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Just lying there, remembering: Improving recall of prose in amnesic patients with mild cognitive impairment by minimising interference

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The hallmark of amnesia is poor explicit long-term memory along with normal short-term memory. It is often stated that information encountered by amnesic patients is forgotten within 1 minute of presentation. However, previous work has not distinguished between forgetting as a function of time versus the interfering material occupying that time. We show that there is a marked benefit of reduced interference in amnesic patients with mild cognitive impairment (MCI), a condition that is characterised by anterograde amnesia in the absence of other neuropsychological deficits and carries an increased risk for Alzheimer's disease. The result suggests that long-term memory is encoded in these patients to a greater extent than had been realised but that their memory is highly vulnerable to interference.

The hallmark of anterograde amnesia is fast forgetting of material to be remembered. Typically, amnesic patients retain verbal information for no longer than 1 minute. If the forgetting were inevitable, it would allow the possibility that the event has not been encoded into the memory system used for voluntary, conscious recollection. In contrast, if memory could be retrieved under conditions of reduced interference, this would indicate that the encoding did occur, at least in a weakened form.

The shallow encoding could take two forms. The information could remain in an active or conscious form continually in memory (i.e., in working memory; see Baddeley, 1986; Cowan, 1995) from the time of its presentation until the time of recall. Alternatively, the information could be encoded in a form that becomes dormant or inactive, leaving consciousness (i.e., in long-term memory), and yet could remain available for retrieval so long as subsequent events are too weak to interfere with the original encoding context.

Every seasoned clinician may notice that anterograde amnesic patients are vulnerable to interference. However, there are few objective data on it and, in clinical situations, it is next to impossible to determine the role of interference as

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opposed to the passage of time because patients (like the rest of us) are rarely free of interference for more than a few minutes. To examine this issue, we investigated the role of interference in verbal recall. To minimise the possible role of active rehearsal we relied on prose memory with immediate and 1-hour-delayed recall. This was prompted by the recent report that amnesic patients show a relative good performance on immediate recall of prose passages (Baddeley & Wilson, 2002). The critical manipulation was the use of ordinary interference and very-low-interference conditions during the hour-long retention interval. If recall in amnesic patients can be improved by reducing interference, that finding would show that they do encode information into a system that can be used for deliberate, verbal recall, despite the popular view to the contrary. The suggestion that amnesic patients may suffer exaggerated effects of retroactive interference can be gleaned from the literature (e.g., Moscovitch, 1994; Shimamura, Jurica, Mangels, Gershberg, & Knight, 1995). However, until now, this hint has not been backed up empirically.

Cowan, Beschin, and Della Sala (2004) used this type of test with six amnesic patients who had a variety of brain lesions and found that four of them benefited profoundly from reduced interference during a 1-hour retention interval, whereas the other two showed no benefit. At this point it is unclear why only some benefited and it would help to observe the effect in a defined subcategory of amnesia. For that purpose, patients with mild cognitive impairment (MCI) were recruited. They are well-suited to this test because they display anterograde amnesia in the absence of overt dementia or other neuropsychological deficits. Fortunately for this work, as well, their immediate recall appears to be fairly comparable to that of normal control participants, allowing valid comparisons of forgetting (see below). They are also of special practical concern because MCI carries an increased risk for developing Alzheimer's disease (Petersen, Smith, Waring, Ivnik, Tangalos, & Kokmen, 1999).

TABLE 1
Demographic features of the MCI patients entering the study and their performance in the diagnostic tests

MCI Patient Number	*Age*	*Education (years)*	*MMSE score*[a]	*Rey-type Word List Delayed*[b]
1	73	8	30	3.9
2	66	5	30	1.8
3	68	5	30	2.4
4	80	5	26.03	3.1
5	72	5	27.03	2.4
6	76	5	30	3.1
7	50	8	29.07	2.6
8	56	5	28.24	0.7
9	66	5	29.99	2.8
10	67	5	30	4.4

[a] Score range, 0–30; cut-off for normal performance, 23.8 (for the Italian population). Scores adjusted for age and education (Measso et al., 1993).

[b] Fifteen-word lists learning delayed recall. Score range, 0–15; cut-off for normal performance, 4.69 (Carlesimo et al., 1996).

METHOD

Participants

Ten patients with MCI (six women and four men, mean age = 67.40 years, *SD* = 8.96; mean education = 5.60 years, *SD* = 1.26) are described in Table 1, which gives ages, education, and criterion scores for the patients, and Table 2, which gives further psychometric test data for them. No MCI patients were included in Cowan et al. (2004). A group of ten age-matched, healthy controls (five women and five men, mean age = 68.30 years, *SD* = 5.79, mean education = 5.4 years, *SD* = 0.96) also participated in this experiment. All MCI patients entering the study had a history of incipient anterograde memory deficits as evinced from clinical notes, relatives' reports, and interview with the patients and their caregivers; no signs of focal lesions (examined in computerised tomography or magnetic resonance imaging); no signs of abnormalities in the neurological examination; a normal Mini-Mental Examination score; and normal blood tests (e.g., cell counts, thyroid hormones levels, syphilis serologic testing, vitamin B_{12} and folic acid levels). Moreover, none of the patients had a history of psychiatric illness or was taking psychoactive drugs at the time of testing, and they showed no hints of depression as assessed by the Beck Depression Inventory (Beck, 1961). They all had a Clinical Dementia Rating Scale (CDR; Hughes, Berg, Danziger, Coben, & Martin, 1982) score equal to 0.5, indicating an overwhelming deficit of memory as compared to all other cognitive domains and activities of daily living, and they scored above 9 (i.e., within the normal range) in the test of Instrumental Activities of Daily Living (IADL; Lawson & Brody,

TABLE 2
Neuropsychological profile of the MCI patients

MCI Patient Numer	*Naming*	*Token Test*	*Phonetic Fluency*	*Semantic Fluency*	*Word List Learning Immediate*	*Digit Span*	*Spatial Span*	*Rey Figure Immediate*	*Rey Figure Delayed*	*Trail Making*
1	9	35	31.7	16.75	28.9	9.25	7.25	36	9.75	136
2	9	33	34.9	21.25	18.1*	5.5	5.5	36	6.75*	145
3	9	35	32.6	20.0	38.0	6.5	6.5	35	6.75*	92
4	9	31	25.7	14.25	36.2	4.75	4.75	36	7.75*	81
5	9	32	26.6	19.6	28.0*	4.5	4.5	36	9.75	116
6	9	31	30.4	16.75	30.0	4.5	4.5	32.75	11.75	168
7	9	35	24.1	18.5	23.3*	6.0	6.0	35.25	3.5*	124
8	9	32	24.8	16.75	17.8*	4.5	4.25	36	5.5*	81
9	9	32	21.25	10.25	20.1*	5.5	4.25	33.25	6.75*	122
10	9	34	28.9	14.25	33.1	5.5	6.25	36	5.5*	114

Scores are age- and education-adjusted. Asterisk (*) indicates performances below the normal cut-off score. Naming test from the *Aachener Aphasie Test*—AAT, 120 stimuli, cut-off score: 8 (De Bleser et al., 1986). *Token Test*, score range: 0–36, cut-off score: 26.5 (De Renzi & Faglioni, 1978). *Phonemic Verbal Fluency*, words beginning with F, A, or S, cut-off score: 17.35 (Carlesimo et al., 1996). *Semantic Verbal Fluency*, names of colours, animals, fruit, cities, cut-off score: 7.25 (Spinnler & Tognoni, 1987). *Rey-type Word List Learning* (15 word list, repeated five times), score range: 0–75, cut-off score: 28. 53 (Carlesimo et al., 1996). *Digit Span* (Orsini et al., 1987), cut-off score: 3.5 (digit span in Italian is generally lower than in English due to the longer pronunciation times of the digits). *Spatial Span* (Orsini et al., 1987), cut-off score: 3.25. *Rey Figure Immediate*, score range: 0–36, cut-off score: 28.87 (Cafarra et al., 2002). *Rey Figure Delayed*, score range 0–36, cut-off score: 9.46 (Caffarra et al., 2002). *Trail Making*, time in seconds, section A—section B, the higher the worse, cut-off score: 187 (Giovagnoli et al., 1996).

1969). Moreover, they scored below the normal cut-off in the delayed recall of the Rey-type Word List Recall Test (Carlesimo, Caltagirone, & Gainotti, 1996). On the other hand, all patients scored above the cut-off in tests assessing language comprehension (including normal performance with the long sentences of the Token Test) and production, and in verbal fluency, immediate copying of a geometrical figure, Trail Making, and verbal and spatial short-term memory (see Table 2). Finally, none of the patients showed signs of dementia when retested to this end after 6 months.

Materials and procedure

All participants were presented with four stories orally (selected from a pool of seven standardised passages), were asked for immediate verbatim recall, and then were asked for delayed recall an hour later. The stories were in Italian, the mother tongue of all participants, and were derived from the available literature (Brazzelli, Della Sala & Laiacona, 1993; Capitani, Della Sala, Laiacona, Marchetti, & Spinnler, 1994; Spinnler & Tognoni, 1987). The length of the stories varied from 21 to 64 content words and verbatim recall was scored with credit for all correct content words that conveyed the correct meaning. Cowan et al. (2004) reported inter-rater reliabilities for recall scoring of > .95 for each condition. The proportion of retention (delayed recall as a proportion of the preceding immediate recall on the same trial) was used in the analyses.

Two of the stories were followed by a 1-hour test delay filled with various psychometric tasks to create a standard amount of interference. The other two stories were followed by a delay in which the participant reclined in a dark, quiet room for the entire 1-hour period to minimise interference. They were not told that delayed recall would be requested, although a participant theoretically might expect this after the first trial. Experimental testing took place in two sessions carried out on different days. The selection of stories for each condition and the order of conditions were random but proved to be well-matched across groups and conditions.

RESULTS

Average proportions of immediate recall (with standard errors of the mean) were similar across groups: .49 (.05) and .46 (.04), respectively, for the healthy controls and the patient group. Retention in delayed tests was measured on each trial as the amount recalled following the delay divided by the amount recalled in the immediate test on the same trial (i.e., delayed/immediate). Healthy controls showed an average retention of .80 (.03) with the usual interference and .89 (.05) with minimal interference. The MCI patients showed a marked difference, from .20 (.03) with the usual interference up to .55 (.05) with minimal interference (see Figure 1).

In an analysis of variance of the retention with the patient group as a between-participant factor and the interference condition as a within-participant factor, both main effects and the interaction all were highly significant, $p < .001$ in each case. Group: $F(1, 18) = 80.48$, $MSE = 0.03$; Interference, $F(1, 18) = 76.96$, $MSE = 0.01$; interaction, $F(1, 18) = 27.19$, $MSE = 0.01$. We do not interpret the interaction because of ceiling effects in the controls, and the poorer overall retention in amnesic patients simply reflects their amnesic deficit in delayed recall.

The key finding is that separate analyses for each of the two participant groups showed that the retention was significantly larger for the minimal-interference condition than for the usual-interference condition in both groups ($p < .001$ in both cases). The improvement of retention by reducing interference perhaps would have been predicted by most investigators for normal controls, but this improvement is newsworthy and informative for amnesic patients.

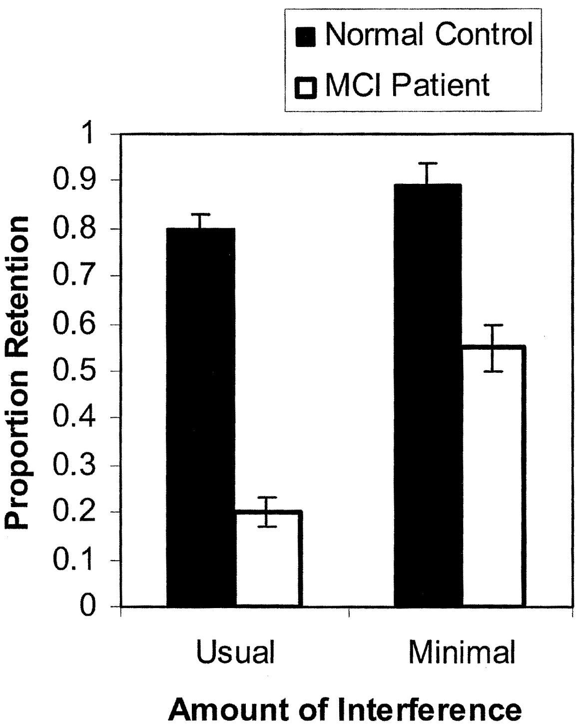

Figure 1. Proportion retention in the experimental story recall task following usual interference (left) and minimal interference (right) for normal control participants (dark bars) and MCI patients (white bars). Retention is calculated on each trial as the proportion of correct verbatim recall in 1-hour-delayed recall relative to (divided by) immediate recall. Error bars are standard errors.

The performance characteristics of each patient on the story recall task are reported in Table 3. There was a large amount of individual difference in the extent to which patients benefited from minimisation of interference. It is not yet clear why this difference occurs. Notice, for example, that Patient 4 went from a retention score of 0 with the usual interference to .38 with interference minimised, whereas Patient 6 went from 0 only to .08, and thus benefited much less than Patient 4. This cannot be easily attributed to differences in their levels of immediate recall, which were fairly similar as the table shows. Among all 10 patients, the relation between retention in the minimal-interference and usual-interference conditions was significant, $r = .67$. However, considering all of the variables presented in Tables 1–3, there were no other correlations with retention in the minimal-interference condition. (There was an almost-significant correlation between the level of immediate recall and retention in the *usual* interference condition, $r = .61$. Immediate recall also was significantly correlated with age, $r = -.72$, and performance on the Token Test, $r = .66$.)

A final important issue is what patients did during the unfilled delay period. It is possible that some of them reminisced about the story for at

TABLE 3
Individual mean performance characteristics of the MCI patients in the experimental prose recall tasks

Patient	*Imm. recall: Prop. correct*	*Interference: Retention (del./imm.)*	*No interference: Retention (del./imm.)*
1	.52	.14	.54
2	.54	.25	.48
3	.58	.40	.59
4	.20	.00	.38
5	.50	.33	.67
6	.32	.00	.08
7	.57	.31	.61
8	.61	.11	.62
9	.40	.32	.88
10	.46	.14	.67

Imm. = immediate, del. = delayed, prop. = proportion.

least part of the interval and thus retained elements of the story in working memory. However, Patients 3 and 7 were observed to snore throughout portions of both unfilled delays and therefore could not have maintained the information in working memory, unless working memory is found to continue during sleep. As Table 3 shows, these patients nevertheless appeared to benefit from the reduction of interference. The case is clearest for Patient 7, who went from .31 retention with usual interference to .61 retention with minimal interference despite snoring under minimal interference.

DISCUSSION

Minimal-interference conditions resulted in much better delayed recall than the usual-interference condition in the MCI patients. Since patients with Alzheimer disease (AD) perform at floor in delayed retrieval of prose passages (e.g., Spinnler & Della Sala, 1988) and in our own pilot studies they did not benefit from the minimal interference condition, this procedure may add to the much sought (see e.g., Petersen et al., 1999) differential diagnosis between MCI and AD.

These findings could hardly be accounted for by postulating the use of subvocal rehearsal during the no-interference condition, for several reasons. First, the delay was long enough to discourage the strategy of sheer rehearsal. Second, several participants fell asleep (and, as noted, some snored) during the retention interval, as testified by the experimenter's regular checks. Third, during the debriefing session, only Patient 7 volunteered that she used subvocal rehearsal as a strategy to optimise recall (and that attempt would have been affected by short-term memory loss during sleep). Hence, long-term retrieval, rather than only short-term rehearsal, seems improved by the lack of interference. As a precursor to this work, Jenkins and Dallenbach (1924) found that memory was spared in two normal participants during sleeping periods compared to when they were awake, and attributed the spared memory to the lack of interference during sleep.

In summary, we have shown that the deficit underlying amnesia in MCI is characterised by increased vulnerability to interference and that reducing the interference can result in a substantial increase in memory performance. These findings indicate that amnesia, or at least that characterising MCI, does not necessarily imply an absence of memory encoding and that new explicit memory representations can be constructed by MCI patients. However, these memory traces are highly susceptible to interference from intervening events.

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