. When variability was reduced by comparing the performance of 9 amnesic patients (6 Korsakoff patients and 3 A-I patients) with the combined performance of both control groups, the amnesic patients were significantly impaired on the faces test in both the immediate, $t(23) = 2.12, p < .05$, and delay, $t(20) = 3.17, p < .005$, conditions.

N.A. performed well on the faces test, both at the immediate and delayed test, a finding consistent with the left diencephalic locus of his lesion (see Figure 4). Because of the variability in the performance of control subjects, face recognition performance of ECT patients was not significantly different from that of alcoholic control subjects, $t(15) = 1.45, p = .17$, and only marginally different from that of healthy control subjects, $t(15) = 1.79, p = .09$.

Possible Hemispheric Asymmetry in Amnesic Patients

The test for words and faces assesses both verbal and nonverbal memory, and it appears to be sensitive to both left and right hemispheric dysfunction, respectively (Warrington, 1984). In the case of amnesic patients who have both verbal and nonverbal memory problems, one usually assumes that bilateral lesions are present and that the lesions are roughly symmetrical. However, when verbal memory test scores are either higher or lower than nonverbal memory test scores, the question arises whether this degree of variability would readily occur in patients with bilaterally symmetrical lesions. Because bilateral ECT affects the two hemispheres symmetrically, the performance of ECT patients provides a way to address this question. Specifically, if amnesic patients do have symmetrical, bilateral brain injury or disease, their discrepancy scores (i.e., each patient's score on the words test minus the same patient's score on the faces test) should be similar to the discrepancy scores obtained by ECT patients. However, to the extent that amnesic patients have asymmetrical brain injury or disease, the amnesic patients should show greater variability in their discrepancy scores than would ECT patients.

With that possibility in mind, we compared the performance of 9 amnesic patients in the no-delay condition (all but N.A., see Table 2) with the performance of 9 patients prescribed ECT. Although the average discrepancy between the words score and the faces score was small for both groups (amnesic patients: 36.6 for words vs. 37.2 for faces; ECT patients: 40.1 vs. 37.1), the amnesic patients, but not the ECT patients, exhibited considerable individual variability. Three amnesic patients (K1, K3, and GD) scored more than 7 points higher on words than on faces, and 4 patients (K4, K5, K6, and AB) scored more than 7 points lower on words than on faces. In contrast, within the ECT group, only 2 patients scored more than 7 points higher on words than on faces, and no patient scored more than 2 points higher on faces than on words. A test of $F$ ratios between the scores of the 9 amnesic patients and the 9 ECT patients indicated that the scores of the amnesic patients were significantly more variable, $F(8, 8) = 4.24, p < .05$. Thus the amnesic patients exhibited larger discrepancies between their words and faces scores than would be expected if the involvement of the two hemispheres were symmetrical. These results suggest that alcoholic brain disease, anoxia, and ischemia—conditions that do lead to global amnesia affecting both verbal and nonverbal material—need not always produce bilaterally symmetrical lesions.

Continuous Recognition: Verbal and Nonverbal Tests

Table 2 shows individual scores for the amnesic patients on the verbal and nonverbal tests. Patients with Korsakoff's syndrome were impaired on both tests relative to the alcoholic control group (verbal test: Korsakoff group mean = 29,0; alcoholic group mean = 41.7, range = 33–49; $t(11) = 2.1, p$
to detect amnesia in some cases because it does not include the left diencephalic locus of his lesion. We administered the same test to him, twice in 1976, and again in 1986. His first scores in 1976 were 17 (verbal) and 45 (nonverbal). However, 1 week later he obtained scores of 43 (verbal) and 45 (nonverbal), using an alternate form. His scores in 1986, using the original form, were similar to his second set of scores (20-44). However, the third patient (LM) performed quite well: a score of 50 on the verbal test and a score of 31 on the nonverbal test.

Patient N.A. was given this test originally in 1964 by Teuber, Milner, and Vaughan (1968). He obtained scores of 20 (verbal) and 30 (nonverbal) at that time, a finding consistent with the left diencephalic locus of his lesion. We administered the same test to him, twice in 1976, and again in 1986. His first scores in 1976 were 17 (verbal) and 45 (nonverbal). However, 1 week later he obtained scores of 43 (verbal) and 45 (nonverbal), using an alternate form. His scores in 1986, using the original form, were similar to his second set of scores in 1976: 41 (verbal) and 44 (nonverbal). N.A. is a bright individual and a sophisticated test subject. This test may fail to detect amnesia in some cases because it does not incorporate a long delay, and because the critical items are repeated several times.

The Boston Naming Test

All patients scored well on the Boston Naming Test, in which subjects supplied the names for line drawings of 72 objects. The test included uncommon objects such as stethoscope, protractor, and trellis. The 6 patients with Korsakoff's syndrome averaged 90.2% correct, the 3 A-I patients averaged 90.3%, and N.A. obtained a perfect score. We also gave this test to a group of 7 normal control subjects (mean age = 55.7 years, mean education = 11.4 years), and they averaged 89.5% correct. The lowest score was 85% correct (a Korsakoff patient).

Finally, we administered the Boston Naming Test to a group of 7 patients prescribed bilateral ECT (4 women and 3 men; mean age = 42.7 years; mean education = 14.4 years). Half of the test (36 items) was given 6 to 8 hr after the fourth, fifth, or sixth bilateral treatment (mean = 5.0), and the other half was given on average 3.6 months after the completion of treatment (range = 2-6 months). The ECT patients averaged 90.9% correct (range = 75%-100%) at the first test session, given during the course of ECT, and 92.1% (range = 86%-97%) at the time of the second, follow-up test.

Dementia Rating Scale

Figure 5 shows the results for the amnesic patients and the alcoholic control group on each subscale of the Dementia Rating Scale (Coblentz et al., 1973). Although there was an overall difference in the dementia score for the amnesic patients in comparison with the alcoholic subjects (amnesic patients = 132.5, alcoholic subjects = 139.1), t(15) = 2.57, p < .05, this difference could be attributed mainly to the memory subscale. Every alcoholic subject scored 100% on the memory part of the test, whereas the 6 patients with Korsakoff's syndrome averaged 75% and the 4 other cases averaged 79%. When the memory subscale score was subtracted from the total Dementia Rating Scale score, the patients with Korsakoff's syndrome averaged 111.5 points (range = 108-118), the four cases averaged 116.2 points (AB = 115, LM = 118, GD = 116, NA = 116), and the alcoholic subjects averaged 114.1 points (range = 106-118). Examination of the subscales other than memory showed that patients with Korsakoff's syndrome, but not the other four other cases, had an impaired score on the initiation and perseveration subscale in comparison with the 4 other amnesic cases, t(8) = 3.0, p < .05, and also in comparison with alcoholic subjects, t(11) = 4.3, p < .01. This subscale assessed word fluency (e.g., "name all the things that a person can buy in a supermarket") and perseveration (e.g., the ability to perform a series of alternating movements). All amnesic patients exhibited good performance on the other components of the test—attention, construction, and conceptualization.

Discussion

This article considers the problem of how best to assess the severity and selectiveness of memory impairment in amnesic study patients. Ten amnesic patients (6 with Korsakoff's syndrome, 3 with amnesia due to anoxia or ischemia, and case N.A.) were evaluated with several cognitive tests: a test of general intellectual capacity (IQ); a standardized test of memory functions (WMS), six specialized neuropsychological tests of memory functions, the Boston Naming Test, and the Dementia Rating Scale. Most of these tests were also given to patients who were amnesic following bilateral electroconvulsive therapy.
The severity of memory impairment can be adequately described by using a combination of neuropsychological tests that have a wide range of difficulty. Despite its shortcomings, the WMS is one useful test for this purpose. It is already widely used, and when given in conjunction with the WAIS, it can facilitate comparisons across study populations. (The revised WAIS-R is now available, but not yet a revised WMS. The WAIS-R–WMS difference score can be expected to be 7 to 8 points lower than the WAIS–WMS difference score.) In the present study, the WAIS–WMS difference scores were useful in suggesting that patients prescribed ECT, and tested at 2 to 8 hr after treatment, exhibit memory impairment comparable to the impairment exhibited by the other amnestic study patients. However, the WMS score is affected by cognitive dysfunction other than amnesia. Accordingly, additional tests are needed to rate the severity of memory impairment reliably.

Tests of delayed recall and the paired-associate learning test are quite sensitive to amnesia. All of the amnesic patients scored close to zero on these tests (see Figure 1). This finding shows that their memory impairment is rather severe; that is, almost no recall of recently encountered material was possible. The tests are easy to administer, and they can play a useful role in a memory assessment test battery. At the same time, these tests provide little information about the relative severity of amnesia in the different patient groups. The tests are simply too difficult to discriminate among different patients, if differences do in fact exist. The usefulness of such tests is in demonstrating that amnesia reaches a particular level of severity, not in establishing exactly how much amnesia is present.

The Auditory-Verbal Learning Test (Rey, 1964) appears to be well suited for establishing the level of impairment (see Figure 2). Performance was poor during the early trials of the recall test and rather good during the later trials of the recognition test. Thus learning ability could be effectively sampled across a wide range. Moreover, testing each patient across several trials increased the reliability of the measure. This test, but not the more difficult recall tests (see Figure 1), permitted some discrimination between groups. Thus, patients prescribed ECT performed better than did patients with Korsakoff’s syndrome. There was no indication, as some have suggested (Hirst et al., 1986), that recognition memory is disproportionately spared in amnesia in relation to recall.

In contrast to the verbal learning test, the Recognition Test for Words and Faces (Warrington, 1984) provides only one score for each kind of material. Nearly all the patients were capable of some learning (i.e., with one exception, they scored above the chance level of 25), but none of them obtained the maximum score of 50. Indeed, there was considerable variability in the performance of all subjects, amnesics, and controls alike, especially on the faces test. One source of this variability may have been the test instructions (see the Method section), which did not emphasize that memory would later be tested. There is mention of a memory test, but then the rating task that will be used during item presentation is explained. We would recommend that the instructions be altered so that the specific memory requirements of the test are explained and emphasized. Despite the variability in our sample, the average scores for our control subjects were within one standard deviation of Warrington’s (1984) age-matched normalization sample.

Some amnesic patients performed well on one or both parts of the words and faces test. Patient K1 performed well on words, patient K5 performed well on faces, and patient LM performed well on both words and faces. One possibility is that when retention is assessed immediately after learning, attention and intelligence are able to play a large role. The 1-day delay test seemed to identify memory impairment more consistently in our sample. For example, patient LM performed normally on the immediate test but was noticeably impaired on the verbal test at the 24-hr delay, scoring outside the range of the control group.

One advantage of this test is that it is relatively easy, in comparison with recall tests, and that it spreads out the scores and potentially discriminates among different groups. In the present study, the patients with Korsakoff’s syndrome consistently performed more poorly than the other groups, though the differences did not reach significance. Another advantage is that the test assesses both verbal and nonverbal memory. This permits comparisons between memory functions subserved by the left and right cerebral hemispheres, respectively. In the present case, the discrepancy between the words and faces scores raised the possibility that the lesions in amnesic study patients need not be bilaterally symmetrical.

The continuous recognition test was the least sensitive to memory impairment. Patients K2, K3, LM, and NA performed normally on the verbal test, and LM and NA performed normally on the nonverbal test. In this test, long delay intervals are not interposed between learning and retention, and the items are repeated several times. It is interesting to note that some of the patients performed so well on these recognition tests that they might have been considered to have intact memory functions. However, the delayed recognition tests (see Figures 3 and 4) and especially the recall tests (see Figures 1 and 2) brought out a clear impairment in the same patients. Moreover, it should be emphasized that all of the amnesic patients were either living in supervised facilities or had family available to assist them, and none of them was working or engaged in significant independent activity. Quantitative data from the tests described here can help determine the severity of amnesia as well as provide a basis for comparing different study populations. On the grounds that WMS scores in study populations are typically less than two standard deviations below IQ scores (i.e., an IQ-WMS difference of 15–30 points), Weiskrantz (1985) concluded that most study patients described in the literature are not severely amnesic, and not as severely impaired as his own study patients. However, assessment of his patients, which placed them more than two standard deviations below the norm, was not based on WMS scores but on a newly developed memory test battery (no WMS scores were presented). The present findings also show that when memory tests other than the WMS are used, amnesic study patients can score more than two standard deviations below normal (see Figure 1).

Yet, an appropriate comparison of the severity of memory impairment between patient groups requires that performance
be assessed with the same tests. Findings with the words and faces test provide one basis for comparing our study patients directly with patients studied by Weiskrantz, because scores on this test for nine British patients were provided by Warrington and Weiskrantz (1978). The British patients scored lower than the patients described here (average score for words: 28.3; average score for faces: 28.9; cf. Table 2). Such comparisons of the severity of amnesia are essential to the process of cumulative neuropsychological research on memory.

The other kind of information that is needed is information about the selectivity of memory impairment. The selectivity of memory impairment in our patients was evaluated by a test of general intellectual capacity (WAIS and WAIS-R), the Boston Naming Test, and the Dementia Rating Scale. All of the amnesic patients had IQs in the normal range, normal Boston Naming Test scores, and normal Dementia Rating Scale scores (except for the memory subscale). All of these tests are known to be sensitive to cognitive dysfunction, and they appear to be of value in assessing the selectiveness of memory impairment in amnesic patients.

Consider two separate observations regarding the Dementia Rating Scale. First, the Scale can detect cognitive impairment in patients with Alzheimer's disease who might otherwise seem suitable for studies of amnesia. In a recent study, 8 patients with clinical diagnoses of mild to moderate Alzheimer's disease had an average Dementia Rating Scale score of 118 (Shimamura, Salmon, Squire, & Butters, in press), which was significantly lower than the 130.2 score of the patients with Korsakoff's syndrome, $t(12) = 2.57, p < .05$. Even when the memory subscale score was subtracted from the total score, the average score of the patients with Alzheimer's disease was lower (104.4 vs. 111.5), $t(12) = 2.82, p < .05$. Yet on independent tests these patients had a memory problem no more severe than that of the Korsakoff patients. The point is that one might show that a group of patients are impaired on certain memory tests to the same degree as a group of amnesic study patients. Yet these same patients may exhibit widespread cognitive deficits (e.g., deficits in perception and attention) that would be expected to influence performance on many memory tests.

A second observation about the Dementia Rating Scale is that it can demonstrate differences even within amnesic groups who are not demented. Thus the patients with Korsakoff's syndrome, but not the other amnesic patients, exhibited impaired scores on the initiation and perseveration subscale of the Dementia Rating Scale. This finding is consistent with a growing body of data that Korsakoff patients have cognitive deficits not shared by all amnesic patients (Moscovitch, 1982; Squire, 1982; Shimamura & Squire, 1986a, 1986b). In this regard, it is worth emphasizing that Korsakoff's disease is a heterogeneous syndrome of amnesia (Lishman, 1981). In our original survey to identify amnesic study patients in 1979, we screened more than 20 patients who carried the diagnosis of Korsakoff's syndrome, but identified only 8 who had both a severe and selective memory impairment. In addition to having an IQ score in the normal range, we have always required that patients be able to draw a cube and a house in perspective. This requirement provides a simple and sensitive measure of constructional ability. However, even these tests are insufficient to identify all patients who have significant cognitive impairment in addition to amnesia. Recently, we evaluated a patient with Korsakoff's syndrome who had an IQ score of 103, a WMS score of 69, recall and recognition scores (Rey test) of 24% and 63%, respectively, and words and faces scores of 22 and 19, respectively. He could also draw in perspective. However, this individual scored only 68% on the Boston Naming Test and only 115 on the Dementia Rating Scale. When memory test scores are unusually poor, one should be especially alert to the possible presence of cognitive deficits in addition to amnesia. Presumably, if the neurological condition causing amnesia was extreme, it is more likely that additional neural damage had occurred. At the same time, amnesia can certainly be both selective and very severe (e.g., surgical patient H. M.: Milner, 1972).

The data presented here suggest some useful guidelines for characterizing amnesic patients. First, for assessing the severity of impairment, the WMS and the recall tests (see Figure 1) are useful. The auditory-verbal test (see Figure 2) is excellent, because it obtains repeated scores and tracks performance over a wide range of ability. The recognition test (see Figures 3 and 4 and Table 2) appears to be too easy to identify every memory-impaired patient who is suitable for neuropsychological study. However, the test could be made more difficult simply by measuring retention after a 1-day delay instead of immediately after learning.

For assessing the selectiveness of memory impairment, the IQ, Dementia Rating Scale, and Boston Naming Tests are all useful. However, the task of determining whether cognitive deficits are present other than amnesia is not simple, and the issue cannot be conclusively settled with just three tests. For example, because signs of frontal lobe dysfunction have been noted in some patients with amnesia (Schacter, Harbluk, & McLachlan, 1984; Squire, 1982), tests sensitive to frontal lobe dysfunction would be useful addition to neuropsychological screening procedures.

Studies of human amnesia have had a long tradition of contributing to our understanding of how normal memory is organized. As hypotheses about the structure of cognition become more sophisticated and more specific, neuropsychological work necessarily comes to depend more heavily on specialized tests that can measure particular aspects of memory function. If published work is to be fully evaluated, and extended in other laboratories with different patient populations, it is critical that each patient population under study be thoroughly characterized. Neuropsychological data, which characterizes both the severity and the selectiveness of memory impairment, should be included routinely in the Subjects section of all experimental articles on human amnesia. We recommend as a minimum list of tests the WAIS-R (or WAIS), WMS, paired-associate learning, delayed story recall, delayed recall of a complex design, the Rey Auditory-Verbal Learning Test, and the Dementia Rating Scale. The words and faces test and the Boston Naming Test would also provide useful information.


Received June 11, 1986