

Korsakoff's Syndrome: A Study of the Relation Between Anterograde Amnesia and Remote Memory Impairment

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Patients with Korsakoff's syndrome were evaluated with nine tests of new learning ability and three tests of remote memory to determine the correlation between anterograde amnesia and remote memory impairment. There was no correlation between the severity of anterograde amnesia and either the overall severity of remote memory impairment (1940s-1970s) or the impairment observed for more remote time periods (1940s-1950s). However, the correlation between remote memory impairment and anterograde amnesia became progressively stronger with the recency of the time period and was significant for the 1960s-1970s or the 1970s alone. The results support the view that the extensive remote memory impairment in Korsakoff's syndrome is, at least in part, distinct from and unrelated to anterograde amnesia. The more severe impairment observed for more recent time periods could be related to anterograde amnesia in that it reflects anterograde amnesia that was either already in place or progressively developing during recent years. The ability to recall very remote events seems therefore to depend on brain mechanisms distinct from those required for new learning or for recall of more recent events.

Studies of human memory pathology have revealed useful information about the structure and organization of normal memory (Baddeley, 1982; Cermak, 1982; Hirst, 1982; Squire & Butters, 1984; Squire & Cohen, 1984). The best-studied example of memory pathology is alcoholic Korsakoff's syndrome, which develops after years of alcohol abuse and is characterized by symmetrical lesions along the walls of the third and fourth ventricles (Butters, 1984; Butters & Cermak, 1980; Mair, Warrington, & Weiskrantz, 1979; Talland, 1965; Victor, Adams, & Collins, 1971). The memory impairment associated with Korsakoff's syndrome includes severe anterograde amnesia (impaired learning ability) and a severe and extensive retrograde amnesia (impairment of remote memory). The remote memory deficit spans several decades, and it is usually more severe for more recent time periods—the most recent decade or two—than for more remote time periods (Albert, Butters, & Levin, 1979; Cohen & Squire, 1981; Meudell, Northern, Snowden, & Neary, 1980).

The basis of the memory deficit observed in patients with Korsakoff's syndrome would be illuminated by a better un-

derstanding of the relation between anterograde and retrograde amnesia. One view has been that remote memory impairment reflects cognitive impairment distinct from and in addition to the impairment that underlies anterograde amnesia (Albert et al., 1979; Cohen & Squire, 1981). That is to say, remote memory impairment could involve damage to brain systems in addition to the damage that affects new learning. In this way the extensive remote memory impairment would be largely unrelated to anterograde amnesia. The greater severity of remote memory impairment for recent time periods could then be due to the fact that anterograde amnesia was either already present at that time or was developing.

At least three pieces of evidence are consistent with this view: (a) The remote memory impairment associated with Korsakoff's syndrome can be more severe and extensive than in other groups of amnesic patients, even though the severity of anterograde amnesia compared across these groups of patients is similar (Butters, Miliotis, Albert, & Sax, 1984; Cohen & Squire, 1981); (b) patients with Korsakoff's syndrome exhibit cognitive deficits that are unique to this form of amnesia and that can be dissociated from the deficit in new learning ability (Moscovitch, 1982; Shimamura & Squire, in press; Squire, 1982a); and (c) alcoholic patients who exhibit mild impairment on tests of new learning also exhibit impairment on tests of memory about events that occurred in recent years, but they do not exhibit impairment across all the decades of remote memory tests (Albert et al., 1979; Cohen & Squire, 1981; Ryan, Butters, & Montgomery, 1980).

An alternative view has been that Korsakoff's syndrome involves a single cognitive deficit that impairs both encoding and retrieval (Jacoby, 1984; Kinsbourne & Winocur, 1980;

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Weiskrantz, 1985); that is, the brain regions damaged in patients with Korsakoff's syndrome impair a common process, which affects the encoding and retrieval of new memories as well as the retrieval of premorbid memories. By this account, impaired learning ability and remote memory loss are caused by the same deficit, and the severity of impaired learning should always be correlated with the severity of remote memory impairment.

These two hypotheses about the relation between anterograde amnesia and remote memory impairment in Korsakoff's syndrome make different predictions about whether measures of new learning ability and measures of remote memory should be correlated. According to the first hypothesis, the two measures should not be correlated, although a positive correlation might be found between new learning ability and memory for events that have occurred since the diagnosis of the disease or during the years of alcohol abuse preceding diagnosis. According to the second hypothesis, the severity of anterograde amnesia and remote memory impairment are linked, and therefore the correlation between the two measures should be positive.

During the past several years, we have administered to our standing population of 8 patients with Korsakoff's syndrome a variety of tests of remote memory and new learning ability. Continuous neuropsychological assessment of this group has made it possible to examine the relation between scores on different tests. The patients were ranked according to their performance on nine tests of new learning ability and three tests of remote memory, and a series of correlation analyses was conducted. In this way, we evaluated the relation between anterograde amnesia and remote memory impairment in a single group of patients.

Method

Subjects

Eight patients with alcoholic Korsakoff's syndrome participated in this study. Testing occurred between 1979 and 1982. This group of 5 men and 3 women averaged 53.8 years of age (in 1982), with an average of 12.4 years of education. Mean full-scale Wechsler Adult Intelligence Scale (WAIS) IQ was 102.6 (range = 91–114). Their average Wechsler Memory Scale (WMS) score was 78 (range = 64–93), and all patients had at least a 15-point difference between their WAIS-IQ and WMS scores. All patients could draw a cube and a house in perspective, and none had aphasia or apraxia. Independent neurological examination confirmed that amnesia was the only notable deficit of higher function. Seven of these patients were included in previous studies of Korsakoff's syndrome (Cohen & Squire, 1981; Graf, Squire, & Mandler, 1984; Squire, 1981, 1982a; Wetzel & Squire, 1982).

Data from previously studied alcoholic control subjects ($n = 6$ –12) were used to illustrate the severity of the anterograde amnesia and remote memory impairment exhibited in patients with Korsakoff's syndrome. A total of 12 tests of anterograde amnesia and remote memory impairment were used to compare control subjects with the patients. The alcoholic control subjects were matched on age, level of education, and intelligence as measured by scores on the information and vocabulary subtests of the WAIS. All of these alcoholic subjects had been free of alcohol for at least 2 weeks. For three tests,

alcoholic control data were not available, and we report instead control data from depressed patients.

Tests of New Learning Ability

Nine tests of new learning ability were administered to each patient. These nine tests included most of the tests of anterograde amnesia employed in our laboratory in the past several years, and except for one test (Test 9, Word Recognition), they have all been described in detail previously (see citations for each test).

1. *Prose Recall.* Subjects were read short prose passages, each containing 19–22 segments. For each passage, recall was tested immediately and 12 min after presentation. Subjects were tested on three separate occasions, with different passages (Squire & Slater, 1978).

2. *Cued Word Recall.* Subjects were read a list of 36 words twice in succession at a rate of 1 word/s. Then the subjects were tested by yes/no recognition, by two-alternative forced-choice recognition, or by cueing with the first three letters of each word (Squire, Wetzel, & Slater, 1978).

3. *Memory for Complex Design.* Subjects copied a complex geometric design and were asked to reproduce it from memory after a 12-min delay. Subjects were tested on three different occasions, with different designs (Squire & Chace, 1975).

4. *Picture Recognition.* Subjects were shown 120 pictures on colored slides taken from magazines, at a rate of 8 s/picture. After a 10-min delay, a yes/no recognition test was given for 40 of these pictures and for 40 new pictures (Squire, 1981).

5. *Sentence Recognition.* Subjects studied a list of 12 sentences, waited 3 min, and then were presented a new list of 12 sentences. After a delay (10 s to 90 min), subjects were given a yes/no recognition test for the 24 sentences and for 24 new sentences (Squire, 1982a).

6. *Incidental Learning.* Subjects were presented 60 words for 5 s each and were asked (a) whether the word was printed in upper- or lowercase, (b) whether the word rhymed with a given word, or (c) whether the word belonged to a given category. One minute after presentation, subjects were given a yes/no recognition test for the 60 words and for 120 new words. Recognition scores were corrected for response guessing bias by the following equation: $pC = (pH - pFA) / (1 - pFA)$, where pC is the corrected score, pH is the proportion of hits, and pFA is the proportion of false alarms (Squire, 1982a).

7. *Recall of Word Triads.* On each of four trials, subjects were shown three words for 2 s, distracted for 15 s, and then asked to recall the words. Trials were separated by 10 s. Subjects were given eight separate administrations of this test (Squire, 1982a).

8. *32-Item Recognition.* This test consisted of 32 items (8 pictures of common objects, 8 photographs of faces, 8 nonsense line drawings, and 8 common words). These items were presented at a rate of 3 s per item. For each set of stimuli, three-alternative forced-choice recognition was assessed 10–12 min later (Squire & Chace, 1975).

9. *Word Recognition Test.* Two different lists of 12 common words were presented at a rate of 2 s per word. Ten minutes after learning, retention was tested by a four-alternative forced-choice recognition test. The score was the proportion of words correct out of 24.

Tests of Remote Memory

The three tests of remote memory allowed assessment of memory for (a) famous faces, (b) public events, and (c) former one-season television programs. In the test of famous faces (Albert et al. 1979; Cohen & Squire, 1981), subjects saw 105 photographs of people who became prominent during a particular decade from the 1940s to the

1970s. Subjects were asked to identify the faces first in an uncued condition and then in a cued condition. In the uncued condition, subjects were asked to produce each person's name from the photograph alone. In the cued condition, subjects were given a name and judged whether the name matched a given face, or they were given three names and were asked to choose the correct name. The type of cue (yes/no or multiple choice) was alternated for the photographs that belonged to each decade. The cued condition was given only for those photographs that could not be identified in the uncued condition.

In the test of past public events (Cohen & Squire, 1981), subjects were questioned about 88 events that had occurred during one of the four decades from 1940 to 1979. Three subtests were used: (a) a four-alternative multiple-choice test, (b) a recall test that required a single word or phrase about each past event, and (c) a detailed recall test that required subjects to recall everything they could remember about each event. The score for the latter test was the number of details recalled per 27 questions (there were 27 questions for the 1970s).

The test of past television programs (Squire & Fox, 1980; Squire & Slater, 1975) sampled memory for 74 television programs that were broadcast for a single season between 1963 and 1977 (approximately five programs for each year). Two subtests were used: (a) a four-alternative multiple-choice test that required subjects to select real program titles from fictional titles and (b) a detailed recall test (Squire & Cohen, 1984) that required subjects to recall everything they could remember about each program.

Results

For 7 of the 8 patients in the present study, data from five tests of new learning ability (Tests 1, 4, 5, 6, 7) and all three tests of remote memory have been presented in previous reports (Cohen & Squire, 1981; Squire, 1981, 1982a; Squire, Wetzel, & Slater, 1978). The focus of this article was the assessment of the relation between the severity of anterograde amnesia and the severity of remote memory impairment. The scores on each separate test are considered first, only to illustrate the severity of amnesia associated with Korsakoff's syndrome. The 8 patients with Korsakoff's syndrome exhibited severe impairment on all nine tests of new learning (see Table 1). Furthermore, on all the tests of remote memory there was significant memory impairment across all time periods (see Table 2), as reported previously for these patients (Cohen & Squire, 1981). In addition, memory for more recent time periods (i.e., 1960s–1970s) was more impaired than memory for more remote time periods (i.e., 1940s–1950s).

The correlation analyses described next were conducted with the data from the amnesic patients, not with the data from control subjects. The question under study concerned the relation between impaired new learning and impaired remote memory, not the pattern of normal performance. We ranked the 8 patients with Korsakoff's syndrome according to their scores on each of the nine tests of new learning ability and on each of the three tests of remote memory. Thus, for the tests of anterograde amnesia, we obtained nine independent rankings of the patients. For the three tests of remote memory, three different and independent rankings were also derived by calculating an average ranking on the subtests of each remote memory test: one ranking for the faces test derived from two subtests, one for public events derived from

Table 1
Performance on Tests of New Learning Capacity

Test	Korsakoff patients (<i>n</i> = 8)	Alcoholic control subjects (<i>n</i> = 6–12)
Paragraph Recall (segments recalled after 12-min delay)	0.25	4.8
Cued Word Recall (36 words; corrected for guessing)	10.1	17.0 ^a
Memory for Complex Designs (features recalled after 12-min delay)	5.1	17.3
Picture Recognition (exposure time needed for 75% correct)	8.0 s	1.0 s
Sentence Recognition (24 sentences; yes/no recognition)	74%	83% ^a
Incidental Learning (60 words; recognition with guessing correction)	18%	31%
Recall of Word Triads (recall after 15-s distraction)	24%	55%
32-Item Recognition	41%	87% ^a
Word Recognition (12 words; 4-choice)	33%	94%

^a Nonalcoholic control subjects.

three subtests, and one for TV programs derived from two subtests.

We first assessed separately the relation among the nine tests of new learning and the relation among the three tests of remote memory. For the nine measures of anterograde amnesia, Kendall's coefficient of concordance (*W*) was significant (*W* = .307, *p* < .01). Thus, despite the fact that the nine tests involved different materials and testing methods,

Table 2
Performance on Tests of Remote Memory

Test	1970s	1960s	1950s	1940s
Famous faces				
Without cues				
Korsakoff patients	.15	.26	.32	.41
Alcoholic controls	.41	.38	.44	.56
With cues				
Korsakoff patients	.63	.70	.77	.84
Alcoholic controls	.81	.83	.86	.90
Public events				
Recognition				
Korsakoff patients	.46	.58	.58	.59
Alcoholic controls	.70	.77	.70	.77
Simple recall				
Korsakoff patients	.07	.15	.33	.18
Alcoholic controls	.37	.46	.49	.44
Detailed recall				
Korsakoff patients	8.4	11.7	11.3	14.1
Alcoholic controls	44.4	42.4	30.1	46.2
Television				
Recognition				
Korsakoff patients	.33	.40	—	—
Alcoholic controls	.45	.45	—	—
Detailed recall				
Korsakoff patients	1.0	.5	—	—
Alcoholic controls	4.4	2.7	—	—

Note. Data are expressed as percentages except for detailed recall, which are the number of details.

the impairment in new learning exhibited by the patients is a global one that to some degree reflects a similar impairment on each test. A coefficient of concordance was also calculated for the three tests of remote memory. The concordance ($W = .694, p < .05$) indicated a significant association among the three measures of remote memory.

Next we determined whether the severity of anterograde amnesia was related to the severity of remote memory impairment. One way to assess this relation would have been to apply multivariate analyses to the data (e.g., confirmatory factor analysis). Unfortunately, the small number of amnesic patients ($n = 8$) precluded this approach. Instead, we calculated Spearman nonparametric correlations between the rankings of patients on each of the nine tests of anterograde amnesia and each of the three tests of remote memory impairment. In this way we obtained 27 independent rank order correlations. The median score of these 27 correlations was .04 (14/27 positive correlations). The number of positive correlations was not significantly above chance as indicated by a binomial (sign) test. Thus, the extent of anterograde amnesia was not correlated with the extent of overall remote memory impairment.

Next, we determined the relation between anterograde amnesia and memory for the four decades 1940–1979. It has been suggested previously that memory impairment for more recent time periods reflects anterograde amnesia rather than retrograde amnesia (Albert et al., 1979; Cohen & Squire, 1981). We therefore ranked the subjects on remote memory performance separately for each of four 10-year time periods (1940s, 1950s, 1960s, and 1970s). Because the test of TV programs was restricted to items from 1963 to 1977, that test was excluded from this analysis. For each decade we calculated Spearman correlations between the rankings of patients on each of the nine independent measures of anterograde amnesia and each of the two independent measures of remote memory. Table 3 shows the median correlation of these 18 independent correlations (nine tests of anterograde amnesia \times two tests of remote memory) calculated separately for each decade. The correlations were highest for the most recent decade (1970s, median $r_s = .36$, 14/18 positive correlations, $p = .015$), and they became progressively lower for more remote decades. The results were the same when the test of TV programs was included in the analysis thus giving nine additional correlations for the 1970s and 1960s (nine tests of anterograde amnesia \times one test of remote memory). With the TV test scores included, the median correlation between anterograde amnesia and remote memory test performance was .35 for the 1970s ($p = .01$), and it was .15 for the 1960s ($p = .06$).

Table 3
Median Correlations Between Nine Tests of Anterograde Amnesia and Two Tests of Remote Memory Impairment Across Four Decades

Measure	1970s	1960s	1950s	1940s
Median r_s	.36	.16	.02	-.09
Proportion of positive correlations	14/18*	12/18	9/18	9/18

* $p = .015$.

It is also noteworthy that the correlation between anterograde amnesia and remote memory performance for recent time periods remained significant when the rankings were based on the combined performance for the 1960s and the 1970s (median $r_s = .30, p = .015$, 14/18 positive correlations). Moreover, when the correlations between each of the nine anterograde amnesia tests and the TV test were included, there was a median correlation of .28 between anterograde amnesia and overall remote memory performance for the 1960s and the 1970s (21/27 positive correlations, $p < .01$). Despite the significant relation between anterograde amnesia and remote memory performance for the 1970s as well as for the 1960s–1970s, this relation was not apparent when the earlier time periods (1940s–1950s) were considered (Figure 1). The median correlation between the tests of anterograde amnesia and overall remote memory performance for the 1940s and 1950s was $-.06$.

To substantiate further the correlational analyses, we also calculated a Mann-Whitney U test to compare the 18 independent correlations obtained between anterograde amnesia and remote memory for the 1960s–1970s with the 18 independent correlations obtained between anterograde amnesia and remote memory for the 1940s–1950s. These sets of correlations were significantly different from each other, $U(18, 18) = 92.5, p < .02$. Thus, the relation between anterograde amnesia and memory for recent time periods is different from the relation between anterograde amnesia and memory for more remote time periods. These data strengthen the conclusion that the remote memory impairment for recent time periods is related to the severity of anterograde amnesia whereas the remote memory impairment as reflected by scores for more remote time periods (i.e., the 1940s–1950s) is unrelated to anterograde amnesia.

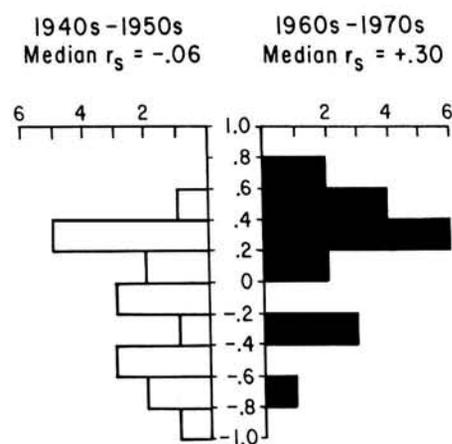


Figure 1. Two frequency distributions of 18 independent correlations computed between the ranks on nine tests of new learning ability and two tests of remote memory. (The left distribution [white bars] shows the correlations for the portion of the remote memory tests that sampled from the period 1940–1959 [8/18 positive correlations]. The right distribution [black bars] shows the correlations for the portion of the remote memory tests that sampled from the period 1960–1979 [14/18 positive correlations]. Thus, new learning ability was correlated with remote memory performance for the 1960s and 1970s, but not for the 1940s and 1950s.)

Discussion

When each decade was considered alone, the correlation between anterograde amnesia and remote memory impairment became progressively stronger with the recency of the time period. Also, there was no correlation when remote memory was measured only by performance on the more remote decades (1940s–1950s). However, a positive correlation was found between the severity of anterograde amnesia and the severity of impairment on the recent decades (the 1960s and 1970s, or the 1970s alone).

These findings are not consistent with the view that a single cognitive deficit causes both anterograde amnesia and extensive impairment in remote memory. If a single cognitive deficit were present, the severity of anterograde amnesia and the severity of remote memory impairment should always be correlated. Instead, the findings are consistent with the view that remote memory impairment in patients with Korsakoff's syndrome is due in part to retrograde amnesia and in part to anterograde amnesia (Albert et al., 1979; Cohen & Squire, 1981). In particular, the results demonstrate that retrograde amnesia is a separate deficit, one that is not inevitably predicted by the severity of anterograde amnesia.

One might suppose that failure to find significant correlations between remote memory impairment and anterograde amnesia is an artifact of differences in the methods used to assess remote memory and new learning capacity. Remote memory tests require subjects to retrieve information learned years ago and acquired incidentally as a part of daily living. By contrast, the tests of anterograde amnesia used here require subjects to attend to and encode new information presented under controlled laboratory conditions. Despite these differences, however, a significant correlation was found between the severity of anterograde amnesia and the severity of remote memory loss for the two recent decades. Accordingly, differences in testing methods cannot account for the failure to find the same kind of correlation when the analyses included the more remote time periods.

The extensive remote memory impairment that is not correlated with anterograde amnesia might be due to cognitive deficits peculiar to Korsakoff's syndrome; for example, there have been reports of deficits in attention (Oscar-Berman, 1980), concept formation (Oscar-Berman, 1973; Squire, 1982b), metamemory (Shimamura & Squire, in press), and the ability to enact appropriate retrieval strategies (Cermak, Reale, & Baker, 1978; Zola-Morgan, Cohen, & Squire, 1983). Indeed, it was stated in some of the earliest reviews that Korsakoff's syndrome involves more than just an impairment of memory (Talland, 1965; Whitty & Zangwill, 1966). These deficits may contribute to the inability to reconstruct and retrieve memories about the remote past. Some of these cognitive deficits are known to be absent in other forms of amnesia and are therefore not obligatory to anterograde amnesia (Moscovitch, 1982; Squire, 1982a).

The additional deficits associated with Korsakoff's syndrome, including perhaps the deficit in remote memory, may be indicative of more widespread neuropathology than in other forms of amnesia. Patients with Korsakoff's syndrome typically have cortical atrophy and other brain damage beyond the diencephalic lesions that have been linked to am-

nesia (Lishman, 1981; Victor et al., 1971; but see Mair et al., 1979, for two cases of Korsakoff's syndrome in which the lesions seemed quite limited). Moreover, neuropsychological data have associated some of the cognitive deficits in Korsakoff's syndrome to frontal lobe dysfunction (Moscovitch, 1982; Squire, 1982a). Also, Jernigan (1984) reported that remote memory performance in aged subjects correlated with CT (computerized tomography) scan measures of cortical atrophy. These findings raise the possibility that cortical atrophy may contribute to the extensive remote memory impairment found in Korsakoff's syndrome. It should be emphasized that these conclusions about Korsakoff's syndrome should not be extended to other forms of amnesia—amnesia due to head injury (Russell & Nathan, 1946), amnesia following electroconvulsive therapy (Cohen & Squire, 1981), or amnesia following temporal lobe resection (Marslen-Wilson & Teuber, 1975; Milner, Corkin, & Teuber, 1968). In other kinds of amnesia, the state of remote memory may be different, and the relation between anterograde amnesia and retrograde amnesia is therefore a separate question (Squire & Cohen, 1984; Zola-Morgan & Squire, 1985).

In summary, the extensive and severe remote memory impairment associated with Korsakoff's syndrome is difficult to explain entirely by the severity of anterograde amnesia. Remote memory impairment seems to constitute, at least in part, a distinct and separate deficit from anterograde amnesia. However, impaired memory for recent time periods is correlated with impaired new learning ability, and this deficit may reflect the fact that anterograde amnesia was gradually developing due to alcohol abuse or was already present in those time periods. The results support the view that the ability to recall remote events depends on brain mechanisms distinct from those required for new learning and recall of recent events.

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