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MEMORY FOR THE TEMPORAL ORDER OF EVENTS IN PATIENTS WITH FRONTAL LOBE LESIONS AND AMNESIC PATIENTS

ARTHUR P. SHIMAMURA, JERI S. JANOWSKY and LARRY R. SQUIRE*

Veteran Administration Medical Center and Department of Psychiatry, University of California, San Diego, California, U.S.A.

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Abstract—Patients with frontal lobe lesions, amnesic patients with Korsakoff's syndrome, other (non-Korsakoff) amnesic patients, and control subjects were given tests of memory for temporal order. In the first experiment, subjects were presented with a list of 15 words and then asked to reproduce the list order from a random array of the words. In the second experiment, they were asked to arrange in chronological order a random display of 15 factual events that occurred between 1941 and 1985. In both experiments, patients with frontal lobe lesions were impaired in placing the items in the correct temporal order, despite normal item memory (i.e. normal recall and recognition memory for the words and facts). The two groups of amnesic patients exhibited impaired memory for temporal order as well as impaired item memory. Patients with Korsakoff's syndrome exhibited poorer temporal order memory than the other amnesic patients, despite similar levels of item memory. These findings demonstrate that patients with frontal lobe lesions have difficulty organizing information temporally. Patients with Korsakoff's syndrome, who have both diencephalic and frontal damage, have memory impairment together with a disproportionate deficit in memory for temporal order.

INTRODUCTION

STUDIES of patients with memory disorders have provided useful information about the organization and structure of normal memory functions [23, 34, 40, 48]. For example, studies of memory-impaired patients, as well as studies of normal subjects, have suggested that fact or event memory should be distinguished from memory for the temporal context in which facts or events have occurred [15, 27, 37, 39, 44, 45, 46]. Indeed, S. S. Korsakoff himself suggested such a distinction based on his clinical examination of patients with memory impairment: "In some cases the facts themselves are remembered, but not the time when they occurred" [19, p. 398]. More recent studies have confirmed this early clinical impression. For example, patients with Korsakoff's syndrome exhibited severe impairment on a test of temporal order memory—a test that asked subjects to judge which of two items had been presented more recently [10, 25, 39].

The deficit in temporal order memory exhibited by patients with Korsakoff's syndrome is out of proportion to their deficits in other aspects of memory. That is, patients with Korsakoff's syndrome—like other amnesic patients—are impaired on many standard tests of memory; yet they also have a disproportionately large impairment on tests of temporal order memory (e.g. recency judgements) [25, 39]. These findings have led some to suggest

*To whom correspondence should be addressed at: Department of Psychiatry (V116-A), Veterans Administration Medical Center, 3350 La Jolla Village Drive, San Diego, CA 92161, U.S.A.

that amnesia is a deficit of *episodic* or *contextual* memory [6, 9, 18, 24]. In other words, it has been suggested that amnesia specifically involves a deficit in the ability to establish memories within a personal spatial–temporal framework. Yet, other findings have suggested that the *disproportionate* deficit in temporal order memory is not observed in non-Korsakoff amnesic patients [39]. Thus, regardless of etiology, amnesic patients appear to have a memory deficit that affects many forms of memory (e.g. verbal, non-verbal, spatial, temporal order). However, for patients with Korsakoff's syndrome the deficit in temporal order memory may occur out of proportion to other memory deficits.

The disproportionate impairment in temporal order memory observed in patients with Korsakoff's syndrome may be the result of frontal lobe damage. Indeed, other neuropsychological findings suggest that frontal lobe damage can contribute to impaired memory for temporal order [17, 27, 28, 31]. Although patients with circumscribed frontal lobe lesions are not amnesic—as indicated by their good performance on standard neuropsychological tests of memory [13, 43], they can exhibit cognitive impairment that affects memory performance, such as impairment in problem-solving, metamemory, verbal fluency, category shifting, and cognitive estimation [13, 14, 28, 33, 38]. Moreover, in an unpublished study (Corsi, as cited by MILNER [27]), patients with frontal lobe lesions performed poorly on a test of recency judgements but were not impaired on a test of recognition memory for the items themselves. Finally, patients with Korsakoff's syndrome have frontal lobe atrophy, as demonstrated in recent quantitative radiological (CT) studies [12, 35]. Thus, damage to the diencephalic and medial temporal regions will cause amnesia and will impair temporal order memory along with other forms of memory. Damage to the frontal lobes may especially affect temporal order memory.

The purpose of the present study was to compare performance on tests of item memory with performance on tests of temporal order memory in patients with frontal lobe lesions, amnesic patients with Korsakoff's syndrome, and non-Korsakoff amnesic patients. To our knowledge, this is the first study in which these three patient groups have been tested together and given concurrent tests of temporal order and item memory. In the first experiment, temporal order memory was assessed by presenting a list of 15 words and asking subjects to reproduce the list order from a random array of the words. In the second experiment, subjects were asked to place in chronological order 15 public events that had occurred between 1941 and 1985. We also assessed recall and recognition memory performance for the words and facts themselves.

Three questions were of interest. First, do patients with frontal lobe lesions exhibit an impairment in memory for temporal order without a significant impairment of item memory? Although this issue has been addressed previously, conclusions have been based only on unpublished data. Second, does impairment of temporal order memory occur only for events that have been presented recently (i.e. several minutes, Experiment 1) or does it occur even for events that span many years (Experiment 2)? Finally, will patients with Korsakoff's syndrome exhibit greater impairment of temporal memory, compared with non-Korsakoff amnesic patients, despite similar levels of item memory?

EXPERIMENT 1—METHODS

Subjects

Patients with frontal lobe damage. Six patients with lesions of the frontal lobes were identified by a review of medical records and CT scans at the Veterans Administration Medical Center, San Diego, and at the University of California, San Diego Medical Center. The patients had lesions restricted to the frontal lobes and had no other diagnoses likely to affect cognition or interfere with participation in the study (e.g. significant psychiatric disease, alcoholism). Four patients had suffered cerebrovascular accidents, and the two other patients had surgical lesions. Of the six patients, four had unilateral frontal lobe lesions (2 left, 2 right) and two had bilateral lesions. The extent and location of the lesions within the frontal lobes were variable and thus finer analyses of regional specificity within the frontal lobes could not be evaluated.

These six patients (three men and three women) averaged 64.3 years of age, had 13.5 years of education, and an average Full Scale Wechsler Adult Intelligence Scale-Revised (WAIS-R) IQ score of 98.5. These patients were impaired on standard tests of frontal lobe dysfunction. For example, they were impaired on the Wisconsin Card Sort test [3, 8], a test that involves problem-solving and the ability to shift categories (number of categories achieved, mean = 2.2; percent of perseverative errors, mean = 46.8). In addition, they were impaired on the 37-point Initiation and Perseveration index of the Dementia Rating Scale [22], averaging 31.2 correct (84%). Finally, the patients with left and bilateral frontal lobe lesions (but not patients with right frontal lobe lesions) were impaired on the Verbal Fluency test ([2]; mean number of words produced by left and bilateral frontal patients = 21.5; right frontal patients = 39.0). Table 1 shows average scores and ranges for neuropsychological tests. Additional neuropsychological data for these patients, together with illustrations of the lesions, can be found in JANOWSKY *et al.* [13].

Table 1. Performance of Patient Groups on Neuropsychological Tests

Group	WAIS-R Full scale	WMS-R Delay	DRS Memory (%)	DRS Init/Pers (%)	WCST Categories
Frontal Patients	98.5 (85–118)	94.5 (80–119)	92 (84–100)	84 (70–97)	2.2 (0–5)
Korsakoff Patients	97.2 (88–106)	56.7 (50–72)	73 (44–92)	88 (78–97)	3.3 (0–5)
Amnesic Patients	109.2 (92–119)	55.0 (50–65)	75 (56–80)	98 (92–100)	5.4 (4–6)

Scores are group means. Ranges are shown in parentheses. WAIS-R = Wechsler Adult Intelligence Scale-Revised; WMS – R = Wechsler Memory Scale-Revised (Delay index); DRS = Dementia Rating Scale (Init/Pers = Initiation and Perseveration index); WCST = Wisconsin Card Sorting test.

The six patients peformed well on standard tests of memory. For example, average Wechsler Memory Scale-Revised (WMS-R) scores were as follows: Attention and Concentration, 83.3; Verbal Memory, 100.7; Visual Memory, 90.5; General Memory, 95.7; Delayed Memory 94.5. As with the WAIS-R IQ test, each of the five indices for the WMS-R yields a mean score of 100 in the normal population with an S.D. of 15 [4, 47]. The patients also scored well on other standard tests of memory. For example, free recall of a short prose passage was 6.2 segments for immediate recall and 4.8 segments for delayed (12 min) recall (total segments = 23). Paired-associate memory of 10 unrelated noun–noun pairs on each of three successive trials was 4.1, 7.2, and 8.3.

Healthy control subjects for patients with frontal lobe lesions. Eight subjects (5 men and 3 women) served as control subjects for the patients with frontal lobe lesions. They were matched to the study patients with respect to age (mean = 60.6 years) and education (mean = 14.3 years). They were also matched to the study patients on the basis of two WAIS-R subtest scores, Information (mean = 22.6; mean = 21.5 for the frontal patients) and Vocabulary (mean = 55.8; mean = 51.7 for the frontal patients). For these control subjects, free recall of a short prose passage was 6.8 segments for immediate recall and 5.9 segments for delayed (12 min) recall. Paired-associate memory of 10 unrelated noun–noun pairs on each of three successive trials was 5.7, 7.4, and 8.7.

Patients with Korsakoff's syndrome. We tested seven amnesic patients with Korsakoff's syndrome (5 men and 2 women) who have participated previously in other studies [13, 36, 41]. These seven patients averaged 57.7 years of age and 11.4 years of education. Their average WAIS-R Full Scale IQ score was 97.1, and their average index scores on the WMS-R were as follows: Attention and Concentration, 90.1; Verbal Memory, 70.6; Visual Memory, 75.1; General Memory, 66.1; Delayed Memory, 56.7. Free recall of a short prose passage was 5.0 segments for immediate recall and 0 segments for delayed (12 min) recall. Paired-associate memory of 10 unrelated noun–noun pairs on each of three successive trials was 0.4, 0.1, and 1.3. On the Wisconsin Card Sorting task, these patients averaged 3.3 categories, which is impaired relative to control subjects [13]. These patients also obtained an impaired score on the Initiation and Perservation index of the Dementia Rating Scale, averaging 32.6 (88%) (see [13]). However, these patients performed as well as control subjects on the Verbal Fluency test [13]. Table 1 summarizes the patient data for some of the neuropsychological tests mentioned above. Additional neuropsychological data for these patients can be found elsewhere [13, 42].

Other patients with amnesia. Five additional amnesic patients (4 men and 1 women) were tested. Three patients (A.B., G.D. and L.M.) became amnesic after an episode of anoxia or ischemia. Two other amnesic patients were also tested. W.H. became amnesic in 1986 without a known precipitating event. The amnesia occurred without head trauma or a known episode of unconsciousness and developed during a period of at most 3 days. Magnetic resonance (MR) scans have identified bilateral medial temporal pathology [30]. M.G. became amnesic in 1986 following a bilateral thalamic infarction, as confirmed by MR scan. As a group, the five patients averaged 55.8 years of age and had an average educational level of 15.6 years. Their average WAIS-R Full Scale IQ was 109.2. On the WMS-R, the average index scores were as follows: Attention and Concentration, 105.4; Verbal Memory, 77.8; Visual Memory, 81.2; General Memory, 73.0; Delayed Memory, 55.0. Free recall of a short prose passage was 6.0 segments for immediate recall and 0 segments for delayed (12 min) recall. Paired-associate memory of 10 unrelated noun–noun pairs on each of three successive trials was 1.0, 1.0, and 2.6. These patients performed well on the Wisconsin Card Sorting task (categories achieved = 5.4). They also performed well on the Initiation and Perseveration subtests of the DRS (average score = 36.2, 98%) and on the Verbal Fluency test [see 13]. Table 1 summarizes the patient data for some of the neuropsychological tests mentioned above. Additional neuropsychological data for these patients can be found elsewhere [13, 42].

Healthy control subjects for amnesic patients. Five men and 3 women served as control subjects for the 12 amnesic patients. These subjects averaged 53.6 years of age and had an average education level of 15.0 years. Their age closely matched the average age of all 12 amnesic patients, but the level of education was more closely matched to the five non-Korsakoff amnesic patients than to the seven patients with Korsakoff's syndrome. The control subjects were matched to the 12 amnesic study patients on the basis of two WAIS-R subtest scores, Information (mean = 21.6, mean = 19.7 for the amnesic patients) and Vocabulary (mean = 59.1; mean = 52.7 for the amnesic patients).

Procedure

Word Sequencing test. Fifteen common words were selected and printed individually on index cards. Each word had 1 or 2 syllables and had a frequency of occurrence of 20 or greater per million (mean = 158, range = 28–492; [20]). The 15 words were presented in random order at a rate of 3 sec per word, and subjects were instructed to read each word aloud and to try to remember the order in which the words appeared. Each subject was presented a different random order of the words. Immediately following the study phase, the experimenter arranged the words on a table in front of the subject in a random, two-dimensional array. A duplicate set of the word cards was used for this test in order to guarantee that the words were arranged randomly and that the subjects were not using any extraneous cues to facilitate performance (e.g. bent cards or stray markings). Subjects were instructed to place the words in the same sequence in which they had just been presented during the study phase—from the first word presented to the last. They were given as much time as needed to reconstruct the temporal sequence of the words. The ability to remember the sequential order of the words was assessed by calculating for each subject a Spearman rank order correlation between the actual study order and the judged order (perfect score = + 1.0). The possibility that short-term memory rehearsal could contribute to performance on this test was reduced by giving subjects instructions between the study and test phases. These instructions took about 15 sec to administer.

Word Recall and Recognition test. On a subsequent test day (average separation of test days = 18.4 days, range = 1–68 days), subjects were presented a different list of common words (1–2 syllables; word frequency per million = 117, range = 23 to 471; [20]) at a rate of 3 sec per word and instructed to read each word aloud and to try to remember the words. Immediately following word presentation, subjects were asked to recall the words from the list. After the free recall test, a yes/no recognition test was given. Performance was based on correct recognition for the 15 study words and 15 new words (i.e hits + correct rejections).

RESULTS AND DISCUSSION

Figure 1 shows the performance by control subjects and patients with frontal lobe lesions on the tests of word recall, word recognition, and word sequencing. The two groups did not differ significantly on the Word Recall test [t (12) = 1.2, $P > 0.2$], though patients with frontal lobe lesions did perform an average of 13% lower than control subjects. On the Word Recognition test, performance by the two groups was similar [t (12) = 1.3, $P > 0.2$]. Because none of the subjects performed perfectly on this test, the similarity in performance between patients with frontal lobe lesions and control subjects could not be attributed to a ceiling effect. On the word sequencing task, control subjects performed significantly better than patients with frontal lobe lesions (correlation measure: 0.62 vs 0.19; [t (12) = 3.1, $P < 0.01$]. Thus, patients with frontal lobe lesions had particular difficulty remembering the sequential order of the words in the list.

Figure 2 shows the performance on tests of Word Recall, Word Recognition, and Word

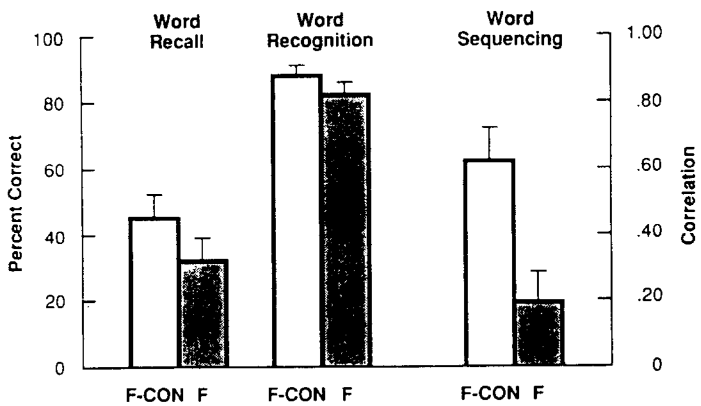

Fig. 1. Following the presentation of 15 words, subjects were asked to recall and recognize the words on the list or, on a different occasion, to reconstruct the order in which the words were presented. $F=6$ patients with frontal lobe lesions; F-CON = 8 control subjects for patients with frontal lobe lesions.

Sequencing by control subjects and two groups of amnesic patients (patients with Korsakoff's syndrome [KOR] and five other amnesic patients [AMN]). A one-way analysis of variance revealed a significant difference across groups for both Word Recall [$F(2, 17)=7.4$, $P<0.01$] and Word Recognition [$F(2, 17)=4.3$, $P<0.05$]. Comparisons between groups showed that both amnesic groups were impaired on the Recall and Recognition Memory tests ($ts>2.7$, $Ps<0.05$); but the two amnesic groups did not differ significantly from each other ($ts<0.4$).

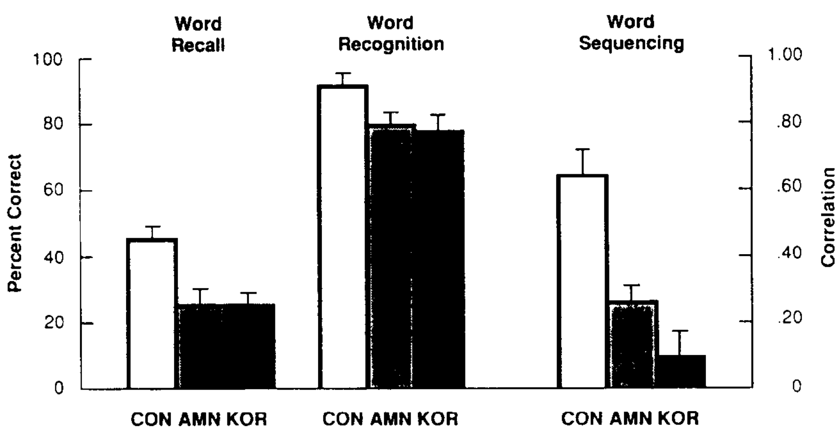

Fig. 2. Following the presentation of 15 words, subjects were asked to recall and recognize the words on the list or, on a different occasion, to reconstruct the order in which the words were presented. AMN = 5 amnesic patients; KOR = 7 amnesic patients with Korskoff's syndrome; CON = 8 control subjects.

On the word sequencing test, the average correlation for the control subjects was 0.64, and the average correlation for the patients with Korsakoff's syndrome and the other amnesic patients was 0.09 and 0.26, respectively. An ANOVA revealed a significant difference across groups [$F(2, 17)=15.9$, $P<0.01$]. Again, comparisons between groups showed that both amnesic groups peformed more poorly than the control group ($ts > 3.7$, $Ps < 0.01$); the difference between the two amnesic groups did not reach statistical significance [$t(10) = 1.7$, $P = 0.1$]. It should be noted, however, that performance by most of the patients with Korsakoff's syndrome was quite impaired relative to the group of five non-Korsakoff amnesic patients. For example, five of the seven patients with Korsakoff's syndrome performed 2 or more standard error units below the mean score obtained by the non-Korsakoff amnesic patients (standard error = 0.053). The failure to find a significant difference between the two amnesic groups was due largely to one patient with Korsakoff's syndrome who performed quite well (correlation = 0.45).

EXPERIMENT 2—METHODS

Subjects

The same individuals who participated in Experiment 1 were tested here, except that one healthy control subject for the amnesic patients was not available for testing. Thus, we tested six patients with frontal lobe lesions, eight age-matched control subjects for the patients with frontal lobe lesions, seven amnesic patients with Korsakoff's syndrome, five non-Korsakoff amnesic patients, and seven age-matched healthy control subjects for the amnesic patients. Experiments 1 and 2 were separated by an average of 38.1 days (range = 1 to 91 days).

Procedure

Fifteen factual events were selected from a test of remote memory for public events ([41], e.g. *Jonas Salk discovered the first Polio vaccine* and *The name of the Polish Labor Movement led by Lech Walesa was Solidarity*). The time when the events occurred was distributed evenly between 1941 and 1985. All subjects were given tests of event recall (e.g. "Who discovered the first Polio vaccine?") and event recognition memory (4-alternative, forced-choice test) for these 15 facts prior to testing temporal order memory (average separation of recall/recognition and temporal order tests = 211 days). The 15 events used in the fact sequencing test were quite familiar, such that on the 4-choice recognition test, control subjects and patients with frontal lobe lesions could recognize about 85% of the correct answers.

The test of fact sequencing was conducted in a similar way as the word sequencing test phase used in Experiment 1. The 15 events were printed on cards and displayed randomly in a two-dimensional array on a table in front of the subject. Subjects were instructed to arrange the events in chronological order from the oldest event to the most recent. Performance for each subject was based on a Spearman correlation measure between the actual chronological order of the events and the subject's judged order.

RESULTS AND DISCUSSION

Figure 3 shows the performance by control subjects and patients with frontal lobe lesions on tests of fact recall, fact recognition, and fact sequencing. The two groups did not differ significantly on the fact recall test [$t\ (12) = 0.9$, $P = 0.4$] or on the fact recognition test [$t\ (12) = 1.3$, $P = 0.2$), though on the recall test patients with frontal lobe lesions did perform on average 9.2% below control subjects. The ability to remember the sequential order of the facts was significantly impaired in patients with frontal lobe lesions [$t\ (12) = 2.6$, $P = 0.02$]. The average correlation for control subjects was 0.86, whereas the average correlation for patients with frontal lesions was 0.70.

Figure 4 shows performance on tests of fact recall, fact recognition, and fact sequencing by control subjects and amnesic patients (patients with Korsakoff's syndrome and five other amnesic patients). A one-way analysis of variance revealed a significant difference across groups for both fact recall [$F\ (2, 15) = 5.1$, $P < 0.05$] and fact recognition [$F\ (2, 15) = 6.3$, $P < 0.01$]. Comparisons between groups showed that both amnesic groups were impaired on the recall and recognition tests compared to control subjects ($ts > 2.3$, $Ps < 0.05$); but the two amnesic groups did not differ significantly from each other ($ts < 0.9$, $Ps > 0.3$). The finding of

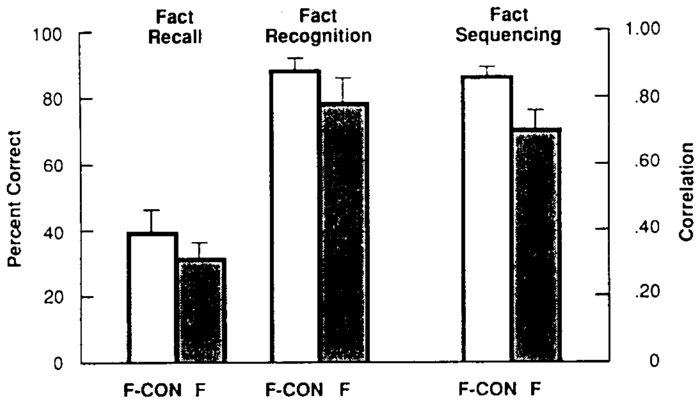

Fig. 3. Subjects were asked (1) to recall the answers to 15 questions about public events that occurred between 1941 and 1985, (2) to recognize the correct answers on a 4-alternative, multiple-choice test, or (3) to arrange the 15 events in correct chronological order. $F=6$ patients with frontal lobe lesions; F-CON $=8$ control subjects for patients with frontal lobe lesions.

impaired remote memory in these same groups of amnesic patients has been described in detail elsewhere [41].

On the fact sequencing test, the average correlation for the control subjects was 0.93, and the average correlation for the patients with Korsakoff's syndrome and the five other amnesic patients was 0.20 and 0.70, respectively. An ANOVA revealed a significant difference in fact sequencing ability across groups [F (2, 16) = 10.2, $P<0.01$]. Comparisons between groups showed that both amnesic groups performed more poorly than the control group (ts > 3.7, Ps < 0.01). In addition, the two amnesic groups differed significantly from each other [t (10) = 2.2, $P=0.05$]. Finally, the patients with Korsakoff's syndrome performed worse than the patients with frontal lobe lesions [t (11) = 2.4, $P<0.05$]. Thus, patients with Korsakoff's syndrome were markedly impaired when asked to arrange facts in chronological order (see Fig. 4).

GENERAL DISCUSSION

Patients with frontal lobe lesions were impaired in their ability to organize information within a temporal context. In Experiment 1, patients with frontal lobe lesions had difficulty reproducing the sequential order of a list of 15 words, despite the fact that these patients performed within the normal range on tests of recall and recognition memory for the words themselves. In Experiment 2, the same patients were impaired in their ability to reconstruct the chronological order of 15 public events that occurred between 1941 and 1985. Thus, impaired memory for temporal order occurred for recently learned information as well as for information acquired across a span of 45 years.

Performance on the fact sequencing test was generally better than the word sequencing test for all subjects, including patients with frontal lobe lesions. Also, the patients with frontal lobe lesions performed better on the fact sequencing test, relative to the patients with Korsakoff's syndrome, than they did on the word sequencing test. It may be that performance on the fact sequencing test was mediated in part by semantic associations, which would likely be more elaborate than the semantic associations for recently presented words. If so, a selective deficit in memory for temporal order might not be very sensitive to the fact sequencing test. In contrast,

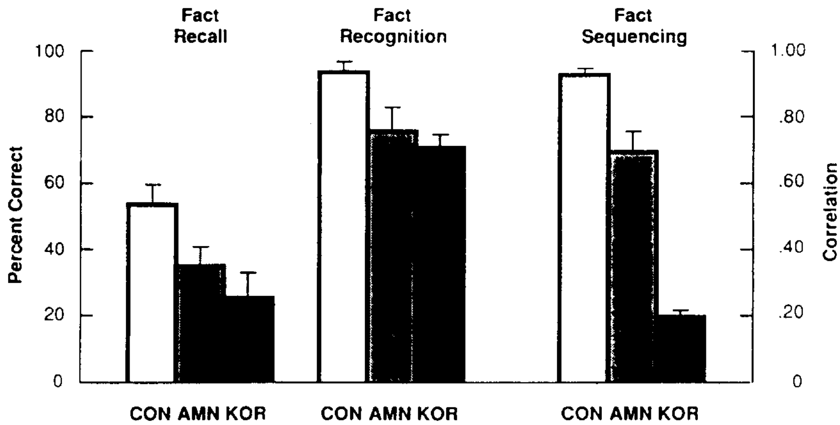

Fig. 4. Subjects were asked (1) to recall the answers to 15 questions about public events that occurred between 1941 and 1985, (2) to recognize the correct answers on a 4-alternative, multiple-choice test, or (3) to arrange the 15 events in correct chronological order. AMN = 5 amnesic patients; KOR = 7 amnesic patients with Korsakoff's syndrome; CON = 7 control subjects.

patients with Korsakoff's syndrome have both diencephalic damage and general cortical atrophy which could contribute to their retrograde amnesia and to their large fact sequencing impairment. These ideas may account for the finding that fact sequencing performance by patients with frontal lobe lesions was considerably better than the performance by patients with Korsakoff's syndrome. Despite their advantage over Korsakoff patients, however, patients with frontal lobe lesions still exhibited significant impairment on the fact sequencing test.

The findings from patients with frontal lobe lesions corroborate previous work showing that the frontal lobes contribute to memory for temporal order [27, 28]. For example, in an unpublished study, patients with frontal lobe lesions were impaired in their ability to judge which of two stimuli occurred more recently in a continuous recognition memory paradigm (see [41]). In other studies, rats with frontal lesions were impaired in remembering the order in which separate events occurred [17], and they were impaired in the ability to remember the expected time of reinforcement [29].

Impaired memory for temporal order may be related to deficits in context or source memory [15, 32, 37]—deficits that have also been reported following frontal lobe damage. In both cases, the deficit occurs when patients are required to place items within a temporal framework. For example, Janowsky *et al.* [15] presented a list of obscure facts (e.g. "The name of the goldfish in the story Pinocchio is *Cleo*"). Patients with frontal lobe lesions could recall the presented information as well as control subjects (e.g. "What was the name of the goldfish in Pinocchio?"), but they had difficulty remembering the source of the facts—that is, when and where the facts were learned.

One important question is whether impaired temporal order memory reflects a specific deficit in temporal processing or whether it is just one example of a broader cognitive deficit. One possibility is that the frontal lobes, or at least parts of the frontal lobes, are specifically involved in processing temporal information. Other parts may be involved in other aspects of cognitive function. Another possibility is that the deficit in temporal order memory observed in patients with frontal lobes lesions is related to other cognitive deficits, such as deficits in planning, problem solving, metamemory, verbal fluency, and cognitive estimation [7, 13, 14, 21, 28, 33, 38]. Such a deficit has been termed a "dysexecutive" syndrome by BADDELEY [1] to capture the idea that the deficit may be a broad one, affecting the ability to plan, initiate, and execute search and retrieval strategies. This interpretation is consistent with the finding that patients with frontal lobe lesions are sometimes impaired on tests of memory that presumably require self-initiated executive processes, such as tests of free recall [11, 13, 16, 38].

If impairment on tests of temporal order memory is linked to frontal lobe dysfunction, then it may be possible to observe significant correlations between tests of temporal order and tests of frontal lobe function in patients with frontal lobe lesions and patients with Korsakoff's syndrome. In amnesic patients with medial temporal damage or with circumscribed diencephalic damage (e.g. the other non-Korsakoff amnesic patients), impairment on tests of temporal order should be related to their general memory impairment. In the present study, none of these correlations were statistically significant, though the trends were weakly in the right direction. The average Spearman correlation between the two sequencing tests and the Wisconsin Card Sorting test was 0.25 for patients with frontal lobe lesions, 0.24 for patients with Korsakoff's syndrome and -0.43 for the other amnesic patients. The correlation between the two sequencing tests and a test of new learning ability (WMS-R General Memory index) was -0.04 for patients with frontal lobe lesions, 0.01 for patients with Korsakoff's syndrome, and 0.21 for the other amnesic patients.

In any case, the finding of such correlations between temporal order data and frontal lobe test data, which has been reported already by SQUIRE [39], cannot be considered very strong evidence for the issues under discussion here. Indeed, it was precisely because we already had this kind of *indirect* evidence that we set out to obtain more direct comparisons between amnesic patients and patients with frontal lobe lesions. The direct evidence now available is: (1) patients with Korsakoff's syndrome (6 of whom participated in the present study) have frontal atrophy, as shown by CT scans [35]; (2) frontal patients are impaired on temporal order tests (present study; also unpublished study cited by [27]); and (3) Korsakoff patients are disproportionally impaired [relative to other (non-frontal) amnesic patients] on the same tests (present study). It remains possible, however, that the quality of the deficit observed in patients with Korsakoff's syndrome is not the same as the additive effects of amnesia plus frontal lobe dysfunction. Clearly, these issues need further study.

Whereas the disproportionate deficit in temporal memory observed in patients with Korsakoff's syndrome may be attributable to frontal lobe dysfunction, the amnesic deficit itself is presumably related to diencephalic damage, not to frontal lobe damage. Several lines of evidence are consistent with this interpretation. First, patients with circumscribed frontal lobe lesions perform within the normal range on many standard neuropsychological tests of new learning ability [see 5, 13, 43]. By contrast, patients with Korsakoff's syndrome are impaired on these same tests [13]. Second, patients with circumscribed lesions of the diencephalic midline (e.g. non-Korsakoff patients M.G. in the present study; patient N.A. in a previous study [39]) exhibit amnesia and also perform no worse on tests of temporal order memory than would be predicted by their general level of memory impairment. By contrast, patients with Korsakoff's syndrome exhibit, in addition to a general impairment of memory, a disproportionately severe impairment of temporal order memory.

In conclusion, findings from this study suggest that the frontal lobes can contribute critically to performance on tests of temporal order memory. The impairment of temporal order memory in patients with frontal lobe lesions may be part of a broader deficit in the ability to organize and retrieve information. Patients with circumscribed damage to diencephalic or medial temporal areas exhibit impaired learning and memory on many tests of memory, including item and temporal order memory. Patients with Korsakoff's syndrome, who have both diencephalic and frontal damage [35], exhibit a disproportionately large deficit in memory for temporal order.

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