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Verbal recall in amnesiacs under conditions of diminished retroactive interference

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Summary

In amnesiacs, stimuli that at first can be recalled are usually forgotten within 1 min, but the conditions required for this severe forgetting have remained unknown. To examine this, six patients with amnesia due to head injury or stroke and six normal controls heard lists of words (Experiment 1) and stories (Experiment 2). These stimuli were to be recalled immediately or after an extended test delay (10 min in Experiment 1; 1 h in Experiment 2). Although severe forgetting occurred in the amnesiacs following activity-filled delays, much less forgetting occurred in four of these patients after delays spent in a dark, quiet room. This was true even when the patients appeared to sleep during the delays. The results show, in a novel manner, that one deficit underlying their amnesias is vulnerability to retroactive interference.

Keywords: retroactive interference; amnesia; anterograde amnesia; memory; interference

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Introduction

Patients affected by anterograde amnesia recollect events normally if tested immediately afterward. However, they will forget these events within ~1 min and thereafter could no longer retrieve them in a direct test (Scoville and Milner, 1957; Baddeley and Warrington, 1970; Cohen, 1984; Schacter, 1987; Squire and Knowlton, 2000; Kopelman, 2002). It is still unclear whether this memory deficit is inevitable or whether the event could be retrieved under conditions of reduced interference indicating that the event has been encoded in the memory system, albeit in a weakened form.

It is common to discuss two types of interference with memory for a target item: proactive interference, or interference from information that was presented before the target item; and retroactive interference, or interference from information that was presented between the target item and the memory test. There is an extensive literature on proactive interference in patients with brain damage, both with classic amnesia syndromes (e.g. Moscovitch, 1982; Freedman and Cermak, 1986; Janowsky *et al*., 1989; Kopelman, 2002) and in patients with amnesia due to frontal lesions (e.g. Janowsky *et al*., 1989; Shimamura, 1995; Baldo and Shimamura, 2002). For example, in a study of a patient with a temporal lobectomy, two Korsakoff's patients and one post-encephalitic patient, Warrington and Weiskrantz (1974) found that cued recall of a 10-word list using semantic category cues was not worse in amnesic patients than in controls, but that a large amnesic deficit emerged when a second list was presented using the same 10 categories as the first list. Based on this and similar proactive interference effects in amnesia, Warrington and Weiskrantz (1970, 1974) formulated an explanation in terms of effects of general interference on recall in amnesic patients, which they later rejected (Warrington and Weiskrantz, 1978). However, only a few studies (discussed below) have examined retroactive interference in any type of amnesia.

It has been assumed that the preservation of information in amnesic patients lasts only as long as attention keeps the information in short-term memory, for a number of seconds (but not minutes). Accordingly, one reason to predict retroactive interference is that it could cause information to be lost from short-term memory through distraction. However, there are other possible reasons why retroactive interference could occur. It could interfere more extensively

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with the consolidation or retrieval of long-term memories; we do not know how long items can be retained by amnesiacs in the absence of retroactive interference.

Some amnesia research has examined retroactive interference, but only for retention intervals of <1 min, traditionally considered within the domain of short-term memory (e.g. Peterson and Peterson, 1959; Baddeley, 1997). Research conducted with monkeys (Malmo, 1942; Bartus and Levere, 1997; Zola-Morgan and Squire, 1985) has invariably shown that, in distraction-filled delay conditions, the lesioned monkeys were impaired in comparison with the control group. In humans, several anecdotal reports point towards the possibility that minimizing retroactive interference may enhance amnesiacs' performance (Drachman and Arbit, 1966). For example, Scoville and Milner (1957) observed that patients with severe memory defects could retain a three-figure number or a pair of unrelated words for several minutes, 'if care was taken not to distract them in the interval. However, they forgot the instant attention was diverted to a new topic' (p. 15). Even the famous patient H.M. could retain verbal items within his span capacity if allowed to rehearse (Milner, 1968; Ogden, 1996). Similarly, Chao and Knight (1995) and Baldo and Shimamura (2000) demonstrated the detrimental effect of filled short delays in human patients with either temporo-parietal or lateral prefrontal lesions, respectively. Finally, it appears tentatively that distractor-filled retention intervals may also be detrimental for patients affected by transient global amnesia (Hodges and Ward, 1989; Quinette *et al*., 2003).

A few studies have looked at processes related to retroactive interference over longer periods. Mayes *et al*. (1994) compared memory for faces under two different filled delay conditions. In the first condition, intervening material during a 12 min retention interval consisted of other faces. In the second, control, condition, the interval was filled with 'conversation and other activities not involving faces'. They found that the difference between interference conditions was equivalent in normal and amnesic participants. Geffen *et al*. (1994) investigated learning of a verbal list across five trials followed by a second list to produce interference, and then another trial with the first list. On the final, post-interference trial, they found less saving from earlier trials in closed-head injury patients than in control participants. These studies reached opposite conclusions. Whereas Mayes *et al*. (1994) concluded that there was no larger effect of retroactive interference in amnesic patients than in controls, Geffen *et al*. (1994) concluded that retroactive interference had a more severe effect on the amnesic patients than in controls. Notice, however, that Mayes *et al*. (1994) compared two potentially distracting test delay conditions (novel faces versus conversation), whereas Geffen *et al*. (1994) simply compared performance before and after a filled test delay. Notice also that neither of them examined what is most critical for an understanding of retroactive interference effects, i.e. performance after test delays that include or exclude interfering stimuli, in amnesic patients and in normal controls.

A prediction about retroactive interference in amnesia with delays longer than 1 min can be derived from recent theoretical treatments of the memory system (e.g. Neath and Nairne, 1995; Chater and Brown, 1999; Cowan *et al*., 2001; Nairne, 2002). Unlike traditional accounts (e.g. Broadbent, 1958; Baddeley, 1997), in which short-term memory for items that are unattended decays as a function of time, in ~20 s or less (Cowan, 1995), the alternative theories suggest that items retain a certain special status in memory until the time at which some other stimulus replaces that memory. According to this alternative conception of the memory system, amnesiacs' memory for the most recently presented stimuli, which they often can retrieve in short-term memory tests (Baddeley and Warrington, 1970), should remain accessible for a considerably longer time, even if the stimuli are not rehearsed continuously, until they are replaced by other stimuli.

These recent predictions also tap into an older tradition. The presence and the nature of interpolated activity have long been thought to play a major role in our ability to recall learned information (see Baddeley, 1997). For example, McGeoch and McDonald (1931) investigated the effect of 10 min delays on the recall of an overlearned list of 10 adjectives. In two different experiments, the delay was filled either with various materials (nonsense syllables, numbers, unrelated words, antonyms or synonyms of the adjectives) or with a period of rest. In the resting condition (unfilled delay), the performance on average was much higher than in any of the other conditions (4.5 out of a possible maximum of 10 versus 1.2–3.7 in the other conditions). Waugh and Norman (1965) also showed that interference, and not temporal decay, was the main source of loss of short-term memory. Specifically, the number of items intervening between presentation and probed recall, and not the amount of time, was the main determiner of performance. If minimizing retroactive interference is so powerful in enhancing recall in healthy controls, our question then is whether it could have a role in amnesia.

Interference or distraction within 1 min or so usually seems inevitable in ordinary life. However, we were inspired to extend the interference-free period by classic research on cockroaches (Minami and Dallenbach, 1946). They were taught to avoid the dark portion of an enclosure with shock punishment and then were retested in that situation after a delay of 1–3 h spent either in a cage (kept in a dark cupboard) that allowed motion or, within that cage, in a smaller box lined with tissue that curtailed motor activity. Inactivity produced savings (i.e. reduced the number of trials needed to relearn the aversion). Thus, 1 h of inactivity yielded 89% savings, as opposed to 59% savings when the test delay was spent in the cage.

In the current study, we used a roughly analogous procedure in humans by presenting lists and stories to be recalled after a retention interval (10 min in the list experiment and 1 h in the story experiment) during which the participant either completed various psychometric tasks or reclined alone in a dark, quiet room. Previously, researchers might have considered it impractical to impose unfilled test delays for this long. However, a feasibility study (Della Sala *et al*., 2004) demonstrated that such a paradigm is possible and reliable. The method of that study was similar to the present Experiment 2 (story presentations with 1 h test delays) but with patients who had minimal cognitive impairment (Petersen *et al*., 1999), rather than specific amnesias as in the present study. The present Experiment 1 used list presentations and 10 min test delays in order to allow better experimental control, and Experiment 2 demonstrated the generality and strength of the findings in the same participants.

Experiment 1

Subjects and methods

We tested six amnesic patients (age range 25–70 years; five male) and six normal control participants (age range 27–70 years; five male) in Italy with their informed consent. Two patients had embolic strokes, three had closed-head injuries and one was affected by the sequelae of an episode of anoxia. CT or MRI scans provided evidence of the site of their lesion. All patients were out-patients with no known pre-morbid psychiatric or neurological histories. The selection criteria included the following: (i) complaints by family members of an abrupt onset of memory loss as a main symptom; (ii) age of ≤70 years; (iii) classification as amnesic according to the Rivermead Behavioural Memory Test; (iv) performance below the cut-off score for normality in verbal and non-verbal delayed recall tasks (figure copy, word list recall); (v) normal performance in short-term memory tasks (digit span, spatial span; Corsi blocks); (vi) score within the normal range on the Token Test (verbal comprehension); (vii) normal performance in all subtests of the Aachener Aphasie Test, a comprehensive battery assessing language across a variety of abilities, administered by a professional speech therapist; (viii) scores above cut-off in a test of verbal reasoning (the Verbal Judgement Test assessing the ability to explain proverbs, identify conceptual differences, discover illogical claims and estimate quantities); and (ix) scores above cut-off in the Raven Progressive Coloured Matrices.

Table 1 provides age- and education-adjusted test results and references for the various tests, for the mean of controls and for the relevant patients (patients 1–6). According to the Italian version of the Rivermead Behavioural Memory Test (Wilson *et al*., 1985; Brazzelli *et al*., 1993) and its scoring criteria, two of the patients were classified as ‘very severely amnesic’, three as ‘severely amnesic’ and one (a stroke patient) as ‘mildly amnesic’. Normal performance on some of the tests shown in Table 1 rules out other neuropsychological diagnoses, including detectable executive deficits (e.g. verbal fluency and sorting tasks) and semantic short-term memory loss (Romani and Martin, 1999) (e.g. the Token Test and immediate recall of word lists).

Tests

The participants were administered a free-recall test with six lists of 15 unrelated, spoken concrete, Italian nouns chosen to have word frequencies in an equivalent range and matched across lists based on a use index (Bortolini *et al*., 1972) and word length.

Procedure

The testing included six conditions, presented in the same order to all participants to ensure that differences between them must be attributed to differential abilities rather than stimulus differences. Repetition of the same condition at multiple points in the procedure demonstrated the consistency of interference condition effects. (We could repeat only some conditions without overly taxing the patients.) The order of the different conditions was as follows: (1) no immediate recall, then delayed recall, with no interference; (2) immediate recall, then delayed recall with no interference; (3) immediate recall, then delayed recall with interference; (4) immediate recall, then delayed recall with interference, as in condition 3 above; (5) no immediate recall, then delayed recall with interference; and (6) immediate recall, then delayed recall with no interference, as in condition 2 above.

We refer to the condition when there was no immediate recall test prior to delayed recall (as in conditions 1 and 5) as ‘delayed first recall’ conditions. In each condition, the interference or no-interference interval lasted 10 min and ended with a delayed test. In total, testing required a single session lasting ~1.5 h.

Whenever recall was requested, the participant was to repeat the words aloud in any order and the experimenter wrote down each word as it was spoken, checking responses later against a tape-recorded record. When the retention (delay) interval included interference, it comprised a planned series of psychometric tests for 10 min. The tests administered in the 30 min of the three filled intervals included verbal and non-verbal psychometric tasks that do not focus on memory, always in the same order: the Wechsler Adult Intelligence Scale (WAIS) Block Design, Phonemic Fluency, Semantic Fluency (requiring retrieval from the categories of colours, animals, fruits and cities), WAIS Digit Symbol Substitution Test and WAIS Vocabulary Test (references in Table 1). There was no overlap in vocabulary between these tests and the memory stimulus materials. If there was time remaining, it was filled with the Trail-making task (Giovagnoli *et al*., 1996) and, if a little time still remained, the participant was engaged in conversation.

When the interval included no interference, the participant was to lie quietly in a darkened room, trying not to fall asleep, for 10 min. In this condition, the experimenter quietly waited in the room and watched for lip movements during the 10 min period (although none were observed). At the end of 10 min in either condition, without warning, the experimenter asked the

Table 1 *Selected characteristics of tests and amnesic patient performance*

Measure	Top of range	Normal cut-off	Mean (SD) of six controls	Patient number 1	2	3	4	5	6	Reference
Age (years)/gender (M or F)			53.33 (19.41)/ 5M, 1F	25/M	70/F	65/M	27/M	64/M	54/M	
Aetiology				h	s	s	h	h	an	
Known lesion sites			–	LRF	RTh	RP	LRF; RP; LT	RF; LP	LRT	
No. of months since damage				3	3	4	17	24	12	
Rivermead Test	12	9	–	4	5	8	2	2	4	Brazzelli *et al.* (1993)
Rivermead category				s	s	m	vs	vs	s	Brazzelli *et al.* (1993)
Aachener Aphasie Test	9	8	–	9	9	9	9	9	9	De Bleser *et al.* (1986)
Token Test	36	29	34.33 (1.97)	29	31	29	30	33	34	De Renzi and Faglioni (1978)
Phonological fluency	–	17.35	34.33 (8.33)	15	38	30	45	35	42	Novelli *et al.* (1986)
Verbal judgements	60	32	55.00 (4.69)	46.25	52.25	50.3	40.25	39.00	52.3	Spinnler and Tognoni (1987)
Raven Matrices	36	18	–	30	18	26	24	26	32	Bassoi *et al.* (1987)
Weigl Sorting Test	15	4.25	–	13	12	11	11	12	15	Spinnler and Tognoni (1987)
Construction apraxia	14	7.75	–	14	14	14	–	14	14	Spinnler and Tognoni (1987)
Digit span	9	3.5	7.00 (1.55)	5.50	4.50	5.50	4.00	5.25	9.00	Orsini *et al.* (1987)
Spatial span	9	3.25	6.17 (1.17)	3.25	4.50	5.50	3.25	5.25	4.00	Spinnler and Tognoni (1987)
Rey Figure copy[h]	36	28.87	36.00	36	31.5	31	14.5	36	36	Caffarra *et al.* (2002)
Figure copy delayed	36	9.46	21.88 (2.76)	0	0	0	0	0	0	Caffarra *et al.* (2002)
Word list recall	15	4.96	7.50 (1.22)	5	5	6	4	4	7	Carlesimo *et al.* (1996)
Word list recall delayed	15	–	4.17 (1.83)	0	0	0	0	0	0	Carlesimo *et al.* (1996)
Word-pair learning	22.5	6.0	18.17 (2.79)	6.50	7.50	5.50	4.50	3.50	3.50	Novelli *et al.* (1986)
Percentage retention in experimental memory tests										
Lists: interference			46 (10)	21	15	20	0	0	0	
Lists: no interference			74 (08)	53	58	60	0	25	0	
Lists: no immediate recall, interference			36 (25)	0	0	16	0	0	0	
Lists: no immediate recall, no interference			77 (13)	41	48	64	0	24	0	
Stories: interference			79 (12)	0	0	27	0	0	0	
Stories: no interference			89 (06)	85	90	63	0	78	0	

Bottom of range = 0 for every test in which top of range is shown. Rivermead Test categories: vs = very severe, s = severe, m = mild. Aetiology: an = anoxia, h = head injury, s = stroke. Lesion site: L = left, R = right, F = frontal, Th = thalamus, P = parietal, T = temporal. For the anoxic patient, precise lesion site = bilateral hippocampus according to MRI. Patient 4 had hemispatial neglect and could not complete the construction apraxia test. Percentage retention = 100 × delayed/immediate scores; for the ‘no immediate recall’ conditions, it was calculated using immediate recall on other trials.

participant to recall any of the words that had been presented in the most recent list.

After the last recall trial, participants were asked whether they used any particular strategy to recall the words; no participant said that they used any strategy. Next they were asked specifically whether they rehearsed the words during the delay; only patient 1 replied ‘yes’ (in the second no interference trial).

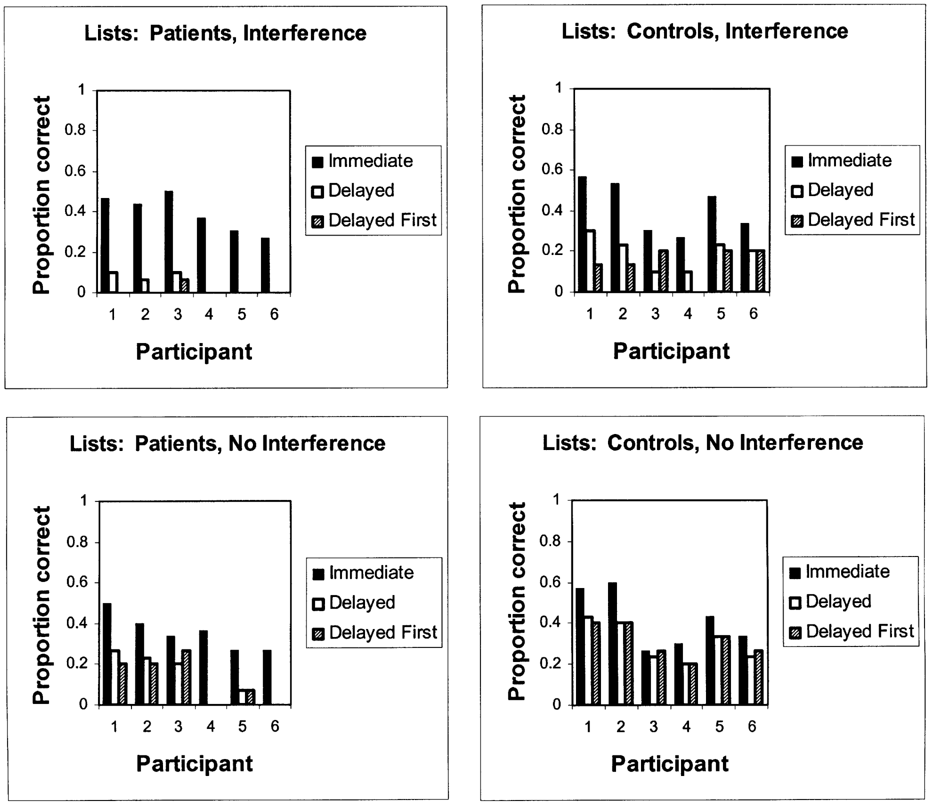

Fig. 1 Proportion of words recalled from lists by amnesic patients (left-hand panels) and normal control participants (right-hand panels) immediately after the list (black bars) and following a 10 min delay, with or without a prior immediate test on that trial (white and grey bars). Sometimes the delay was filled with extraneous cognitive tasks (top panels, interference), whereas other times the participant rested in a quiet, dark room during the delay (bottom panels, no interference). The loss of memory during the delay was greatly reduced in the no interference condition.

Results and discussion

Figure 1 shows the proportion of words recalled in each condition for every participant. An analysis of variance (ANOVA) of percentage correct with participant group (patient versus control), interference condition (interference present or absent) and test delay (immediate, delayed or delayed first recall) as factors produced several effects. The only significant ones with participant group as a factor were a main effect of group, $F(1,10) = 6.71$, $P < 0.05$, and an interaction of the delay condition with the group, $F(2,20) = 7.48$, $P < 0.01$. The basis of both effects was that patients had poorer performance than controls in delayed recall.

Both groups showed better delayed performance with no interference than with interference, leading to two additional effects: a main effect of interference, $F(1,10) = 22.76$, $P < 0.001$, and an interaction of the interference condition with the delay condition, $F(2,20) = 19.56$, $P < 0.001$. For immediate, delayed and delayed first recall, respectively, the patients went from 39, 4 and 1% correct in interference conditions to 36, 13 and 12% correct in no interference conditions. Controls went from 41, 19 and 14% correct in interference conditions to 42, 31 and 31% correct in no interference conditions. There was no interaction between the interference condition and the group, $F(1,10) < 1$ (not significant).

As another means to quantify the results, the percentage of retention was calculated as 100 times the proportion correct in the delayed recall condition divided by the immediate recall condition for the same list, and as 100 times the proportion correct in the delayed first recall condition divided by the mean of all immediate recall trials (see Table 1). These results illustrate that four of the six patients (patients 1–3 and 5) were able to benefit substantially from the absence of interference during the delays. The results are very similar for delayed recall and delayed first recall conditions.

The results cannot be attributed to differences in level of immediate recall. On average, the amnesiacs performed about the same as controls in immediate recall (see Fig. 1). In an ANOVA with two measures of immediate recall (preceding interference and no interference delays) in the patient and control groups, no effects approached significance. Moreover, the results do not appear to be governed by the trial order. Table 2 shows list memory performance according to the chronological order in which trials were presented, separately in all six patients, in just the four patients who benefited from

Table 2 *Trial-by-trial proportions of list items correct (with SDs) in Experiment 1*

List	Test interval	Interference? (yes/no)	All patients	Select 4 patients	Controls
1	Delayed	Yes	0.01 (0.03)	0.02 (0.03)	0.21 (0.08)
2	Immediate	No	0.38 (0.08)	0.42 (0.06)	0.40 (0.14)
	Delayed	No	**0.16** (0.13)	**0.23** (0.07)	**0.31** (0.10)
3	Immediate	No	0.42 (0.10)	0.45 (0.11)	0.47 (0.18)
	Delayed	Yes	0.03 (0.06)	0.05 (0.06)	0.19 (0.10)
4	Immediate	No	0.36 (0.11)	0.40 (0.09)	0.36 (0.08)
	Delayed	Yes	0.06 (0.07)	0.08 (0.06)	0.20 (0.07)
5	Delayed	No	**0.12** (0.11)	**0.18** (0.08)	**0.38** (0.08)
6	Immediate	No	0.33 (0.13)	0.33 (0.16)	0.43 (0.19)
	Delayed	No	**0.10** (0.12)	**0.15** (0.11)	**0.30** (0.11)
All	Immediate	No	0.37	0.40	0.41
	Delayed	No	**0.13**	**0.19**	**0.33**
	Delayed	Yes	0.03	0.05	0.20

The ‘select 4’ are patients 1, 2, 3 and 5, who benefited from the absence of interference. Delayed retention in the absence of interference is shown in bold.

an absence of interference, and in control participants. The patients’ benefit from the absence of interference was almost as large on trial 6 as it was on the earlier trial in the same condition, trial 2. The four patients shown in the fifth column of the table had a substantial amount of retention on these tests with no interference, measured as the delayed score divided by the immediate score (trial 2, 55%; trial 6, 45%). In contrast, in the presence of interference, these four patients had lower levels of retention (trial 3, 11%; trial 4, 20%). For the four immediate recall attempts, there were stable individual differences among the six patients, and inter-trial reliability was high (Cronbach’s alpha = 0.83). For the three recall attempts following unfilled delays (two of which were preceded by immediate recall of the same list), reliability was very high (Cronbach’s alpha = 0.96). For recalls following a filled delay, because patients’ performance was low overall (see Fig. 1 and Table 1), Cronbach’s alpha was more moderate at 0.70.

We checked for the possible involvement of proactive interference by counting the number of intrusions (words recalled that were not actually in the particular lists being recalled). Patients 1–6 made a total of two, 10, 15, nine, five and zero intrusions summed across all conditions, respectively. The control participants made an average of 12.00 (SD = 6.60) intrusion errors summed across conditions. This difference was not significant by a Mann–Whitney *U* test. Cross-list interference during recall of word lists has been reported in patients with dysexecutive problems due to frontal lesions (Baldo *et al*., 2002). Thus, the relatively low number of intrusion errors in our patients provides additional evidence (along with the test results summarized in Table 1) that our patients were not suffering primarily from deficits related to executive dysfunction.

To explore the generality of the findings, we report further testing, using sentence stimuli and 1 h retention intervals.

Experiment 2

In this second experiment, to examine the longevity of memory under conditions of no interference, we extended the retention interval to 1 h, which placed severe restrictions on how many trials we could include per participant. A recent study showed that many amnesiacs have good immediate recall but poor delayed recall of prose from stories (Baddeley and Wilson, 2002). Rehearsing this type of material verbatim for prolonged periods would be difficult. Therefore, as the stimuli to be remembered, we selected prose memory tests that had been used in prior studies.

Subjects and methods

All of the participants from Experiment 1 entered Experiment 2, with their informed consent.

Tests

The same procedure as in the study of Della Sala *et al*. (2004) with patients with minimal cognitive impairment was used. Stories were drawn from a pool of seven Italian passages from several previous studies (Novelli *et al*., 1986; Brazzelli *et al*., 1993, 1994; Capitani *et al*., 1994).

Procedure

Each participant listened to four stories, on two separate days (two stories per day). Participants were to listen to each story and repeat it verbatim. Immediate recall was required for each story (in contrast to the lists in Experiment 1). Each immediate recall test was followed by a filled or unfilled delay as in the first experiment, but lasting 1 h. Therefore, out of the four stories a participant received, there were two delayed recall trials with interference and two with no interference. Inasmuch as this was an exploratory study, story order was varied (with comparable orders among patients and controls). Patients 1–3 and three matching controls received the two no interference trials before the two interference trials, patient 4 received an alternating order beginning with a no interference trial, patient 5 received an alternating order beginning with an interference trial, and patient 6 received the interference trials first. There was no indication in the results that trial order was important.

Responses, which were scored verbatim, received credit for correct content words in an order that reflected the correct meaning. Words with slight grammatical changes (such as making a singular noun plural) were scored as correct. Verbatim scoring of recall by two raters, one of whom was blind to the conditions, had a high inter-rater reliability (among the patients, based on means for immediate recall, 0.95; recall after filled delays, 1.00; after unfilled delays, 0.96).

As in Experiment 1, during the interference-filled delay condition, diagnostic tests were carried out. The tests during the 1 h interval included both verbal and non-verbal tasks, with brief periods of conversation between tests.

In the no interference delay condition, the participant was told that he or she would be left there for an hour as part of the experiment (without receiving any reason why, and there were no queries). However, the experimenter unobtrusively looked and listened in every 15 min to observe signs of sleep or rehearsal. After either type of delay, the experimenter said the Italian equivalent of the following: ‘One hour ago I read you a story; would you now please tell me all that you remember about that story?’

Results and discussion

Figure 2 shows the proportions of correct story recall for each participant in the interference and no-interference conditions. An ANOVA similar to the one conducted in Experiment 1 produced all of the effects noted for that experiment: a main effect of group, $F(1,10) = 20.52$, $P < 0.001$, an interaction between the group and the test delay, $F(1,10) = 5.84$, $P < 0.05$, an overall effect of the interference condition because of better retention with no interference, $F(1,10) = 6.91$, $P < 0.05$, and an interaction of condition × delay, $F(1,10) = 6.07$, $P < 0.05$. The control participants in the condition with interference went from 62% immediate recall to 50% delayed recall and, in the condition with no interference, from 63% immediate recall to 57% delayed recall. The patients in the condition with interference went from 21% immediate recall to only 2% delayed recall; however, in the condition with no interference, they went from 29% immediate recall to 15% delayed recall.

In the participants who received the two no interference trials first (patients 1–3 and three controls), the results were very comparable with the other patients and controls. Patients 1–3 recalled 29% of the stories in immediate recall, 26% in delayed recall with no interference, and only 3% in delayed recall with interference. The corresponding percentages for these conditions in the controls with the same trial order were 60, 52 and 50%, respectively.

Table 1 shows the percentage of retention of stories with and without interference (delayed recall as a proportion of immediate recall). This table illustrates that, as in Experiment 1, only four of the patients actually benefited from omission of interference. These were the same ones as in the list study (patients 1–3 and 5). They went from an average of 7% retention with interference up to 79% with no interference. Patients 4 and 6 once more showed no benefit from minimizing interference.

As a further analysis, we checked for possible signs of sleep during the unfilled retention intervals because sleep would be incompatible with uninterrupted rehearsal throughout the retention interval. Participants were checked unobtrusively during the unfilled delay at 15 min intervals for possible signs of sleep (snoring, deep breathing, no movement, post-recall question about whether they slept). Snoring was encoded only if it was loud and lasted several seconds. There were apparent signs of sleep in 79% of all trials in patients. Snoring, which we take as our strongest suggestion of sleep, was accompanied by good performance. Patient 1 snored in one unfilled delay interval and achieved 92% retention in that trial, whereas patient 5 snored in both unfilled delay intervals and achieved 75 and 80% retention in them. In contrast, these same two patients showed 0% retention in the high interference condition. Processes taking place during sleep may have improved memory consolidation (Jenkins and Dallenbach, 1924; Maquet *et al*., 2000; Stickgold *et al*., 2000), but clearly would not allow uninterrupted maintenance rehearsal as it is generally understood. Physiological indices of sleep would be desirable in future studies of this phenomenon.

General discussion

In six amnesic patients and six control participants, the present study focused on the delayed recall of lists and stories following drastically reduced retroactive interference, as compared with retention intervals of the same lengths filled with verbal and non-verbal psychometric tests. The filled and unfilled delays were much longer than those that have been used in most previous studies of retroactive interference: 10 min in Experiment 1 and 1 h in Experiment 2. The most important finding is simply that some patients benefited a great deal from an omission of retroactive interference. For example, in three of the patients, as shown in Table 1, after 1 h long intervals (in Experiment 2), the retention of what had been recalled before the interval was 0% when the interval included interference but 63, 78 and 85% of that material after no interference. Notably, this marked benefit of reduced interference accrued even though the interfering materials were not words from the same set as the memoranda. In Experiment 2, over an hour long test delay, the benefit accrued even when participants presumably did not engage in

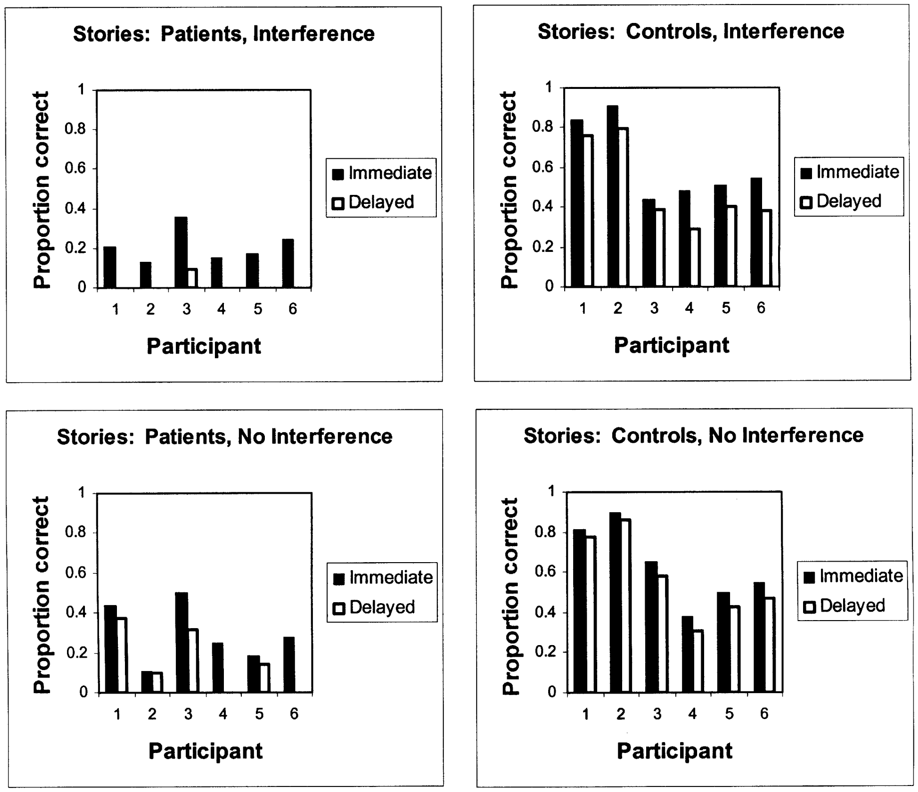

Fig. 2 Proportion of words recalled from stories by amnesic patients (left-hand panels) and normal control participants (right-hand panels) immediately after the story (black bars) and in a retest following a 1 h delay (white bars). Sometimes the delay was filled with extraneous cognitive tasks (top panels, interference), whereas other times the participant rested in a quiet, dark room during the delay (bottom panels, no interference). The loss of memory during the delay was greatly reduced in the no interference condition.

continuous rehearsal (given the long time period and the presence of snoring in several patients displaying improved delayed retention).

The findings are relevant to the theoretical view in which a unitary set of rules underlies both short- and long-term memory (e.g. Nairne, 2002) because it suggests that the most recently presented stimuli may not inevitably fade from memory within a matter of seconds, as in the traditional view. Instead, the most recently presented stimuli may remain accessible until additional stimuli are presented.

Researchers previously have advocated that memory performance in brain-damaged patients may be overwhelmingly affected by interference (Incisa della Rocchetta and Milner, 1993; Moscovitch, 1994; Shimamura *et al.*, 1995; Thompson-Schill *et al.*, 2002). However, these studies mainly focused on the effect of proactive interference on the ability to retrieve newly learned information by patients with frontal lobe lesions (reviewed in Baldo and Shimamura, 2002). The point has not been established empirically until now for amnesiacs who do not have executive function deficits (some of whom do not even appear to have frontal lobe damage), and it has not often been investigated for the case of retroactive interference. This kind of interference is pervasive in daily life, given that the target and interfering items need not be similar for interference to occur. No previous article has predicted our finding of a marked improvement in memory retention in amnesiacs following a protracted, no interference test delay.

Given the patients' poor performance in all tests assessing long-term memory functions, including visual and verbal delayed recall and paired-associate learning, it is unlikely that some of the retention we observed in the absence of retroactive interference is due to sparing of long-term memory functions as tested by classic tests. Our findings lead to a revised view of the deficit in some cases of amnesia due to stroke or head injury. Amnesia in at least some such patients results in the formation of memory representations that do not remain accessible once their status as the most recent stimuli is lost. Thus, items in memory would be lost on the basis of displacement but not on the basis of the passage of time *per se*.

With this revised view of memory, it remains to be explained why patients 4 and 6 could not retrieve the most recent material following a long, empty retention interval. Perhaps in addition to an impairment of long-term memory, a short-term episodic buffer (Baddeley, 2000) is impaired in these patients.

As this discrepancy between patients suggests, our procedure may be of use in distinguishing between different types of amnesia. Ever since the seminal papers by Huppert and Piercy (1978, 1979), there has been considerable emphasis in trying to tease apart the putative differences between patients whose amnesia results from diencephalic versus medial temporal lobe lesions, with only qualified success (e.g. Warrington and Weiskrantz, 1970, 1974; Stanhope *et al*., 1998; Mayes and Roberts, 2001; Kopelman, 2002; Conway and Fthenaki, 2003; Mayes *et al*., 2003). Using our procedures, the two patients whose lesion involved the temporal lobe (patients 4 and 6 in Table 1) did not show any benefit from minimizing interference. These patients differed from the others very little in their behavioural performance. They did not differ noticeably in the severity of their amnesia except in no interference conditions. Age is not the critical issue, nor is aetiology. Performance in the target test cannot account for the different outcome either, because these two patients did not perform less well than the others on immediate recall. The pattern obtained in the general neuropsychological examination is not indicative of a different cognitive profile. The only apparent difference between these two patients and the others is the anatomical locus of the lesion, which includes the temporal lobes in patients 4 and 6 but not in the other four patients. Similarly, Della Sala *et al*. (2004) reported that patients with minimal cognitive impairment benefited from no interference conditions, whereas patients with mild Alzheimer's disease did not; once more, a salient difference between these groups is the more severe atrophy of the hippocampus in the latter group (Dickerson *et al*., 2001). Therefore, as a very tentative hypothesis (to be investigated in future studies with larger groups and precise measures of lesion sites), we suggest that temporal lobe amnesia may not be moderated by retroactive interference over a period of 10 min or more, but that amnesia associated with lesions that do not encroach upon the temporal lobes or the hippocampus is moderated by it.

Finally, the study also suggests the possibility of therapeutic applications. At least patients 1 and 2 were aware of the substantial benefit of the low interference condition for their memory performance and were excited about it, and patient 1's wife was quite surprised at its success. They in fact asked for training using the technique. Reduced interference may be useful within a rehabilitation regimen for some cases of amnesia.

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References

Baddeley AD. Human memory. Theory and practice. Rev edn. Hove (UK): Psychology Press; 1997.

Baddeley A. The episodic buffer: a new component of working memory? Trends Cogn Sci 2000; 4: 417–23.

Baddeley AD, Warrington EK. Amnesia and the distinction between long- and short-term memory. J Verb Learn Verb Behav 1970; 9: 176–89.

Baddeley A, Wilson BA. Prose recall and amnesia: implications for the structure of working memory. Neuropsychologia 2002; 40: 1737–43.

Baldo JV, Shimamura AP. Spatial and color working memory in patients with lateral prefrontal cortex lesions. Psychobiology 2000; 28: 156–67.

Baldo JV, Shimamura AP. Frontal lobes and memory. In: Baddeley AD, Kopelman, MD, Wilson BA, editors. The handbook of memory disorders. 2nd edn. Chichester (UK): John Wiley; 2002. p. 363–79.

Baldo JV, Delis D, Kramer J, Shimamura AP. Memory performance on the California Verbal Learning Test—II: findings from patients with focal frontal lesions. J Int Neuropsychol Soc 2002; 8: 539–46.

Bartus RT, Levere TE. Frontal decortication in rhesus monkeys: a test of the interference hypothesis. Brain Res 1997; 119: 233–48.

Basso A, Capitani E, Laiacona M. Raven's Coloured Progressive Matrices: normative values on 305 adult normal controls. Funct Neurol 1987; 2: 189–94.

Bortolini U, Tagliavini C, Zampolli A. Lessico di frequenza della lingua Italiana contemporanea. Milan: Garzanti; 1972.

Brazzelli M, Della Sala S, Laiacona M. Taratura della versione Italiana del Rivermead Behavioural Memory Test: un test di valutazione ecologica della memoria. Supplemento al Manuale del TMCR. Florence: Organizzazioni Speciali; 1993.

Brazzelli M, Capitani E, Della Sala S, Spinnler H, Zuffi MA. Neuropsychological instrument adding to the description of patients with suspected cortical dementia: the Milan Overall Dementia Assessment. J Neurol Neurosurg Psychiatry 1994; 57: 1510–7.

Broadbent DE. Perception and communication. Oxford: Pergamon Press. 1958.

Caffarra P, Vezzadini G, Dieci F, Zonato F, Venneri A. Rey–Osterrieth complex figure: normative values in an Italian population sample. Neurol Sci 2002; 22: 443–7.

Capitani E, Della Sala S, Laiacona M, Marchetti C, Spinnler H. Standardizzazione ed uso clinico di un test di memoria di prosa. Boll Psicol Appl 1994; 209: 47–63.

Carlesimo GA, Caltagirone C, Gainotti G. The Mental Deterioration Battery: normative data, diagnostic reliability and qualitative analyses of cognitive impairment. The Group for the Standardization of the Mental Deterioration Battery. Eur Neurol 1996; 36: 378–84.

Chao LL, Knight RT. Human prefrontal lesions increase distractibility to irrelevant sensory inputs. Neuroreport 1995; 6: 1605–10.

Chater N, Brown GDA. Scale-invariance as a unifying psychological principle. Cognition 1999; 69: B17–24.

Cohen NJ. Preserved learning capacity in amnesia: evidence for multiple memory systems. In: Squire LR, Butters N, editors. Neuropsychology of memory. New York: Guilford Press; 1984: 83–103.

Conway MA, Fthenaki K. Disruption of inhibitory control of memory following lesions to the frontal and temporal lobes. Cortex 2003; 39: 667–86.

Cowan N. Attention and memory: an integrated framework. Oxford Psychology Series, No. 26. Oxford: Oxford University Press; 1995.

Cowan N, Saults S, Nugent L. The ravages of absolute and relative amounts of time on memory. In: Roediger HL III, Nairne JS, Neath I, Surprenant A, editors. The nature of remembering: essays in honor of Robert G. Crowder. Washington (DC): American Psychological Association; 2001. p. 315–30.

De Bleser R, Denes F, Luzzatti C, Mazzucchi A, Poeck K, Spinnler H, et al. L'Aachener Aphasie Test (AAT). Problemi e soluzioni per una versione italiana del test e per lo studio crosslinguistico dei disturbi afasici. Arch Psicol Neurol Psichiatria 1986; 47: 209–37.

De Renzi E, Faglioni P. Normative data and screening power of a shortened version of the Token Test. Cortex 1978; 14: 41–9.

Della Sala S, Cowan N. Beschin N. Perini M. Just lying there, remembering: improving recall of prose in amnesic patients with mild cognitive impairment by minimizing interference. Memory. In press 2004.

Dickerson BC, Goncharova I, Sullivan MP, Forchetti C, Wilson RS, Bennett DA, et al. MRI-derived entorhinal and hippocampal atrophy in incipient and very mild Alzheimer's disease. Neurobiol Aging 2001; 22: 747–54.

Drachman DA, Arbit J. Memory and the hippocampal complex. Arch Neurol 1966; 15: 52–61.

Freedman M, Cermak LS. Semantic encoding deficits in frontal lobe disease and amnesia. Brain Cogn 1986; 5: 108–14.

Geffen GM, Butterworth P, Forrester GM, Geffen LB. Auditory verbal learning test components as measures of the severity of closed-head injury. Brain Inj 1994; 8: 405–11.

Giovagnoli AR, Del Pesce M, Mascheroni S, Simoncelli M, Laiacona M. Capitani E. Trail making test: normative values from 287 normal adult controls. Ital J Neurol Sci 1996; 17: 305–9.

Hodges JR, Ward CD. Observations during transient global amnesia: a behavioural and neuropsychological study of five cases. Brain 1989; 112: 595–620.

Huppert FA, Piercy M. The role of trace strength in recency and frequency judgements by amnesic and control subjects. Q J Exp Psychol 1978; 30: 347–54.

Huppert FA, Piercy M. Normal and abnormal forgetting in organic amnesia: effect of locus of lesion. Cortex 1979; 15: 385–90.

Incisadella Rocchetta I, Milner B. Strategic search and retrieval inhibition: the role of the frontal lobes. Neuropsychologia 1993; 31: 503–524.

Janowsky JS, Shimamura AP, Kritchevsky M, Squire LR. Cognitive impairment following frontal lobe damage and its relevance to human amnesia. Behav Neurosci 1989; 103: 548–60.

Jenkins JG, Dallenbach KM. Oblivescence during sleep and waking. Am J Psychol 1924; 35: 605–12.

Kopelman MD. Disorders of memory. Brain 2002; 125: 2152–90.

Malmo RB. Interference factors in delayed response in monkeys after removal of frontal lobes. J Neurophysiol 1942; 5: 295–308.

Maquet P, Laureys S, Peigneux P, Fuchs S, Petiau C, Phillips C, et al. Experience-dependent changes in cerebral activation during human REM sleep. Nat Neurosci 2000; 3: 831–6.

Mayes AR, Roberts N. Theories of episodic memory. Philos Trans R Soc Lond B Biol Sci 2001; 356: 1395–408

Mayes AR, Downes JJ, Symons V, Shoqeirat M. Do amnesics forget faces pathologically fast? Cortex 1994; 30: 543–63.

Mayes AR, Isaac CL, Holdstock JS, Cariga P, Gummer A, Roberts N. Long-term amnesia: a review and detailed illustrative case study. Cortex 2003; 39: 567–603.

McGeoch JA, McDonald WT. Meaningful relation and retroactive inhibition. Am J Psychol 1931; 43: 579–88.

Milner B. Disorders of memory after brain lesions in man. Neuropsychologia 1968; 6: 175–9.

Minami H, Dallenbach KM. The effect of activity upon learning and retention in the cockroach. Am J Psychol 1946; 59: 1–58.

Moscovitch M. Multiple dissociations of function in amnesia. In: Cermak LS, editor. Human memory and amnesia. Hillsdale (NJ): Lawrence Erlbaum; 1982. p. 337–374.

Moscovitch M. Memory and working with memory: evaluation of a component process model and comparisons with other models. In: Schacter DL, Tulving E, editors. Memory systems. Cambridge (MA): MIT Press; 1994. p. 269–310.

Nairne JS. Remembering over the short-term: the case against the standard model. Annu Rev Psychol 2002; 53: 53–81.

Neath I, Nairne JS. Word-length effects in immediate memory: overwriting trace decay theory. Psychon Bull Rev 1995; 2: 429–41.

Novelli G, Papagno C, Capitani E, Laiacona M, Cappa SF, Vallar G. Tre test clinici di memoria verbale a lungo termine. Taratura su soggetti normali. Arch Psicol Neurol Psichiatria 1986; 47: 278–96.

Ogden JA. Marooned in the moment. In: Ogden JA. Fractured minds. A case-study approach to clinical neuropsychology. New York: Oxford University Press; 1996. p. 41–58.

Orsini A, Grossi D, Capitani E, Laiacona M, Papagno C, Vallar G. Verbal and spatial immediate memory span: normative data from 1355 adults and 1112 children. Ital J Neurol Sci 1987; 8: 539–48.

Petersen RC, Smith GE, Waring SC, Ivnik RJ, Tangalos EG, Kokmen E. Mild cognitive impairment. Clinical characterization and outcome. Arch Neurol 1999; 56: 303–8.

Peterson LR, Peterson MJ. Short-term retention of individual verbal items. J Exp Psychol 1959; 58: 193–8.

Quinette P, Guillery B, Desgranges B, de la Sayette V, Viader F, Eustache F. Working memory and executive functions in transient global amnesia. Brain 2003; 126: 1917–34.

Romani C, Martin R. A deficit in the short-term retention of lexical–semantic information: forgetting words but remembering a story. J Exp Psychol Gen 1999; 128: 56–77.

Schacter DL. Implicit memory: history and current status. J Exp Psychol Learn Mem Cognit 1987; 13: 501–18.

Scoville WB, Milner B. Loss of recent memory after bilateral hippocampal lesions. J Neurol Neurosurg Psychiatry 1957; 20: 11–21.

Shimamura AP. Memory and frontal lobe function. In: Gazzaniga MS, editor. The cognitive neurosciences. Cambridge (MA): MIT Press, 1995. p. 803–13.

Shimamura AP, Jurica PJ, Mangels JA, Gershberg FB, Knight RT. Susceptibility to memory interference effects following frontal lobe damage: findings from tests of paired-associate learning. J Cogn Neurosci 1995; 7: 144–52.

Spinnler H, Tognoni G, editors. Standardizzazione e taratura italiana di test neuropsicologici. Ital J Neurol Sci 1987; 6 Suppl 8: 1–120.

Squire LR, Knowlton BJ. The medial temporal lobe, the hippocampus, and the memory systems of the brain. In: Gazzaniga MS, editor. The new cognitive neurosciences. 2nd edn. Cambridge (MA): MIT Press; 2000. p. 765–79.

Stanhope N, Guinan E, Kopelman MD. Frequency judgements of abstract designs by patients with diencephalic, temporal lobe or frontal lobe lesions. Neuropsychologia 1998; 36: 1387–96.

Stickgold R, James L, Hobson JA. Visual discrimination learning requires sleep after training. Nat Neurosci 2000; 3: 1237–8.

Thompson-Schill SL, Jonides J, Marshuetz C, Smith EE, D'Esposito M, Kan IP, et al. Effects of frontal lobe damage on interference effects in working memory. Cogn Affect Behav Neurosci 2002; 2: 109–20.

Warrington EK, Weiskrantz L. Amnesic syndrome: consolidation or retrieval. Nature 1970; 228: 628–30.

Warrington EK, Weiskrantz L. The effect of prior learning on subsequent retention in amnesic patients. Neuropsychologia 1974; 12: 419–28.

Warrington EK, Weiskrantz L. Further analysis of the prior learning effect in amnesic patients. Neuropsychologia 1978; 16: 169–77.

Waugh NC, Norman DA. Primary memory. Psychol Rev 1965; 72: 89–104.

Wilson BA, Cockburn J, Baddeley AD. The Rivermead behavioural memory test. Bury St Edmunds (UK): Thames Valley Test Company; 1985.

Zola-Morgan S, Squire LR. Medial temporal lesions in monkeys impair memory on a variety of tasks sensitive to human amnesia. Behav Neurosci 1985; 99: 22–34.