9 Forgetting due to retroactive interference in amnesia

Findings and implications

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Imagine the improbable. A man with a dense anterograde amnesia is lying in bed at night, at home, watching television while his wife, who generally strives to be at his side, steps out of the room to take a shower. During that time, there is a power failure and both the man and his wife are left in the dark and the silence, separated for all of 7 minutes while she gropes around for her towel, glasses, and so on. She is worried because he might have time to become disoriented, forget what he was doing, and come looking for her. When she finally makes it back to the bedroom, it is still dark and her husband, who hears her coming, states, "I was just watching a show about dog tricks." The wife is astounded, as her husband has not remembered anything for this long since before his stroke.

This is a fictional scenario but we have been recently confronted with data even more astounding than this (Cowan, Beschin, & Della Sala, 2004; Della Sala, Cowan, Beschin, & Perini, 2005; Dewar, Fernandez Garcia, Cowan & Della Sala, 2009). What follows is a description of what we have found, and our attempt to reconcile it with other evidence on the nature of amnesia and the memory system. We believe that there are profound implications.

Anterograde amnesia

Envisage a life in which all currently perceived and experienced information and events fade away as soon as they are no longer the focus of your attention. Life would be spent in the here and now; nothing would remain for more than a few seconds. Currently perceived information, such as this paragraph, or the librarian who may have just given you this book, would appear entirely novel if encountered again, even after the briefest of delays. The philosopher

Friedrich Nietzsche (1844–1900) tried to see the bright side of such plight, arguing that: "The advantage of a bad memory is that one enjoys several times the same good things for the first time."

However, for people who have suffered anterograde amnesia as a consequence of head injury, illness or a degenerative disease (e.g., Alzheimer's disease, AD), such forgetting is a most debilitating condition. This is perhaps most evocatively displayed by Clive Wearing, a professional musician who in his forties was left densely amnesic following viral encephalitis. Clive's amnesia was so severe that he repeatedly stated that he had only just now recovered consciousness. Even if his wife left his room for only a few minutes he would greet her on her return with great emotion, as if they had not seen each other for a very long time. Patients like Clive are clearly stuck in a moment, seemingly unable to retain anything for more than a few seconds. Is such severe forgetting inevitable though? Our recent work indicates that it need not be.

Studies on retroactive interference in anterograde amnesia

Cowan et al. (2004) presented 6 densely amnesic patients with a list of 15 words, which they were asked to recall immediately afterwards as well as after a 10-minute delay. This delay interval either simulated a standard memory assessment in that it was filled with further cognitive tasks, or it remained unfilled, meaning that the patient was left alone in a quiet, darkened testing room. Remarkably, 4 of the 6 patients showed substantially greater retention of the word list material that had been reproduced in immediate recall following the unfilled (49%) than the filled delay (14%). The data were even more astonishing when the delay was increased to 1 hour, and when short stories were used instead of word lists. When the retention period was filled with cognitive tasks, one patient recalled just 27% of what was recalled an hour earlier and the other 5 patients recalled nothing. When the retention period was spent in the quiet, dark room, however, the patient who had recalled 27% in delayed recall now went up to 63% in delayed recall. What is more amazing is that 3 patients who had recalled 0% with a task-filled retention interval now went up to 85%, 90%, and 78% in the absence of cognitive tasks. On average, these 4 patients (the same 4 as in the word list trials) went from 7% retention over a task-filled hour to an astounding 79% retention over an hour with no stimulation (see Figure 9.1).

Why some patients benefited from the minimization of interference while others did not is unclear, but differences in lesion loci and aetiology are likely candidates (Cowan et al., 2004). In order to minimize individual differences in aetiology and lesion loci, Della Sala et al. (2005) replicated Cowan et al.'s (2004) prose memory study with a sample of patients diagnosed with amnestic mild cognitive impairment (aMCI) (Petersen, Smith, Waring, Ivnik, Tangalos, & Kokmen, 1999). Such patients present with a degenerative isolated anterograde amnesia, which is often a harbinger of Alzheimer's

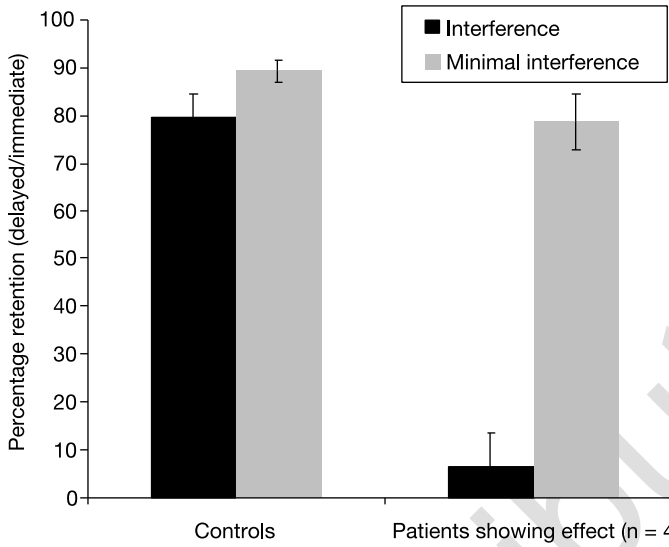

Figure 9.1 Mean percentage retention (delayed recall/immediate recall) of story material for 4 severely amnesic patients and 6 controls following a 1-hour delay interval, which was either filled with cognitive tasks (*retroactive interference*) or was spent alone in the quiet, darkened testing room (*minimal retroactive interference*). While the amnesic patients performed extremely poorly following the retroactive interference delay, all 4 showed remarkably high story retention following the minimal retroactive interference delay. Two further amnesic patients were tested but retained no story material in either delay condition. (Error bars = Standard error of the mean.) (Cowan et al., 2004)

disease. Again patients performed significantly better following the unfilled (55%) than the filled delay interval (20%). (Age- and education-matched controls showed a group mean percentage retention of 80% following the filled and 89% following the unfilled condition.) This is shown in Figure 9.2.

These remarkable findings clearly demonstrate that at least some amnesic patients can retain new information for much longer than is typically assumed if the time following learning is devoid of further information. This in turn suggests that forgetting in amnesia might be largely attributed to retroactive interference, i.e., the interference generated by material and tasks that follow new learning.

Can these novel findings be readily accounted for by existing cognitive theories of forgetting and models of memory? It seems not.

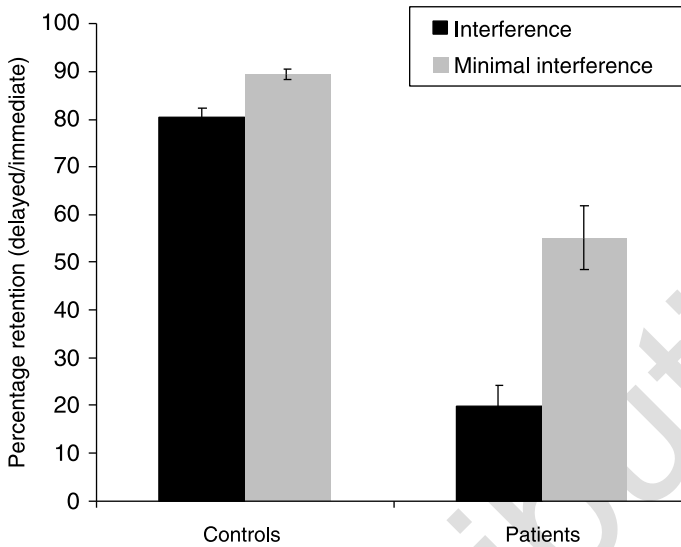

Figure 9.2 Mean percentage retention (delayed recall/immediate recall) of story material for 10 patients diagnosed with amnestic mild cognitive impairment (aMCI), a frequent harbinger of Alzheimer's disease, and 10 controls, following a 1-hour delay interval. The amnesic patients retained much more story material when the delay interval was spent alone in the quiet, darkened testing room (*minimal retroactive interference*) than when it was filled with cognitive tasks (*retroactive interference*). (Error bars = Standard error of the mean.) (Della Sala et al., 2005)

Existing cognitive theories of amnesia

The standard dual store account

Anterograde amnesia has been traditionally interpreted within a two-store model of memory, in which new information is passed from a temporary short-term memory (STM) store to a permanent long-term memory (LTM) store (Aktinson & Shiffrin, 1968). Amnesic patients are said to have intact STM but no new LTM, meaning that they are entirely reliant upon STM for retention of new information. However, in neurologically intact people as well as amnesic patients information in STM is said to decay rapidly (~ 30 seconds) unless it is maintained within consciousness, e.g., via explicit rehearsal. This traditional model is illustrated in Figure 9.3.

With this in mind, could it be that minimizing retroactive interference simply allows amnesic patients to consciously maintain new information within STM, thus effectively protecting it from STM decay? It is known already that amnesic patients, including the famous patient HM, can retain new information such as a three-figure number or a pair of unrelated words for longer than usual (several minutes) if they are not

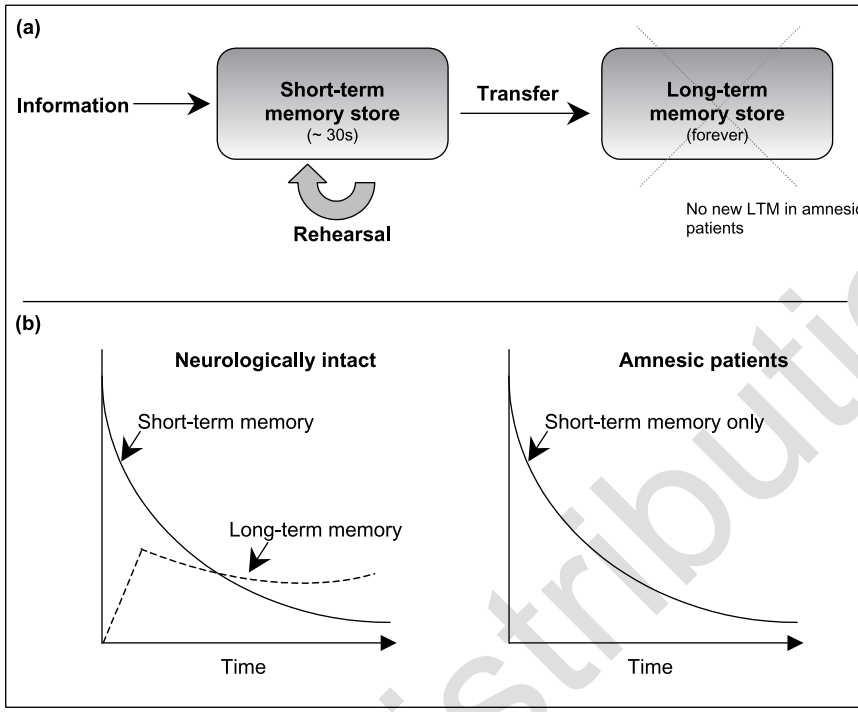

Figure 9.3 The traditional two-store model of memory (adapted from Aktinson & Shiffrin, 1968). New information is said to be transferred from a temporary short-term memory store to a permanent long-term memory store (a). Amnesic patients are postulated to have intact short-term memory but no new long-term memory. They are thus said to rely exclusively upon short-term memory for retention of new material. However, material within short-term memory decays rapidly (~30s) unless it is actively maintained within consciousness (e.g., via explicit rehearsal) (b).

distracted from such information (Milner, 1968; Ogden, 1996; Scoville & Milner, 1957).

However, several findings by Cowan et al. (2004) and Della Sala et al. (2005) speak against such a conscious rehearsal account of the data. First, the initial delayed recall came as a surprise, meaning that participants had little or no incentive to consciously rehearse the material for up to an hour, yet that did not lead to poorer recall than later trials. Moreover, two patients were observed to be sleeping through at least part of the retention interval with minimal retroactive interference, yet benefited from minimal retroactive interference as much as on other trials, and as much as other patients did.

Even stronger evidence against a mere conscious rehearsal account of the minimal retroactive interference-induced memory enhancement in amnesic patients comes from our subsequent work (Dewar et al., 2009). We hypothesized that if the augmented retention following minimal retroactive

interference in amnesic patients were solely the result of continuous STM maintenance based on rehearsal, with no additional LTM memory processing, amnesic patients should forget to-be-retained material as soon as retroactive interference interrupts rehearsal, irrespective of the prior duration of such rehearsal. If, on the other hand, a period of minimal retroactive interference allowed for some enhanced LTM processing in amnesic patients, some memory retention may persist even in the presence of retroactive interference, provided that such retroactive interference is preceded by a sufficient period of minimal retroactive interference (see Figure 9.4).

We presented 12 patients with aMCI and 12 age and IQ matched controls with a list of 15 words, which they were asked to recall immediately following word list presentation, and again after a 9-minute delay. This delay was either entirely unfilled (as in Cowan et al., 2004 and Della Sala et al., 2005), or it was filled with a 3-minute rehearsal-blocking interference task (naming presented line drawings). The critical manipulation was the temporal placement of this retroactive interference task within the otherwise unfilled delay. Retroactive

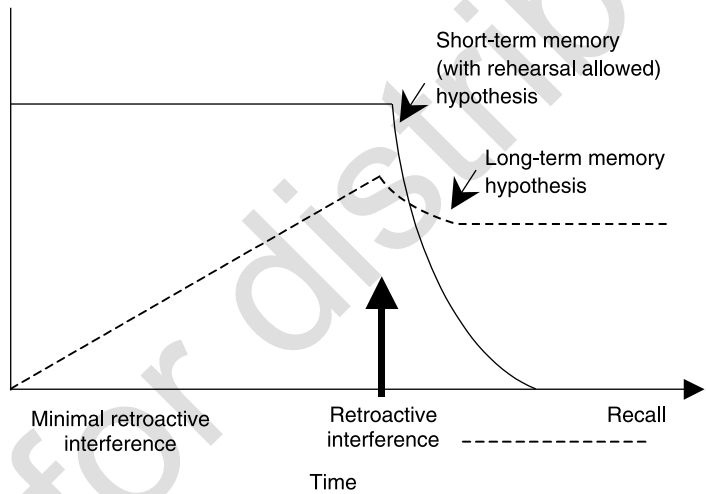

Figure 9.4 The benefit of minimal retroactive interference. Predictions made by a short-term memory hypothesis and a long-term memory hypothesis of the phenomenon. The short-term memory hypothesis predicts that a period of minimal retroactive interference allows amnesic patients to consciously maintain new information within their intact short-term memory. This new information, however, decays rapidly from short-term memory as soon as such conscious maintenance is interrupted via retroactive interference, leading to very poor retention. The long-term memory hypothesis, on the other hand, predicts that a period of minimal retroactive interference enhances long-term memory processing of the new material in amnesic patients. This enhanced processing is predicted to render new material less susceptible to subsequent retroactive interference. Some retention should therefore persist in the presence of retroactive interference, so long as this retroactive interference is preceded by a period of minimal retroactive interference.

interference was either placed in the first (early retroactive interference), the middle (mid-retroactive interference) or the last (late retroactive interference) portion of the delay.

As predicted from our previous retroactive interference work, the patients performed significantly better than usual when no retroactive interference was present during the delay interval. Most importantly, the patients also retained significantly more word list material when retroactive interference was delayed by 6 minutes (late retroactive interference) than when it was delayed by only 3 minutes (mid-retroactive interference), or when it occurred at the very beginning of the delay interval (early retroactive interference) (see Figure 9.5). All 12 patients showed the improvement from the early to the late condition, and 8 patients showed the improvement from the mid to the late condition, indicating that these findings were very robust indeed. Most remarkable was the finding that 8 of the tested patients recalled nothing when retroactive interference occurred at the start of the delay, yet they recalled between 30% and 70% when retroactive interference was delayed by 6 minutes.

These striking findings of an effect of the temporal placement of retroactive interference clearly conflict with an account of the minimal retroactive interference-induced memory enhancement in amnesia based only on STM with rehearsal. The early, mid and late interference conditions all included the same amount of rehearsal-disrupting interference. Mere rehearsal, in the absence of any LTM processing, should have thus only led to improved memory in the condition in which no interference was present. Memory performance in the early, mid and late conditions should have been equally poor.

Further evidence against such an STM-with-rehearsal notion comes from an unpublished case study on a 72-year-old highly educated patient who, as a consequence of limbic encephalitis, was left severely amnesic (Dewar, Cowan, & Della Sala, unpublished). This patient, PB (not his real initials), was entirely unable to recall a previously presented story following a 10-minute delay filled with a simple tone detection task. In striking contrast, when the delay was unfilled, PB was able to recall 66% of what he had repeated back 10 minutes before. Remarkably, he could still recall most of this information after a further 5-minute delay, during which we engaged him in a casual conversation entirely unrelated to the story. Indeed, we found that PB continued to be able to recall some of the story material following a further few of these short conversation-filled delays, a finding that resulted in much amazement in both himself and his wife. It would have certainly been near to impossible for PB to have continuously maintained the story material within consciousness while engaging in such unrelated conversations. Nonetheless, he was able to remember some new information.

The above findings indicate a clear incompatibility between our data and the standard two-store theory of forgetting in amnesia. Indeed, our data imply that some LTM functioning is spared in a number of amnesic patients, and that it is a LTM process, not merely STM maintenance, that is enhanced when retroactive interference is minimal.

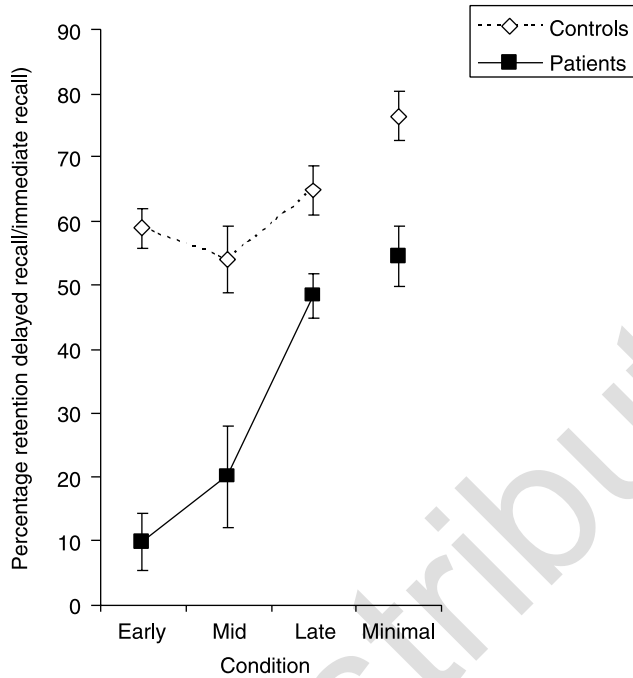

Figure 9.5 Mean percentage retention (delayed recall/immediate recall) of a word list for 12 severely amnesic patients (diagnosed with amnestic mild cognitive impairment) and 12 controls following a 9-minute delay interval, in which retroactive interference occurred either in the first 3 minutes (early), the middle 3 minutes (mid) or the last 3 minutes (late). An entirely unfilled delay (minimal) was also included. In line with a long-term memory hypothesis the patients were able to retain some word list material following retroactive interference, provided that this retroactive interference was preceded by at least 6 minutes of minimal retroactive interference (see early and mid vs. late conditions). According to a short-term memory hypothesis of the benefit of minimal retroactive interference patients should have only shown improved retention in the entirely unfilled (minimal) condition. Memory performance in the early, mid and late conditions should have been equally poor. The results strongly suggest that minimal retroactive interference enhances long-term memory in amnesic patients. (Dewar et al., 2009)

Long-term memory interference in amnesia

Which LTM process might minimal retroactive interference enhance in amnesic patients? There are two key possibilities. It may be the case that new information can reach LTM in amnesic patients but that their memory retrieval is greatly impaired, and thus that minimal retroactive interference facilitates LTM retrieval. Alternatively, it could be that minimal retroactive interference enhances an impaired LTM formation (consolidation) process in

amnesic patients. Both assume that at least some new LTM formation is possible in amnesic patients, thus conflicting with the standard cognitive theory of amnesia. We will discuss these two possibilities in turn.

Retrieval interference

Memory retrieval is essentially driven by retrieval cues, which activate the memory traces that best match that cue. Such cues can be explicit in that they aid a conscious memory search. For example, on being asked what one did for one's birthday 4 years ago, various memory traces matching "my birthday" will be activated and help one narrow down the search. Retrieval cues can also be implicit, relating to context (e.g., environmental factors and internal states). The powerful effect which such implicit retrieval cues can have on memory is beautifully illustrated by Marcel Proust who, upon tasting madeleine crumbs in his tea, is taken on a vivid and emotion-filled time travel back to his boyhood when his aunt indulged him with such treats on Sunday mornings.

Memories are said to be retrieved best if the encoding context matches the retrieval context closely, i.e., when features such as location, auditory, and visual information present at initial encoding are also present at retrieval (Tulving & Thomson, 1973). This was perhaps most famously demonstrated by Godden and Baddeley (1975), who showed that deep-sea divers learning a list of words under water recalled these better when under water than on land, and vice versa.

If a particular retrieval cue activates two or more memory traces, these memory traces are said to compete for retrieval, thus effectively inhibiting each other. In the above birthday example, it is possible that memory traces from a birthday party 2 years before and 7 years before interfere with the to-be-recalled birthday 4 years before. In the lab such retrieval interference can be induced experimentally via the presentation of two or more stimuli which are similar and/or share a retrieval cue (Dewar et al., 2007; Postman & Alpner, 1946; Skaggs, 1933; Wixted, 2004). For example, two subsequently presented lists of word pairs, which share a common cue word, such as *tree*–glass (List 1) and *tree*–train (List 2) tend to produce interference at retrieval when the cue (*tree*) is presented. Moreover, similar items learned in the same context are also more likely to interfere at retrieval when this context is also present during retrieval (Anderson & Bjork, 1994; Mensink & Raaijmakers, 1988).

Might minimal retroactive interference enhance retrieval in amnesic patients by keeping competing memory traces at bay? Such a hypothesis would imply that amnesic patients can form new memories but struggle to retrieve these when competing memory traces are present.

Research has shown that some patients with subtle memory impairment associated with executive dysfunction, who have difficulty planning their behaviours to meet their goals, present with such problems exactly (e.g.,

Baldo & Shimamura, 2002; Shimamura, Jurica, Mangels, Gershberg, & Knight, 1995). For example, Shimamura et al. (1995) report that in their dysexecutive patients the learning of a list of paired associates such as *lion–hunter* interfered substantially with the subsequent learning of a second list of paired associates, in which the cue word matched that of the first list, e.g., *lion–circus*. Their work hints that such increased interference also occurs in dysexecutive patients when to-be-retained information is followed by highly similar material (i.e., similar retroactive interference).

In the 1970s Warrington and Weiskrantz (1970, 1974) also proposed such a hypothesis for anterograde amnesia. However, they soon rejected this theory for various reasons, one being the lack of a benefit from a reduction of potentially competing memory traces (Warrington & Weiskrantz, 1978). Two decades later, Mayes, Isaac, Holdstock, Carriga, Gummer, and Roberts (1994) examined the effects of 12 minutes of similar retroactive interference (photos of faces) versus 12 minutes of unrelated retroactive interference (conversation and other activities that did not contain faces) on the retention of photos of faces in amnesic patients and also failed to find any evidence for a benefit from the reduction of competing memory traces (similar retroactive interference).

Unlike these studies, our own retroactive interference material bears little close resemblance to the to-be-retained material used in our studies. Therefore, if the observed minimal retroactive interference-induced memory enhancement were the sole product of a reduction of competing memory traces (i.e., similar retroactive interference), one would predict that our retroactive interference material would be ineffectual, and that amnesic patients therefore would perform similarly in our filled and unfilled conditions. This clearly is not the case, though.

Perhaps the threshold for similarity of memory traces is lower in amnesic patients than it is in neurologically intact people, meaning that memory traces need not be very similar for a substantial retrieval interference to occur in amnesia. But how might one account for the fact that the same material poses a greater detrimental effect on retrieval when placed at the beginning of the delay than at the end of the delay, as in the Dewar et al. (in press) data?

One could argue that the placement of the interfering material affects the context of that material. Mensink and Raaijmakers (1988) suggest that contexts fluctuate over time. Such contextual fluctuation might result in greater contextual overlap between to-be-retained material and immediately following retroactive interference stimuli than between to-be-retained material and delayed retroactive interference stimuli. Indeed, work in the immediate recall domain suggests that list items which are temporally isolated from other list items are retrieved more easily than list items that are in close temporal proximity to other list items (see Chapter 4). Importantly, however, with a contextual fluctuation conception one would also predict a larger contextual overlap between the retrieval context and the retroactive interference occurring at the end of the delay than between the retrieval context and earlier

retroactive interference. Thus, both early and late retroactive interference would be predicted to interfere somewhat with retrieval, more than mid-retroactive interference. Indeed, work on neurologically intact individuals on similar retroactive interference has elucidated such an "inverted U" response pattern exactly (e.g., Newton & Wickens 1956; Postman & Alpner, 1946; see Wixted, 2004 for a review). However, such was not the case in the study by Dewar et al. (2009).

Moreover, retrieval interference often results in the emergence of intrusions (i.e., falsely activated memory traces) during recall of to-be-recalled material. If retroactive interference occurring early in the delay interval led to more retrieval interference than did retroactive interference occurring later in the delay, one might expect a larger number of intrusions in the former than latter condition. However, Dewar et al. (2009) did not find that. Instead, the average number of such intrusions was extremely low in all conditions (< 1) and did not differ from that of controls.

On a more observational note it should be highlighted that patients with anterograde amnesia are typically able to retrieve memories normally from a long time ago. Unless the mechanisms for retrieval of such retrograde memory differ from those of anterograde memory, any retrieval difficulties should manifest themselves during retrieval of both types of memory (cf., Curran & Schacter, 2000; Squire, 1980, 1982, 2006; Wilson, 1987).

While we do not for one moment doubt that forgetting can be induced by retrieval interference, a retrieval interference hypothesis currently appears to be unable to provide an adequate account of the amnesia data summarized here.

In order to derive a better-fitting account for our data we might well need to move away from traditional cognitive memory models and incorporate what pharmacological and behavioural neuroscience work has revealed about a physiological phenomenon, memory consolidation.

Consolidation interference

The term "consolidation" was coined over a century ago by the experimental psychologist Georg Müller (see Figure 9.6) and medical student Alfons Pilzecker (Dewar, Cowan, & Della Sala, 2007; Lüer, 2007; Müller & Pilzecker, 1900; Wixted, 2004). The term comes from the Latin word *consolidare*, meaning "to make solid" (from *cum* + *solidus* "solid"). Consolidation has been mostly ignored within modern psychology, with a few notable exceptions (e.g., Bosshardt et al., 2005a, 2005b; Gaskel & Dumay, 2003). It has, however, proven to be a popular and widely researched process within neuroscience and psychopharmacology, where it is defined as "the progressive postacquisition stabilization of long-term memory" and "the memory phase(s) during which such presumed stabilization takes place" (Dudai, 2004, p. 52).

The first clinical evidence for consolidation came from observations made by Théodule Armand Ribot (1881, 1882), who reported that brain injury had

Figure 9.6 Georg Elias Müller (1850–1934).

a more detrimental effect on recent than remote premorbid memories. Such finding has been replicated extensively during the last century and today is known as "temporally graded retrograde amnesia". One of the first explanations for such temporally graded retrograde amnesia can be gleaned from Burnham (1903):

> The fixing of an impression depends upon a physiological process. It takes time for an impression to become so fixed that it can be reproduced after a long time interval; for it to become part of a permanent store of memory considerable time may be necessary. This we may suppose is not merely a process of making a permanent impression upon the nerve cells, but also a process of association, of organization of the new impressions with the old ones . . . Now suppose a shock occurs which arrests these physiological processes in the nervous tissue. What will be the result? Not only will the mind be a blank for the period of insensibility following the shock, but no impressions will be remembered which were not already at the time of the accident sufficiently well organized to make their persistence for a considerable interval possible. Hence the amnesia will be "retroactive".
>
> (Burnham, 1903, pp. 128–129)

He goes on to state: "The essential characteristic of these cases of retroactive

amnesia is that the memory is lost because it was never fully organized" (Burnham, 1903, p. 129).

These early clinical findings and hypotheses clearly indicate that the formation of memories takes time and cannot be compared to the instantaneous long-term "memorizing" of files by a computer. Thus, while a personal computer is capable of "memorizing" documents such as this very book within milliseconds, our brains require time, up to many years, to consolidate the often highly complex information and episodes which we perceive and experience.

More recent evidence for a consolidation process comes from animal neuroscience work on protein synthesis inhibitors. Protein synthesis inhibitors, typically antibiotics or toxins, interfere with the neural processes associated with memory formation in animals (Agranoff, Davis, & Brink, 1966; Dudai, 2004) (see Chapter 6). Retention of recently learned material is low if a protein synthesis inhibitor is introduced shortly following learning, but improves steadily with augmenting delay in the introduction of the protein synthesis inhibitor (see Figure 9.7). Such reduction in interference susceptibility over time clearly indicates that memories strengthen as a function of time. Importantly, such "temporal gradient" of interference is also found when interference is behavioural as opposed to pharmacological. Izquierdo, Schröder, Netto, and Medina (1999), for example, trained rats not to step off a platform by administering a mild shock if they did so. The rats were subsequently allowed to explore a novel environment for 2 minutes either 1 hour or 6 hours following learning. When tested 24 hours following initial learning, memory was found to be impaired in those rats who had explored the new environment 1 hour postlearning, but not in those who had explored the new environment 6 hours postlearning.

Interestingly, such temporal gradient of "behavioural" interference has also been reported in neurologically intact humans. In their aforementioned pioneer work on consolidation and retroactive interference, Müller and Pilzecker (1900) presented participants with a to-be-retained syllable list. Either 17 seconds or 6 minutes following the learning of the to-be-retained syllable list the participants were presented with a new syllable list. The participants' retention increased from 28% in the 17-second condition to 49% in the 6-minute condition. Müller and Pilzecker argued that the first syllable list could consolidate thoroughly during the 6-minute interval, thus being less susceptible to the subsequent interfering effect of the interpolated syllable list. They therefore reasoned that new memory traces are initially fragile and vulnerable to retroactive interference but strengthen, i.e., consolidate, over time (Dewar et al., 2007).

Further behavioural work on such consolidation interference hypothesis was undertaken by Skaggs (1925). He presented participants with a chessboard containing five chessmen, whose positions the participant had to remember after a 5-minute delay. During this delay simple algebra problems were interpolated at one of 4 onset times. In keeping with the consolidation

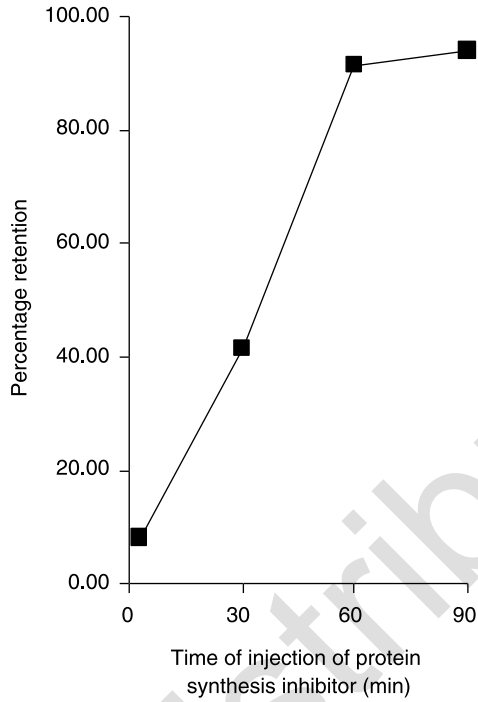

Figure 9.7 Percentage retention as a function of time of injection of a protein synthesis inhibitor (puromycin) in the goldfish. Goldfish were placed at one end of a shuttle box tank, which was divided into two sections by an underwater barrier. The fish were trained to swim across the barrier whenever a light was flashed within the section of the tank that they were placed in. The training was achieved via administration of an electric shock. When the protein synthesis inhibitor was injected immediately following training, the goldfish showed near to no retention of the task following a delay interval (i.e., their performance reverted to that of naive, untrained fish). However, when the time of injection of the protein synthesis inhibitor was delayed, the goldfish showed some retention of the task. Indeed, their retention increased with augmenting temporal delay in the injection of the protein synthesis inhibitor, revealing a reduction in interference susceptibility and thus a strengthening of the memory trace over time. (Figure adapted from Agranoff et al., 1966; see also Dudai, 2004.)

interference hypothesis, the average number of errors was highest when the interpolated task occurred immediately following learning but levelled thereafter.

It should be highlighted that interference stimuli need not be similar to to-be-retained material for a consolidation interference effect to occur. Such was not only elucidated by the aforementioned study by Skaggs (1925), but also by pioneer work by Müller and Pilzecker (1900), as well as more recent

work by ourselves (Dewar et al., 2007; see also Wixted, 2004 for a review). Such a finding is important given that modern psychologists tend to define retroactive interference in terms of interference by subsequent similar information (Dewar et al., 2007; Wixted, 2004).

Taken together, these behavioural and pharmacological findings strongly suggest that various kinds of interference, occurring immediately or shortly following the learning of to-be-retained information, have a detrimental effect on the consolidation of the to-be-retained material in neurologically intact neural systems.

The aforementioned findings of a temporal gradient of retroactive interference in amnesic patients by Dewar et al. (2009) are in close accordance with such data. This suggests that: (a) minimal retroactive interference may allow for enhanced memory consolidation in at least some amnesic patients; (b) that forgetting in at least some amnesic patients might well be the result of a disruption of memory consolidation by retroactive interference.

Unlike protein synthesis inhibitors, "behavioural" retroactive interference, such as the one applied in the reported studies, is of course the norm in everyday life, and neurologically intact individuals are easily able to consolidate new memories in the midst of such interfering information. In amnesic patients, however, this ability seems to have broken down.

The reasons behind such potential breakdown in normal consolidation ability in amnesic patients remain to be examined. One possibility is that resources required for the consolidation of new memory traces are greatly reduced in amnesic patients, presumably due to lesions to, or degeneration of, vital memory structures (i.e., medial temporal lobe/hippocampus). Wixted (2004) maintains that in neurologically intact individuals the resources required for consolidation are not infinite. He hypothesizes that when to-be-retained stimuli are followed by further information, resources have to be divided between the processing of the to-be-retained stimuli and the processing of further information. This division of resources is hypothesized to lead to the small reduction in retention that is observed in neurologically intact individuals when performance following a filled delay is compared with that following an unfilled delay.

In amnesic patients who do not benefit from the removal of postlearning material, consolidation resources may be entirely absent or too few to allow for any consolidation, even when new learning is followed by an unfilled interval. In amnesic patients who do benefit from the removal of new postlearning material, consolidation resources may be greatly depleted, but not absent. A considerable depletion of such consolidation resources could render the consolidation mechanism unable to process more than a few memory traces at any one time. Newly learned information may thus not be consolidated properly if further information, competing for greatly restricted resources, follows immediately. If, however, the onset of further information is delayed, there may be sufficient resources for the newly learned information to be adequately strengthened. Of course the absence or delaying of new

presented material in unfilled delay intervals does not imply that no new events are consolidated during such intervals. After testing, neurologically intact individuals remember well that they were left alone in a dark quiet room during this interval, even if they were never asked to try and remember such episodic information. As highlighted by Martin (1999), such memory demonstrates that any new events are automatically processed in the intact brain, irrespective of whether or not participants are asked to remember them. This processing of the unfilled delay episode in normals would also be expected to occur, at least in part, in those amnesic patients in whom some consolidation function is spared. Perhaps it is interference from such information that explains why even in unfilled conditions amnesic patients retain less new information than do controls.

Irrespective of whether or not this is the case, the possibility of at least some enhanced consolidation in amnesic patients following minimal retroactive interference is clearly an exciting prospect. Does this interpretation imply that amnesic patients can form new permanent long-term memories if care is taken to reduce any retroactive interference immediately following new learning?

So far we have been unable to find sound evidence for durable long-term memory (following several months) for specific material learned prior to minimal retroactive interference in the lab, even when cues were provided. Of course, even neurologically intact people tend to struggle somewhat when trying to recall details as specific as experimental stimuli after several months. A better indication of retention may thus be a more general episodic memory test of the original test session. Neurologically intact individuals tend to remember well that they attended a testing session (Martin, 1999). They may even be able to recall something specific about the laboratory or the experimenter.

What about amnesic patients? Preliminary data suggest that, when explicitly asked, some patients do indeed state that they can remember general information such as taking part in the study. When phoned a year after initial testing, one of our severely amnesic patients freely recalled that there had been an "English doctor". This memory was clearly not a mere intelligent guess. The patient was Italian and tested at his local Italian hospital where "English doctors" are rather seldom found. However, on the day of testing the team of experimenters did indeed include a visiting UK psychologist. Whether this lasting memory was the result of minimal retroactive interference or some other entirely unrelated factor can of course not be deduced from this observation. Further work is thus necessary to examine whether or not minimal retroactive interference can lead to memory traces that persist over long durations as predicted by the consolidation theory.

Would a failure to reveal such long-term memory go against a consolidation theory of the minimal retroactive interference-induced memory enhancement? Not necessarily. Neuroscience research suggests that there are in fact two types of consolidation, a fast and short-lived kind of consolidation (as

initially proposed by Müller & Pilzecker, 1900) as well as a slow and long-lived kind of consolidation. Dudai (2004) refers to such fast and slow kinds of consolidation as "synaptic" and "systems" consolidation respectively (see Chapter 6). Minimal retroactive interference might enhance both kinds of consolidation, or it might enhance only synaptic consolidation.

In short, *synaptic consolidation*, which has been the focus of molecular research, refers to a fast and short strengthening process, taking place in synapses and neurons immediately following encoding (Dudai, 2004; Dudai & Morris, 2000). Such consolidation is, as Dudai puts it, "universal" (Dudai, 2004, p. 56) in that it has been identified in all species. Synaptic consolidation is alleged to render new memories resistant to interference by distraction, drugs, seizures, and lesions within a matter of seconds to hours (Dudai, 2004). Moreover, it is frequently associated with long-term potentiation (LTP; Bliss & Lomo, 1973; see Lynch, 2004 and Morris, 2003 for reviews), which is a long-lasting strengthening of the synapses (i.e., the connections) between two neurons that are simultaneously active, and takes place within the hippocampus. The main evidence for synaptic consolidation comes from the aforementioned findings of a temporal gradient of the detrimental effect of protein synthesis inhibitors.

Systems consolidation refers to a much slower type of memory strengthening: a "progressive reorganisation of memory traces throughout the brain" (Dudai & Morris, 2000, p. 149) that can last years (Dudai, 2004). Such a process is assumed to take place between the medial temporal lobe (MTL) structures/hippocampus and the neocortex, by way of repeated activation of the memory trace, either implicitly (e.g., during sleep) or explicitly via retrieval/rehearsal (Dudai, 2004). While the standard consolidation account holds time per se responsible for the strengthening of such LTM, a newer theory, termed "multiple trace theory" (Nadel & Moscovitch, 1997), posits that it is the number of reactivations of a memory trace that determines its relative strength. Evidence for systems consolidation comes from the elucidation of temporally graded retrograde amnesia (i.e., the larger apparent effect of brain lesion on recent than distant pre-morbid memories) in neurological patients. To date it is unknown whether systems consolidation occurs in parallel to or as a consequence of synaptic consolidation (Dudai, 2004).

While the bulk of evidence for such division of consolidation processes comes from neuroscience, some behavioural evidence is beginning to emerge from the neuropsychological investigation of temporal lobe epilepsy and transient epileptic amnesia. This work has revealed that some epilepsy patients show normal retention of new information following short filled delays (around 30 minutes) but abnormally low retention following longer delays of weeks (Blake, Wroe, Breen, & McCarthy, 2000; Butler, Grahan, Hodges, Kapur, Wardlaw, & Zeman 2007; Kapur, Millar, Colbourn, Abbot, Kennedy, & Docherty, 1997; Manes, Graham, Zeman, de Lujan Calcagno, & Hodges, 2005; Mayes, 2003; O'Connor, Sieggreen, Ahern, Schomer, & Mesulam, 1997; Zeman, Boniface, & Hodges, 1998; see also Chapter 10).

On a purely observational note, there also seems to be evidence from everyday life for such division of consolidation processes. For example, on leaving a new art gallery following a longish and enjoyable browse, we tend to remember where we parked our car. However, we do not usually remember such information following a few days or weeks. Similarly, when visiting a city abroad, we will probably remember which bus to catch to get us from the airport to our hotel and back, but we are unlikely to remember such information once we have returned to our day-to-day business at home. Yet there are other events and pieces of information that we tend to remember for a long time, and possibly forever.

To return to amnesia and retroactive interference: this standard consolidation model makes various predictions as to how and for how long minimal retroactive interference may enhance memory in amnesic patients. Given the findings of minimal retroactive interference-induced memory enhancement over short delays (i.e., up to an hour), it may be that synaptic consolidation is impaired but not entirely defective, and that it benefits hugely from an absence of retroactive interference in those amnesic patients who show some memory enhancement.

Systems consolidation may be entirely defective or unresponsive to minimal retroactive interference occurring immediately following learning, meaning that any memory enhancement would be short-lived in amnesic patients. Alternatively, systems consolidation may also benefit from minimal retroactive interference, either directly at the time of minimal retroactive interference (if the processes act in parallel), or indirectly because material has been adequately strengthened by synaptic consolidation for further processing (if the processes occur serially).

In patients who do not show any minimal retroactive interference-induced memory enhancement, both consolidation types would be predicted to be defective.

Criticisms of the consolidation theory

Like any theory, the consolidation theory is not free of opponents and sceptics. In particular, advocates of retrieval models of forgetting and amnesia have criticized the consolidation theory for its apparent inability to account for instances of memory recovery following longer delays or cues (cf., Spear & Riccio, 1994). Given that we have not yet administered any further extensive free recall or cued recall tests as part of our amnesia retroactive interference work, it is unknown whether any of the previously nonrecalled material may have been retrievable by our patients under such conditions. Moreover, a null finding in such tests still could not remove all doubt in this regard. Also, a positive finding would not necessarily speak against a consolidation account of our data (Dewar et al., 2009). Retroactive interference may not block all consolidation of newly learned material in amnesic patients. It could simply lead to a greatly weakened memory trace that is only retrievable via

specific reminders or contextual cues (cf., Dudai, 2004; Squire, 2006). Indeed, Dudai (2004) as well as Miller and Matzel (2006) have argued that perhaps we should not simply consider consolidation as the strengthening of a memory trace per se, but also as the strengthening of that memory trace's retrieval cues. When viewed in this way, consolidation not only strengthens a memory trace but also renders it more retrievable (Dudai, 2004; Miller & Matzel, 2006). Therefore, retroactive interference may not only weaken a memory trace, but it may also make it less retrievable in the future.

If a memory trace has been sufficiently consolidated it should presumably be resistant to all future interference. However, animal work has shown this not to be the case. Reactivation of an apparently stable memory trace via appropriate external retrieval cues can, in some cases, render the memory trace susceptible to immediately following interference again (e.g., Lewis, Bregman, & Mahan, 1972; Misanin, Miller, & Lewis, 1968, see also Sara, 2000 for a review). At first glance these findings appear to be incompatible with a theory that holds that memories become immune to interference over time. However, in recent years it has been proposed that memory traces might not be simply consolidated once, but that they can also be "reconsolidated" (Nader, Schafe, & LeDoux, 2000; Sara, 2000) on various future occasions. Such reconsolidation appears necessary for the modification of existing memory traces and the integration of existing memory traces with new memory traces (Dudai, 2004; Nader et al., 2000; see also Hupbach, Gomez, Hardt, & Nadel, 2007 for work on reconsolidation in neurologically intact people). Nader et al. (2000) thus suggest that it is not simply new, but "active" memory traces which are rendered fragile and in need of strengthening. While previously stable memory traces may, at times, become damaged via interference, the resulting vulnerability to interference might, as Dudai (2004) nicely puts it, simply be "the price paid for modifiability" (p. 75). Moreover, as argued by Dudai (2004), we are not generally at risk of pharmacologically induced reconsolidation blockers (i.e., large doses of protein synthesis inhibitors) and should thus be relative safe from any substantial memory corruption.

Nonetheless, given the apparent high vulnerability to behavioural retroactive interference in some amnesic patients, it is possible that such behavioural retroactive interference could also be highly detrimental to the reconsolidation of recently retrieved retrievable (i.e., retrograde) memory in such patients.

A revised cognitive model of forgetting

Given our findings and consideration of existing cognitive and neuroscience theories, we propose a revised model of forgetting. In a nutshell, we propose a cognitive model containing an *intermediate memory/consolidation* stage. This is illustrated in Figure 9.8. We hypothesize that currently attended (and interpreted) information is temporarily held in STM which might act as a funnel,

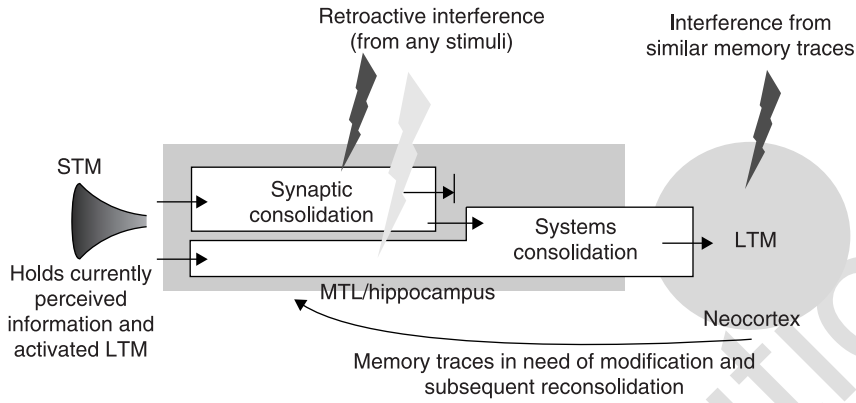

Figure 9.8 A revised cognitive model of forgetting. Currently attended (and interpreted) information is temporarily held in STM, which might act as a funnel, enabling a synaptic consolidation process (probably within the hippocampus) to rapidly strengthen and bind memory for currently relevant stimuli. This consolidation process allows for only the short-term retention of new information (minutes to hours). Additional or subsequent systems consolidation is required for this new information to become an enduring memory trace. In neurologically intact individuals synaptic consolidation is mildly susceptible to interference by any subsequent material. The same might be true for systems consolidation. Items within the long-term memory store are mildly susceptible to interference by competing memory traces (retrieval interference) or to interference with reconsolidation. In patients with anterograde amnesia synaptic consolidation is hypothesized to be highly susceptible to interference by any subsequent material. It remains to be established whether this might also be the case for systems consolidation.

allowing a synaptic consolidation process (probably within the hippocampus) to rapidly strengthen and bind memory for currently relevant stimuli. This synaptic consolidation process is likely to be capacity limited in that it can only maintain or process a limited number of items at any one time. As a consequence this type of consolidation presumably only allows us to remember new information for minutes to hours. An activated and temporarily strengthened memory trace can either be further strengthened by systems consolidation (via implicit or explicit rehearsal and reactivation), or it is simply displaced from the "intermediate memory" generated by synaptic consolidation.

Whether a memory trace is consolidated further may depend on the importance placed upon it, and thus perhaps on the amount of rehearsal/reactivation. It may also depend on other factors such as emotional salience (cf., McGaugh, 2000).

Synaptic consolidation is predicted to be susceptible to retroactive interference (by which we mean interference from any new stimuli). Systems consolidation may also be susceptible to retroactive interference. However, it remains

to be established whether systems consolidation occurs in parallel to or as a consequence of synaptic consolidation.

Items that are successfully consolidated and stored in LTM may be forgotten temporarily via retrieval interference (by competing memory traces) or interference with reconsolidation (cf., Nader et al., 2000). Patients with executive dysfunction are hypothesized to be especially susceptible to retrieval interference.

In neurologically intact humans the effects of retroactive interference are predicted to be mild, yet significant when compared to minimal retroactive interference (cf., Dewar et al., 2007; Müller & Pilzecker, 1900; Skaggs, 1925). However, in patients with anterograde amnesia, retroactive interference is predicted to be highly detrimental to synaptic consolidation (as well as perhaps to systems consolidation). In such patients minimal retroactive interference is therefore hypothesized to lead to enhanced synaptic consolidation. It remains to be established whether systems consolidation also benefits from minimal retroactive interference in amnesic patients.

Summary and conclusions

To summarize, the amnesia research reported and discussed in this chapter demonstrates that at least some amnesic patients can retain new information for much longer than is typically assumed if the period that follows new learning is devoid of further material. This minimal retroactive interference-induced memory improvement appears to underlie enhanced memory consolidation. Thus, it strongly appears that at least some patients with anterograde amnesia are in actual fact (still) able to consolidate new information, but that a high susceptibility to retroactive interference impairs such process substantially. Whether minimal retroactive interference leads to a long-term benefit in amnesic patients remains to be established, and is likely to be dependent upon the functioning of systems consolidation.

The reported data and interpretation have important implications. On a practical note, the findings strongly indicate that some patients with anterograde amnesia may be more capable of forming new LTM traces than previously assumed. Future research on minimal retroactive interference could thus lead to fruitful memory training techniques.

With respect to theoretical implications, the reported work clearly highlights the necessity for modern psychology to follow in the footsteps of both Müller and Pilzecker (1900) and contemporary neuroscience and (re-)incorporate an intermediate consolidation stage into its standard two-stage model of memory.

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