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Acquisition and Transfer of New Verbal Information in Amnesia: Retrieval and Neuroanatomical Constraints

Suparna Rajaram
State University of New York at Stony Brook

H. Branch Coslett
Temple University School of Medicine

Four experiments examined new associative learning in amnesia by contrasting the performance of 2 amnesic participants—1 (C.C.) with basal forebrain damage and the other (R.H.) with medial temporal lobe damage—and 3 controls. Both amnesic individuals were severely impaired on explicit memory measures but showed intact perceptual priming. On the new associations measures, only C.C., not R.H., exhibited learning by producing correct targets (*HIJACKER*) in the absence of perceptual cues for them (e.g., *STAFF shot ???*). When the perceptual cue (e.g., *MEDICINE cured _ I _ C _ P*) was provided, both C.C. and R.H. showed learning. Transfer to information containing conceptually related targets (e.g., *TERRORIST* or *BELCH*) was reliably observed only in C.C. This finding was replicated with further reduction in perceptual overlap across original (*LIGHTNING torched JUNGLE*) and transfer (*LIGHTNING burned WILDERNESS*) sentences. Together, these findings delineate the role of experimental conditions, severity of amnesia, and different neuroanatomical structures in mediating new verbal learning in amnesia.

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Theories of memory have been greatly influenced in the last three decades by the dissociations in performance exhibited on various memory tasks by amnesic participants. The amnesic syndrome is characterized by a failure to remember episodes that occur subsequent to the onset of the disorder (also known as anterograde amnesia) and a debilitating impairment in the ability to acquire new information (Rozin, 1976). Loss of memories for the period immediately preceding the onset of amnesia (also known as retrograde amnesia) is also common. These memory deficits are typically noted in the context of at least relative preservation of a number of other cognitive functions, such as perception, attention, language, thought, reasoning, intelligence, and short-term memory (Mayes, 1988; Parkin, 1988; Rozin, 1976).

A large body of research, however, has demonstrated that amnesic participants exhibit striking discrepancies in memory performance as a function of task demands. These participants typically perform poorly in recall and recognition tasks in which they receive explicit memory instructions to consciously access previously presented or learned information. In contrast, amnesic participants perform at normal levels on tasks involving implicit retrieval instructions. In these implicit memory tasks, participants are asked not to recall or recognize the target but rather to provide the first response that comes to mind (Warrington & Weiskrantz, 1968, 1970). Preserved implicit memory for past information may be revealed, for example, by perceptual priming (improved performance in resolving perceptually degraded information; e.g., _ *a b _ e*, as a result of prior presentation within the experimental context, i.e., *table*; see Moscovitch, Vriezen, & Goshen-Gottstein, 1993; Roediger, 1990; Shimamura, 1986). Amnesic individuals may also exhibit preserved perceptual–motor and procedural skills on tasks involving mirror tracing (Milner, 1962), rotary pursuit (Brooks & Baddeley, 1976; Cermak, Lewis, Butters, & Goodglass, 1973), mirror reading (Cohen & Squire, 1980), solving the Tower of Hanoi puzzle (Cohen & Corkin, 1981), and learning the mathematical Fibonacci principle (Kinsbourne & Wood, 1975).

A number of current theories of amnesia postulate multiple memory systems to account for these discrepancies in performance. For example, distinctions have been drawn between an episodic memory system considered to be impaired in amnesia and procedural and perceptual representation systems considered to be preserved in amnesia (Tulving & Schacter, 1990). Similar distinctions have been drawn between the declarative memory system (impaired in amnesia) and the procedural memory system (preserved in amnesia; Cohen & Squire, 1980) and between memory and habit (Mishkin & Appenzeller, 1987). These and other

Suparna Rajaram, Department of Psychology, State University of New York at Stony Brook; H. Branch Coslett, Department of Neurology, Temple University School of Medicine.

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Correspondence concerning this article should be addressed to Suparna Rajaram, Department of Psychology, State University of New York at Stony Brook, Stony Brook, New York 11794-2500. Electronic mail may be sent to srajaram@psych1.psy.sunysb.edu.

similar theoretical distinctions assume that different neural circuits mediate the functioning of the various memory systems.

On the basis of both human and animal work, explicit memory appears to be critically dependent on three brain regions: the medial temporal lobes, the midline diencephalon, and the basal forebrain (Rajaram, 1997; Zola-Morgan & Squire, 1993). In addition, in recent years, memory loss has also been attributed to damage to prefrontal cortex (Moscovitch & Winocur, 1992; Wheeler, Stuss, & Tulving, 1995) and the mammillary bodies (Bolton et al., 1998; Dusoir, Kapur, Byrnes, McKinstry, & Hoare, 1990; Tanaka, Miyazawa, Akaoka, & Yamada, 1997). Regions of the brain subserving the functioning of the perceptual representation system (Tulving & Schacter, 1990) or the procedural memory system (Cohen & Squire, 1980; Squire, 1986, 1992) are not yet well identified. However, the right occipital lobe (Gabrieli, Fleischman, Keane, Reminger, & Morrell, 1995) and the right posterior cortex (Squire et al., 1992) have been implicated in visual perceptual priming for words.

Although accounts of amnesia that posit multiple memory systems generally agree that the declarative/episodic memory system is impaired and the procedural/perceptual representation systems are preserved, these accounts differ with respect to the status of the semantic memory system in amnesia. Semantic memory constitutes knowledge about world events, history, language, and also personal events that over the course of time take on an impersonal quality (Tulving, 1983) and, thus, can be contrasted with episodic memory that includes memory for daily events and personal experiences anchored within a spatio-temporal context. Most theorists agree that semantic memory for premorbid events and knowledge remains intact even after the onset of amnesia. The divergence in theoretical positions concerns the acquisition of new semantic knowledge after the onset of amnesia. According to some theorists (Parkin, 1982; Shallice, 1988; Tulving, 1983, 1985; Tulving & Schacter, 1990; Wood, Ebert, & Kinsbourne, 1982), amnesia is characterized by impairment in episodic memory whereas the semantic memory system can be intact such that this system can support the learning of new information. In contrast, others (Cermak, Talbot, Chandler, & Wolburst, 1985; Cohen, 1984; Cohen & Squire, 1980; Gabrieli, Cohen, & Corkin, 1988; Squire, 1986, 1992) argue that amnesia results in impairment in both the episodic and semantic components of memory, and such impairments result in an inability to acquire new factual or semantic information at normal rates. Thus, according to these theorists, the ability to acquire new procedural skills or rule-based learning is preserved in amnesia, but the ability to acquire new semantic information is impaired.

Within these theoretical frameworks that attempt to map the preserved and impaired functions in amnesia, two key questions have received a great deal of empirical scrutiny in recent years. The first question concerns the integrity of perceptual and conceptual processes that mediate memory functions (Blaxton, 1989; Rajaram & Roediger, 1993; Roediger, 1990; Roediger, Weldon, & Challis, 1989; Srinivas & Roediger, 1990). As mentioned earlier, a large body of data demonstrates that perceptual priming of preexisting information, as measured by tasks such as word identification, word fragment completion, word stem completion, and picture naming, is typically preserved at normal levels in amnesia (Cermak et al., 1985; Graf, Squire, & Mandler, 1984; Hamann & Squire, 1996; Shimamura & Squire, 1984; Vaidya, Gabrieli, Keane, & Monti, 1995; Verfaellie, Cermak, Letourneau, & Zuffante, 1991; Verfaellie, Gabrieli, Vaidya, Croce, & Reminger, 1996; Warrington & Weiskrantz, 1968, 1970). The evidence is more mixed on the status of priming that is mediated by conceptual processes. Several studies indicate that conceptual priming can indeed be obtained on a number of conceptual priming tasks, such as category exemplar production (given the category *animals*, participants produce exemplars where a low-frequency exemplar, such as *donkey*, may constitute the target item; Gardner, Boller, Moreines, & Butters, 1973; Hamann, 1990; Keane et al., 1997; Vaidya et al., 1995), production of two-word idioms (*sour-grapes*; Schacter, 1985), and production of preexperimentally associated words (e.g., *table–chair*, Shimamura & Squire, 1984; Warrington & Weiskrantz, 1982; Winocur & Weiskrantz, 1976). Others have, however, reported impaired levels of conceptual priming in amnesic participants compared with memory-intact participants on similar tasks (Blaxton, 1992; Cermak, Hill, & Wong, 1998; Keane et al., 1997).

The second key question concerns the ability to learn new information after the onset of amnesia. Within this domain, three lines of research can be identified. In the first line of research, studies have investigated the acquisition of new semantic information after the onset of amnesia. For example, in one study Gabrieli et al. (1988) reported that the well-known patient H.M. failed to learn the meaning of hitherto unknown English words even after repeated exposures. In another report, Grossman (1987) reported that the participants with Korsakoff's amnesia failed to develop the knowledge of the meaning and grammatical form for a new word (e.g., *bice*). In contrast, Wood, Brown, and Fulton (1989) reported that a young girl who became amnesic in childhood following an episode of herpes simplex encephalitis was able to make progress in the academic domain. Others have found evidence for acquisition of new French vocabulary at normal levels (Hirst, Phelps, Johnson, & Volpe, 1988), and yet others have reported positive evidence for single word interpretations of ambiguous descriptions (McAndrews, Glisky, & Schacter, 1987) and normal levels of implicit frequency judgments (Dopkins, Kovner, & Goldmeier, 1994). One study also reported intact ability of the participants with Korsakoff's amnesia to develop new concepts and concept rules (Van der Linden, Meulemans, & Lorrain, 1994), although this finding was obtained for only one of the two amnesic patients tested. Thus, the evidence of learning in this set of studies appears to be mixed, and the ambiguity of results may be attributable to differences in etiology or severity of amnesia as well as to differences in the experimental conditions used across different studies.

The second line of research on the issue of new learning has examined the retention of individual novel items that were unknown prior to the onset of amnesia. For example,

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many researchers have examined priming for nonwords and novel shapes across a variety of perceptual priming tasks, such as perceptual identification, word reading, and lexical decision. Although significant priming for novel items has been reported, one concern in many studies has been that priming in amnesic participants for novel information is not always at normal levels (Cermak et al., 1985; Diamond & Rozin, 1984; Gordon, 1988; Smith & Oscar-Berman, 1990). However, this pattern may be attributable to the potential use of explicit memory by memory-intact participants (Bowers & Schacter, 1993). Later studies in the literature have now documented intact priming for nonwords in amnesia (Cermak, Blackford, O'Connor, & Bleich, 1988; Cermak, Verfaellie, Milberg, Letourneau, & Blackford, 1991; Gabrieli & Keane, 1988; Haist, Musen, & Squire, 1991; Musen & Squire, 1991) even when the contribution of sublexical components is ruled out (Keane, Gabrieli, Noland, & McNealy, 1995). In a similar manner, priming in amnesia for individual novel shapes also appears to be preserved (Gabrieli, Milberg, Keane, & Corkin, 1990; Knowlton & Squire, 1993; Musen & Squire, 1992; Schacter, Cooper, Tharan, & Robens, 1991; Schacter, Cooper, & Treadwell, 1993; Verfaellie, Milberg, Cermak, & Letourneau, 1992).

A third line of research on the issue of new learning relates more directly to the hypotheses examined in this article and concerns the status of new associative learning of verbal information after the onset of amnesia. A number of studies have investigated this issue by using the novel word association paradigm. In this paradigm, participants are presented with unrelated word pairs at study (e.g., *window–reason, march–shave*) and are later presented the word pairs in the same configuration as the study episode or in a recombined fashion (e.g., *march–reason*). In the initial reports that used implicit memory measures of word stem completion (*window–rea____*) in amnesic individuals (Graf & Schacter, 1985), intact priming for new associations was reported. However, subsequent studies reported intact priming only in cases of mild to moderate but not severe amnesia, suggesting that such learning was likely mediated by residual episodic memory (Cermak, Bleich, & Blackford, 1988; Mayes & Gooding, 1989; Schacter & Graf, 1986; Shimamura & Squire, 1989; but see Cermak, Blackford, et al., 1988). It is interesting that recent studies have demonstrated intact and normal levels of priming on the new associations paradigm when priming was measured on implicit tasks, such as rapid word identification (Gabrieli, Keane, Zarella, & Poldrack, 1997, but see Paller & Mayes, 1994), reading time (Moscovitch, Winocur, & McLachlan, 1986), and color–word naming (Musen & Squire, 1993).

Evidence in support for new learning in amnesia has also been obtained in studies that required amnesic individuals to learn simple computer vocabulary and programming commands (Glisky & Schacter, 1988; Glisky, Schacter, & Tulving, 1986a, 1986b), name–face associations (Thoene & Glisky, 1995), simple facts (e.g., Angel Falls is located in Venezuela; Shimamura & Squire, 1987), and specified targets as a part of sentences (Shimamura & Squire, 1988). Once again, across these reports of new associative learning in amnesia, the rate of learning is not always found to be at normal levels. The general pattern of results in all the studies of new learning in amnesia reviewed so far may be summarized as follows: New learning after the onset of amnesia may be reliably observed when the to-be-learned stimuli can be treated as a single perceptual unit (nonwords, novel shapes) and do not contain an associative component (Gabrieli et al., 1997). In contrast, preserved priming for new stimuli may not be consistently observed in amnesia when the to-be-learned information requires the formation of associations (e.g., Curran & Schacter, 1997).

In fact, it is reasonable to argue that development of new associations may be at the crux of learning not only in the different paradigms just described, but also in the studies cited earlier that examined the acquisition of semantic information in amnesic participants and reported mixed evidence (Gabrieli et al., 1988; Grossman, 1987; Hirst et al., 1988; McAndrews et al., 1987; Van der Linden et al., 1994; Wood et al., 1989). Therefore, a systematic investigation of the experimental conditions and neural underpinnings that govern the nature of new associative learning in amnesia is central to an understanding of memory and amnesia. The present article reports four experiments designed to explore various aspects of this critical question.

With this goal in mind, we now turn to the hypotheses that have been proffered in the literature to account for the inconsistent findings of new associative learning in amnesia. Many researchers have postulated that differences in task demands and experimental procedures, such as different encoding and retrieval conditions, may significantly influence the extent of new learning in amnesia (Hayman, Macdonald, & Tulving, 1992; Tulving, Hayman, & Macdonald, 1991; Van der Linden et al., 1994). In a recent set of reports, Tulving and coworkers (Hayman et al., 1992; Tulving et al., 1991) extensively examined a number of experimental factors that may determine learning of new associations in dense amnesia. Tulving et al. (1991) reported long-lasting learning of new associations in an amnesic participant, K.C., who became profoundly amnesic following a closed-head injury sustained in a traffic accident in 1980. In this study, a number of plausible but presumably unfamiliar sentences (e.g., *STAFF shot HIJACKER*) were presented for study across a number of sessions, and K.C.'s retention for the target words (e.g., *HIJACKER*) was tested with implicit instructions under different retrieval conditions. In addition to perceptual priming obtained from the fragment completion task (e.g., *_ I J _ _ KE _*), priming for the target word *HIJACKER* was also obtained in response to relatively nonperceptual cues, for example, exposure to the sentence cues such as *STAFF shot ???*. This latter finding was taken as evidence of semantic learning, because K.C. was able to generate newly learned targets without the aid of perceptual cues for the target itself (see also Hayman et al., 1992). In addition, Tulving and his coworkers concluded that new learning in amnesia is slow and laborious compared with that seen in memory-intact persons (see also Squire, 1992), but that there is long-term retention of such learning. Finally, Hayman et al. (1992) also reported in their

study that across the conditions, repetition facilitated performance whereas associative interference had a deleterious effect on the learning of new semantic associations in amnesia. Furthermore, they reported that new learning occurs under implicit but not explicit retrieval conditions. Thus, specification of experimental conditions and selection of tasks appear to be important factors in observing new learning in amnesia.

A second possibility may be that discrepancies in new learning arise from differences in the severity of amnesia (Ostergaard & Squire, 1989; Schacter & Graf, 1986; Shimamura & Squire, 1989; Verfaellie, Croce, & Milberg, 1995). Learning of new verbal associations is assumed to occur in mild to moderate amnesia but not following profound memory impairment (Cermak, Bleich, et al., 1988; Ostergaard & Squire, 1989; Schacter & Graf, 1986; Verfaellie et al., 1995). Furthermore, if learning does occur after severe amnesia, such learning is found to be slow, laborious, and inflexible in nature (Hayman et al., 1992; Squire, 1992; Van der Linden et al., 1994).

A third possibility may be that differences in new learning arise from differences in the loci of pathology causing the amnesia (Shimanura & Squire, 1989; Squire, 1992). The need to take into account different pathology and the concomitant nature of impairment in memory has been noted previously (e.g., Gordon, 1988; Mayes, 1991; Parkin, 1984). For example, disruption in temporal memory is typically reported in frontal lobe amnesia whereas impairment in content memory is noted in hippocampal amnesia (Kolb & Wishaw, 1990; Moscovitch, 1994b; Moscovitch & Winocur, 1992). Differences in recall and recognition performance as a function of different brain pathologies have also been noted (see Aggelton & Saunders, 1997; Mayes & Downes, 1997). Parkin and Hunkin (1997) recently recommended the case study approach that differentiates amnesic individuals on the basis of etiology and lesion type in order to properly elucidate functional and processing differences among different amnesic individuals.

Differentiation of amnesic participants on the basis of underlying brain pathology is particularly relevant within the context of recent theoretical accounts of new associative learning in amnesia. In these accounts, associative priming impairment has variously been conceptualized as impairment in developing "complex associations" (Mayes & Downes, 1997) and binding information (Curran & Schacter, 1997). Furthermore, in current models of animal and human amnesia, the function of binding information is attributed to the medial temporal lobes (Cohen & Eichenbaum, 1993; Cohen, Poldrack, & Eichenbaum, 1997; Cohen et al., 1994; Johnson & Chalfonte, 1994; McClelland, McNaughton, & O'Reilly, 1995; Moscovitch, 1994a; O'Reilly & McClelland, 1994). Thus, damage to the medial temporal lobe structures is assumed to disrupt the forming of new associations (see also Gabrieli et al., 1988), and the extent of damage may determine the magnitude of impairment in priming of new associations (Squire, 1992). If the medial temporal lobe structures play a unique role in mediating the formation of new associations, then it is important to determine whether other forms of brain damage that underlie amnesia can produce better learning of new associations.

Research reported in this article was undertaken to examine the acquisition and transfer of new information in amnesia within the context of a number of empirical and theoretical issues reviewed so far. We compared two severely amnesic participants, one (R.H.) with extensive but selective bilateral lesions to the medial temporal lobe region and another (C.C.) with damage restricted to the gyri recti and basal forebrain region. The specific aims of each experiment are described separately in the forthcoming sections. The four overarching goals that guided these experiments are described here.

The first goal was to determine whether amnesic participants would exhibit new associative learning within the verbal domain when tested under experimental conditions that have produced learning in severely amnesic participants in other reported studies. As noted earlier, study and test conditions often vary across studies, making it difficult to reconcile the differences in the findings across different patient populations. In order to minimize discrepancies attributable to methodological differences, Experiment 1 was partially modeled after Tulving et al.'s (1991) study in which positive evidence of learning in profound amnesia was reported. We used the materials and several aspects of the procedure used by Tulving et al. in order to equate the critical factors involved in learning across our two amnesic participants.

The second goal was to delineate the experimental conditions that facilitate or obstruct new associative learning in amnesia. The goal here was to determine whether different retrieval conditions would account for the differences in performance observed across amnesic individuals. To this end, we assessed new learning with retrieval cues that provided conceptual and perceptual information and retrieval cues that limited the perceptual information.

The third goal was to investigate the role of different loci of main pathology in the learning of new information in amnesia. To this end, in our study two amnesic participants were treated identically in all the experiments in order to determine whether new learning can be obtained in amnesic individuals with different pathologic substrates. This approach allowed us to conduct a comparison between medial temporal lobe amnesia and basal forebrain amnesia in mediating new associative learning. Despite the neural interconnectivity between these structures, many researchers have noted that anterior communicating artery (ACoA) amnesia (mediated by basal forebrain damage) may be anatomically distinguishable from the hippocampal system (that includes hippocampus, fornix, mammillary bodies, and anterior thalamic nuclei; Aggleton & Saunders, 1997; Parkin & Leng, 1993). If this neuroanatomical distinction is meaningful with respect to new associative learning, then a comparison of performance between a participant with basal forebrain amnesia and a participant with medial temporal lobe amnesia was expected to reveal differences. Initial reports in the literature suggest that new associative learning can occur when the underlying pathology does not reveal complete damage of the medial temporal structures, as was

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the case with patient K.C. (Tulving et al., 1991). However, the well-known medial temporal patient H.M. failed to show such learning (described in Squire & Knowlton, 1995). Thus, on the basis of these findings and the theoretical accounts described earlier, we expected to find impairments in learning in the medial temporal lobe amnesic participant but expected to see better performance in the basal forebrain amnesic participant.

The fourth goal was to determine whether newly acquired information, if any, facilitates implicit learning of related information more rapidly than unrelated information. In other words, we sought to determine whether the new learning is inflexible in nature and restricted to the materials presented repeatedly or whether it can facilitate the learning of related information. On the basis of recent theories of amnesia (e.g., Cohen & Eichenbaum, 1993), we expected learning to be generally inflexible in medial temporal lobe amnesia. If inflexibility of learning is a hallmark of medial temporal amnesia per se, and not of amnesia in general, then some transfer to related information was expected to occur in the basal forebrain amnesic participant's performance.

Patient Description

C.C.

At the time of testing, C.C. was a 23-year-old amnesic woman. C.C. was noted by her family to have become increasingly rebellious and belligerent at the age of 16. Over the ensuing 2 years, her behavior and school work slowly worsened; formerly a good student, she quit high school in the 11th grade. She sought medical attention at the age of 18 for evaluation of memory loss and headaches. Neurologic examination revealed her to be anosmic (unable to smell) and amnesic but otherwise normal. A magnetic resonance imaging (MRI) scan revealed an approximately 5 × 5 × 5 cm meningioma extending from the floor of the anterior fossa into the under surface of the frontal lobes. The benign tumor was successfully resected.

Postoperatively, C.C. gradually regained her warm and cheerful disposition but remained profoundly amnesic. At the time of testing reported here, C.C. was living with her family. She was unable to work but spent part of her time caring for toddlers. She required supervision in this task, however, as when distracted she forgot about her charges. Although a fluent and practiced reader, C.C. read very little as she quickly forgot what she had read. In a similar manner, although she enjoyed movies, she often became confused because of a failure to retain information from earlier scenes; C.C. confided that she watched the same movie countless times as she could not recall the plot. C.C. was accompanied by a relative when coming for testing as she could not remember the purpose of her outings. She maintained an active and varied social life, often meeting old friends, who reported that C.C. repeated the same anecdotes at every meeting. In general, throughout the testing period, C.C. was found to be animated, motivated, and socially engaging without any signs of apathy or disinterest.

An MRI scan obtained 1 year after resection of the meningioma demonstrated focal encephalomalacia of the bilateral gyri recti and inferior portions of the cingulate gyri (see Figure 1). A T2 weighted image demonstrated abnormal signal involving the basal forebrain and other subfrontal structures (see Figure 2). Finally, temporal lobe structures were intact (see Figures 2 and 3).

The neuropsychological examination at the time of experimental testing revealed C.C. to have a full scale IQ of 94 on the Wechsler Adult Intelligence Test—Revised (WAIS–R) with a verbal IQ of 101 and a performance IQ of 88. She achieved a scaled score of 12 in the Vocabulary subsection, indicating normal language function. In contrast, her memory quotient as measured by the Wechsler Memory Scale (WMS) was only 87. Substantial discrepancies were noted on the subtests of WMS. She performed normally, for example, on measures of short-term memory (Digits Forward = 7, Digits Backward = 6). Performance on the Logical Memory Test, in contrast, was quite impaired. C.C. was able to recall an average of 4.5 out of 23 concepts in immediate testing and could not remember being presented with a story after a 10-min delay. She was impaired in other subsections of WMS (Information = 4/6; Associate Learning = 12/21). C.C. scored below the 5th percentile for her age group on Warrington's Forced Choice Memory Test (Faces = 35/50; Words = 24/50).

The absence of any behavioral signs of frontal dysfunction in C.C. were confirmed by her normal performance on the Wisconsin Card Sorting Test: categories achieved = 6 (norm for age-matched controls: $M = 5.4$, $SD = 1.3$), perseverative responses = 3 (norm for age-matched controls: $M = 15.6$, $SD = 11.5$), and perseverative errors = 10 (norm for age-matched controls: $M = 12.6$, $SD = 10.2$).

R.H.

R.H. was a 47-year-old man at the time of testing who was in good health until he began to experience seizures in

Figure 1. A coronal T1 weighted magnetic resonance imaging section demonstrating encephalomalacia involving the bilateral gyri recti and inferior portions of the cingulate gyri.

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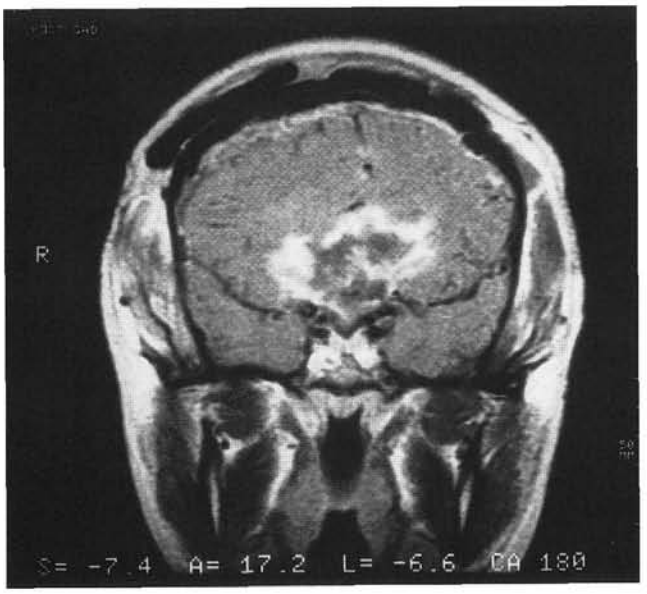

Figure 2. A T2 weighted section demonstrating multiple small areas of abnormal signal in the basal forebrain.

his early twenties while a college student. After graduating from college, R.H. attended graduate school at night and worked as a chief lab technologist. Following this, he held an administrative position at a university for a brief period before his memory deficits became incapacitating. At the time of testing, R.H. had been living with his father and brother. He could not retain information long enough to enjoy reading or watching movies and television. He enjoyed watching sports but did not know what teams were playing or who was winning. R.H. enjoyed crossword puzzles and word-play; when shown the word *napkins*, for example, he remarked, "You mean sleepy relatives."

In a number of respects, R.H. appeared to be stuck in the period when his amnesia developed. He dressed in clothes that were in vogue in the early 1970s and claimed that his current favorite athletes were Johny Unitas and Willie Mays (stars of the 1960s). R.H. related stories from his college days with animation, but the stories had a schematic flavor with little deviation in detail from one telling to the next. Even after weekly visits to our laboratory for over 1 year, R.H. was unable to recall the name of the first author with whom he had regular contact, or the purpose of his visit.

Neurological examination revealed evidence of a profound amnesia, but R.H. was otherwise normal. An MRI scan obtained at the time of testing revealed circumscribed areas of encephalomalacia involving the medial temporal structures, including the amygdala and hippocampal gyri bilaterally. Atrophy of the left lateral temporal lobe was also noted (see Figures 4 and 5).

Neuropsychological examination at the time of experimental testing confirmed the remarkable dissociation between R.H.'s intellectual ability and memory loss. On the WAIS–R, R.H. achieved a full scale IQ score of 126 (Verbal IQ = 121, Performance IQ = 123). R.H. obtained a scaled score of 13 on the Vocabulary subsection, consistent with the superior language function evident in conversation. In contrast, his memory quotient on the WMS was only 86. As with C.C., substantial discrepancies in performance were noted on the subtests. He performed normally on tests of short-term memory (Digits Forward = 7, Digits Back-

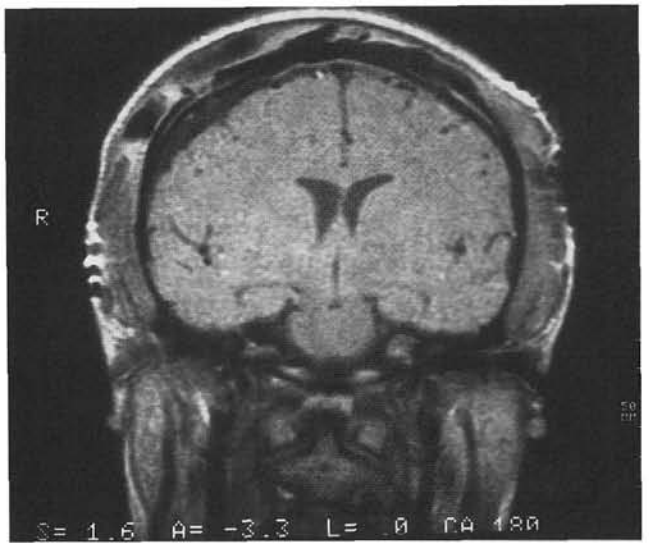

Figure 3. A T1 weighted section at the level of the caudate nuclei and anterior portion of the lateral ventricles demonstrating no abnormalities.

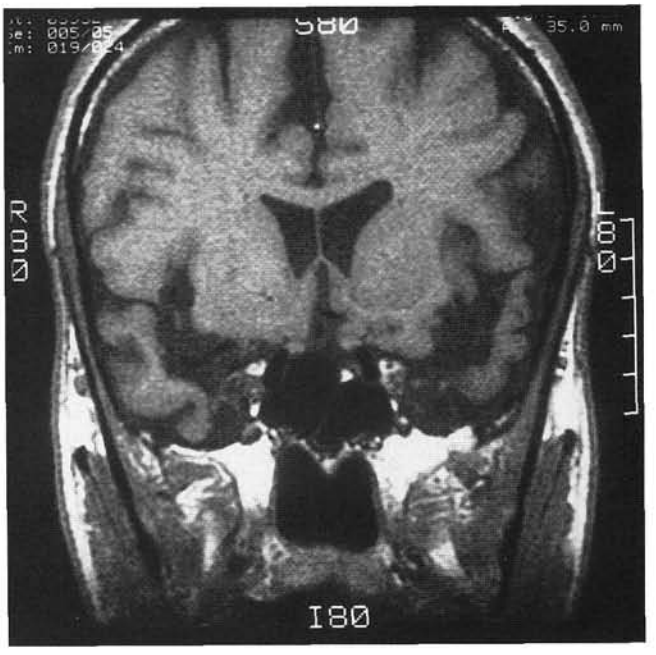

Figure 4. A coronal T1 weighted magnetic resonance imaging section demonstrating encephalomalacia involving the amygdala and hippocampal gyri bilaterally as well as atrophy of the left lateral temporal lobe.

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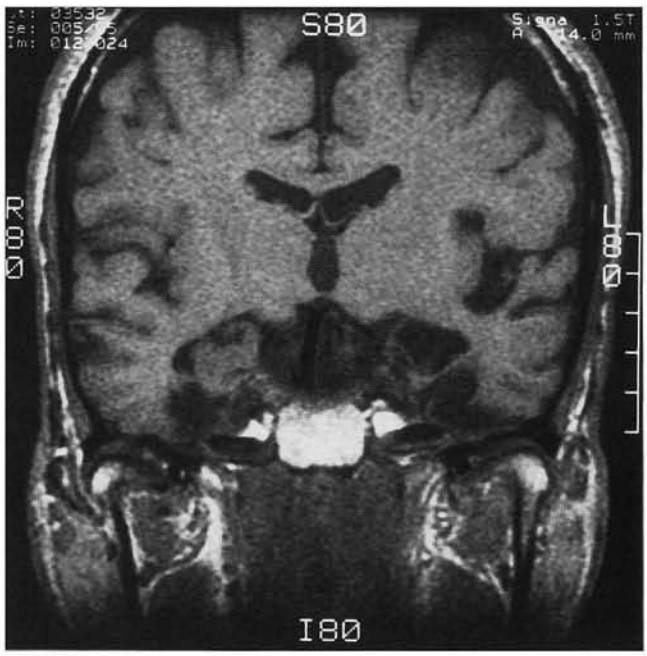

Figure 5. A more rostral section demonstrating encephalomalacia involving the hippocampal gyri and left hippocampus.

ward = 5). In contrast, he recalled only 4 of 23 concepts on the Logical Memory subtest without delay and had no memory of having been told a story when queried 10 min later. He obtained a score of 1/6 on the Information subtest and 7/21 on the Associate Learning subtest. R.H. performed at chance on Warrington's Forced Choice Memory Test for Faces and Words (both 28/50).

Control Participants

Three control participants were tested in all four experiments. One participant (CON1) was matched for age (22 years) and education (14 years) with patient C.C. Two participants (CON2 and CON3) were matched for age (CON2 = 46 years; CON3 = 50 years) and education (CON2 = 16 years; CON3 = 18 years) with patient R.H. Control participants were treated identically to amnesic participants except where we note a specific change in the procedure.

General Method

In all experiments, the 2 amnesic participants and 3 control participants were tested individually. Each experiment (except for the recognition memory tests) consisted of multiple sessions held 1 to 3 weeks apart. Each session consisted of three phases occurring in the following order: study phase, retention interval, and test phase. During the study phase, participants were presented with a series of sentences for incidental and conceptual encoding. For each sentence, the participants were asked to decide whether or not the sentence made sense. Participants were told that there were no right or wrong answers. This task was self-paced, and the study phase lasted for an average of approximately 5 min. In the 5-min retention interval, the experimenter and the participants engaged in informal conversation. In the following test phase, the test items were individually presented and the participants were instructed to complete either the sentence or the fragment (see below) with the first word that came to mind—no mention of the study phase was made. The specific retrieval conditions varied across sessions and experiments and are described shortly. Recognition tasks were also given in Experiments 1 and 3 in order to measure explicit memory for the studied sentences.

Experiment 1

Experiment 1 was motivated by conflicting reports of associative learning in amnesic individuals in case studies (e.g., Gabrieli et al., 1988; Hayman et al., 1992; Tulving et al., 1991). On the one hand, the densely amnesic participant H.M. was unable to associate certain definitions with unfamiliar words even after repeated exposures (Gabrieli et al., 1988). On the other, another densely amnesic participant, K.C., did demonstrate learning for new definitions and new sentences (Hayman et al., 1992; Tulving et al., 1991).

There are two notable differences in these two sets of studies that could potentially account for the differences in learning between these two dense amnesic individuals. One difference is that the loci of neurological damage resulting in amnesia differed in the two patients. H.M.'s amnesia is a result of the extensive but selective surgical removal of the medial temporal lobes bilaterally (Scoville & Milner, 1957). Patient K.C. became amnesic following a closed-head injury in a traffic accident that resulted in damage to multiple neural structures without selective or extensive damage to the medial temporal lobes (see Hayman et al., 1992; Tulving et al., 1991). Thus, H.M.'s failure to learn new associations could be attributed to the special role the hippocampus and related structures might play in mediating such learning. This possibility is supported by several theories of amnesia reviewed earlier in the article that ascribe the role of binding information to the medial temporal lobe structures.

A second explanation for the discrepancy is that the differences in learning are due to the differences in conditions under which such learning was tested. The procedure used by Gabrieli et al. (1988) permitted the selection of several incorrect alternatives provided by the experimenter before the correct response was elicited, thereby creating interference that may have obstructed learning. In contrast, the procedure used by Tulving and his collaborators (Hayman et al., 1992; Tulving et al., 1991) was designed to reduce interference and increase repetition, thereby creating improved conditions for learning to occur.

In the present experiment, we compared the learning of a participant with medial temporal lobe amnesia with a participant with basal forebrain amnesia under learning conditions similar to those used by Tulving et al. (1991) to determine whether new verbal learning can consistently occur in amnesia. Because positive evidence of learning was observed in patient K.C., we used the materials used by Tulving et al. (1991) and designed study and test conditions that were similar, although not identical, to those used by Tulving et al. (1991). We predicted that if new learning is solely a function of encoding and retrieval conditions, then

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both amnesic participants should exhibit similar learning as Tulving et al.'s patient. However, if medial temporal lobe structures are crucial for learning of this sort to occur, then R.H., who had suffered extensive bilateral medial temporal lobe damage, would not be able to learn new verbal information.

Method

Materials. Eighty of the three-word sentences used by Tulving et al. (1991) were used in this experiment. These sentences were constructed to be semantically plausible and yet unfamiliar to the participants. Forty-eight sentences were selected at random to be presented at study in all the sessions. The remaining 32 sentences were presented as nonstudied sentences during the test phase across all the sessions to measure baseline performance. Thus, at test 48 studied sentences and 32 nonstudied sentences were presented in different retrieval conditions such that each sentence was nested within a particular retrieval condition across sessions. In other words, a given sentence was tested in the same retrieval condition across all sessions.

In this and subsequent experiments, we took care to equate all critical aspects of the methodology, including materials, design, and procedure across the two amnesic participants. Thus, the same set of materials was presented to the two amnesic participants in every condition. We deemed this procedure important because we wanted to enable a direct comparison of performance of the two amnesic individuals. Therefore, both amnesic participants (C.C. and R.H.) received the same set of 48 sentences at study. In a similar manner, at test, the same sentence was presented in a particular retrieval condition for both amnesic participants.

In addition to the 48 study sentences, we included 12 buffer sentences, 8 at the beginning of the study list and 4 at the end of study list, to eliminate primacy and recency effects. In a similar manner, at test, we presented 8 nonstudied buffer items in different retrieval conditions at the beginning of the test list.

Finally, a recognition memory task was designed to measure explicit memory for new information at the end of the acquisition and testing sessions described above. It consisted of all the 48 studied sentences arranged in a new random order in a booklet. This recognition measure was similar to the one used by Tulving et al. (1991). All the details of the procedure described so far were identical for the control participants as well.

Design and procedure. We conducted multiple sessions in Experiment 1. C.C. participated in 8 sessions, R.H. in 12 sessions, and control participants in 5 sessions. In each session, during the study and the test phase, a new random order of presentation was used with the constraint that within a session, the same random order be used for each participant. The study phase was identical in all sessions—C.C., R.H., and control participants were presented with one sentence at a time on the Macintosh computer screen, and their task was to determine whether each sentence made sense to them (e.g., *MEDICINE cured HICCUP*, *STAFF shot HIJACKER*). After the experimenter typed in the response (yes or no), the next item appeared on the screen. The amnesic participants as well as the control participants gave both "yes" and "no" responses, particularly in the initial study sessions.

The presentation of the test items varied across sessions in the following manner. In Sessions 1, 3, 5, and 7 for C.C.; Sessions 1, 3, 7, 9, and 11 for R.H.; and Sessions 1, 3, and 5 for control participants—called the sentence cues sessions—test items were presented in two retrieval formats. The same set of 24 studied sentences and 16 nonstudied sentences were presented in the sentence+fragment condition (e.g., *MEDICINE cured _ I _ C _ P*) across all the above stated sessions for all the participants. The participants' task was to complete the fragment with the first word that came to mind. The remaining set of 24 studied sentences and 16 nonstudied sentences was presented in the sentence+??? condition (e.g., *STAFF shot ???*) across all the above stated sessions for all the participants, and again the participants' task was to complete the sentence with the first word that came to mind. The sentence+??? retrieval condition was considered to be the best measure of new learning by Tulving et al. (1991). In order for an amnesic participant to produce the correct response in this retrieval condition, new associations have to be made across words that have little or no preexisting links; therefore, we used this condition in the present experiment as well to obtain a comparable measure of new learning. The sentence+fragment retrieval condition was used here because this condition provided both the conceptual (the conceptual information provided by the sentence stem) and the perceptual (the perceptual information provided by the sentence stem and the fragment) cues to provide maximal support for performance (see Tulving et al., 1991).

In Sessions 2, 4, 6, and 8 for C.C.; Sessions 2, 4, 6, 8, 10, and 12 for R.H.; and Sessions 2 and 4 for control participants—called the fragments-only cues sessions—only the fragments of the targets from the studied and nonstudied sentences were presented (e.g., *_ I J _ _ K _ R* [*hijacker*], *_ I _ C _ P* [*hiccup*]), and the participants were asked to complete the fragment with the first word that came to mind. These sessions were included to demonstrate perceptual priming for stimuli tested in the sentence+fragment and sentence+??? conditions. Because perceptual priming is preserved in amnesia, it was important to determine that both amnesic participants would exhibit perceptual priming for the very materials that were used in two different retrieval conditions in other sessions in case differences in performance between the two patients emerged in the two retrieval conditions (i.e., sentence+fragment and sentence+???) in the sentence cues sessions.

We also administered a recognition memory test to both amnesic participants as well as the control participants. Following Tulving et al.'s (1991) procedure, 1 week after the completion of the last session (i.e., Session 8 for C.C., Session 12 for R.H., and Session 5 for control participants), participants were presented with the recognition memory task without a preceding study phase. All 48 sentences that were presented during the study phases of the preceding sessions were presented in a booklet, and the participants' task was to determine whether the sentences were familiar to them. In this experiment, only the study sentences were presented for the recognition test in order to facilitate as much familiarity with the materials as possible for the amnesic participants. Note that in Experiment 3, we administered the recognition test that included studied as well as nonstudied sentences in order to obtain a measure of memory as well as bias.

Results

Tables 1 and 2 present the sentence completion and fragment completion performance, respectively, of C.C. and R.H. for the studied and nonstudied items in different retrieval conditions across all the sessions conducted in Experiment 1. For each retrieval condition (sentence+???, sentence+fragments, and fragments-only cues), we determined the proportions of correctly completed studied and nonstudied items. The standard priming scores can be calculated by subtracting the proportion of correctly reported nonstudied targets from the proportion of correctly reported studied targets.

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Table 1
Performance of Participants C.C. (Basal Forebrain Amnesia) and R.H. (Medial Temporal Lobe Amnesia) in Experiment 1 When Sentence Cues Presented

	Sentence cues					
	Sentence+??? condition (e.g., *STAFF shot ???*)			Sentence+fragment condition (e.g., *MEDICINE cured _I_C_P*)		
Participant & session	Old	New	AP	Old	New	AP
Participant C.C.						
Session 1	.13	0	.13	.29	.06	.24
Session 3	.58	0	.58	.79	.06	.78
Session 5	.63	0	.63	.88	.19	.85
Session 7	.88	0	.88	.92	.13	.91
Participant R.H.						
Session 1	.00	0	.00	.29	.19	.12
Session 3	.04	0	.04	.67	.38	.47
Session 5	.08	0	.08	.88	.50	.66
Session 7	.04	0	.04	.92	.50	.84
Session 9	.04	0	.04	.88	.50	.66
Session 11	.08	0	.08	.88	.56	.73

Note. Old = studied items; New = nonstudied items; AP = adjusted priming scores.

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We analyzed the data in this and all the subsequent experiments in the following manner unless noted otherwise: To analyze the single-subject data for each amnesic participant, we calculated the total number of correct responses across sessions for each studied and nonstudied item in each retrieval condition. Following this, we carried out an independent t test (by items) to determine whether the difference in the rate of responding to studied items compared with nonstudied items (standard priming) was significant in each retrieval condition for each amnesic participant. The alpha level for the computation of significance was set at $p < .05$ unless noted otherwise.

Finally, we calculated adjusted or relative priming scores (Snodgrass, 1989) individually for amnesic as well as control participants in each retrieval condition where the standard priming scores (i.e., studied minus nonstudied completions) were divided by the corresponding value obtained from the following equation: 1 – nonstudied completion rate. The adjusted priming measure adjusts the effects for nonstudied performance and is particularly useful in comparing individual performances (see also Tulving et al., 1991, for the use of this measure). The adjusted priming scores for each amnesic participant in each retrieval condition are displayed in Tables 1 and 2 under the column titled AP (adjusted priming).[1]

Table 1 contains data from the sentence cues conditions that were critical in determining whether new associative learning can occur in amnesia. The priming scores in the sentence+??? condition clearly indicate that only C.C. was able to demonstrate learning for new sentences by generating the target items in the absence of any perceptual cues for those targets. Furthermore, the increment in learning was very impressive as indicated by the high priming score in Session 7. This advantage for studied items for C.C. was confirmed by the significant independent t test carried out for items as described previously, $t(38) = 6.77$. In contrast, R.H. showed little learning of the target items when no perceptual cue for the target aided the retrieval of the appropriate word. In fact, despite an attempt to expose the study sentences in additional sessions (Sessions 9–12), we failed to find any evidence of new associative learning as measured by the sentence+??? cues in R.H., $t(38) = 1.12$.

The second sentence cues condition (i.e., the sentence+fragment condition) provided a measure of new learning when perceptual cues for the target items were provided. In this condition, both amnesic participants (C.C. and R.H.) demonstrated significant priming: for C.C., $t(38) = 7.31$, and for R.H., $t(38) = 2.83$. Thus, C.C. was able to exhibit new learning in the sentence cues conditions whether or not the perceptual cues for the targets were provided, whereas R.H. was only able to show priming when the perceptual constraints for the retrieval of target items were present.

Finally, Sessions 2, 4, 6, and 8 (and in R.H.'s case, 8 and 10 as well) provided a measure of perceptual priming for the target items in the absence of sentence cues. Table 2 displays the data for the fragments-only cues conditions. Perceptual priming scores for target items that belonged to sentences used in the sentence+??? condition are shown on the left. Amnesic participant C.C. produced significant levels of priming for these target items, $t(38) = 4.74$. More important, amnesic participant R.H., who had failed to produce these items in the absence of perceptual cues (i.e., the sentence+??? condition), was able to demonstrate significant perceptual priming for the same set of target items, $t(38) = 2.59$. On the right side, the perceptual priming

[1] It should be noted that the pattern of performance yielded by the standard and the adjusted priming scores were similar for both amnesic participants. All the interpretations of the amnesic data in this and the subsequent experiments are based on the statistical analyses carried out on the more conservative standard priming scores.

Table 2
Performance of Participants C.C. (Basal Forebrain Amnesia) and R.H. (Medial Temporal Lobe Amnesia) in Experiment 1 When Only Fragments of Targets Presented

	Fragment-only cues					
	Sentence+??? condition (e.g., *__IJ___K__R*)			Sentence+fragment condition (e.g., *__I__C__P*)		
Participant & session	Old	New	AP	Old	New	AP
Participant C.C.						
Session 2	.71	.31	.58	.63	.19	.54
Session 4	.71	.13	.67	.79	.19	.74
Session 6	.83	.25	.77	.92	.19	.90
Session 8	.88	.25	.84	.92	.13	.91
Participant R.H.						
Session 2	.54	.25	.39	.54	.31	.33
Session 4	.50	.44	.11	.58	.38	.32
Session 6	.75	.31	.64	.88	.50	.66
Session 8	.66	.56	.23	.88	.50	.66
Session 10	.71	.38	.53	.92	.56	.82
Session 12	.83	.31	.75	.88	.63	.68

Note. Old = studied items; New = nonstudied items; AP = adjusted priming scores.

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scores for target items from the sentences used in sentence+fragment retrieval condition are shown. Again, both C.C. and R.H. exhibited significant perceptual priming for these items: for C.C., $t(38) = 6.32$, and for R.H., $t(38) = 2.57$.[2]

The adjusted priming scores of control participants along with those of the amnesic participants for Experiment 1 are displayed in Figures 6 and 7. Figure 6 presents the adjusted priming scores for the sentence conditions (i.e., sentence+??? and sentence+fragment), and Figure 7 presents adjusted priming scores for the fragments-only conditions. The graphical representation of the data suggest that in all the conditions, the priming scores of amnesic participant C.C. were within the range of scores produced by control participants. Amnesic participant R.H.'s adjusted priming scores in the sentence+fragment condition of the sentence cues sessions were also close to the range of the scores of control participants. In the sentence+??? condition of the sentence cues sessions, R.H. performed abysmally compared with control participants. In the fragment-only sessions, R.H.'s adjusted priming scores for perceptual priming were significant, as noted above. These scores appear to be below that of control participants owing to R.H.'s higher base-rate performance (average nonstudied score across Sessions 2, 4, 6, 8, 10, and 12 was .38 for sentence+??? items and .48 for sentence+fragment items) compared with control participants (average across Sessions 2 and 4 for sentence+??? items: CON1 = .10, CON2 = .10, and CON3 = .13; sentence+fragment items: CON1 = .06, CON2 = .19, and CON3 = .09).

In the recognition memory test, both amnesic participants exhibited impaired recognition memory for repeatedly studied sentences. C.C. checked only 24/48 sentences as familiar, and R.H. checked only 18/48 sentences as familiar; this difference in performance between the two amnesic participants was not statistically significant by a chi-square analysis with continuity correction, $\chi^2(1, N = 96) = 1.06$, $p = .30$. In contrast, control participants performed near ceiling on the recognition test (CON1 = 42/48, CON2 = 45/48, CON3 = 48/48).

Discussion

Four clear findings emerged in this experiment. First, learning of new associations can be obtained in amnesic individuals with different etiologies under retrieval conditions where perceptual constraints are provided (i.e., the sentence+fragment condition). Second, new verbal learning of the kind reported by Tulving et al. (1991), and as assessed by the sentence+??? condition, is exhibited by some other amnesic individuals because C.C. (basal forebrain amnesia) exhibited impressive learning in this condition across sessions. Equally important to note is that, contrary to the previous reports (Tulving et al., 1991), R.H. (medial temporal lobe amnesia) failed entirely to produce the studied targets in this condition. Third, both R.H. and C.C. exhibited significant perceptual priming (i.e., in the fragments-only cues conditions) for all sets of studied material. Particularly noteworthy is the finding that R.H. showed significant perceptual priming for the very same set of targets that he failed to produce in the sentence+??? condition. Finally, in light of these differences and similarities in implicit learning of new verbal information, both C.C.

[2] Tables 1 and 2 show a numerical rise in the nonstudied fragment completion rate for the sentence+fragment and fragments-only conditions. This rise is attributable to the use of the same set of nonstudied items across sessions in order to keep as many factors constant as possible across sessions. It is important that this rise in the nonstudied completion rate was lower than the rise in the completion rate for the studied items for both amnesic participants, thereby yielding an increase in the magnitude of priming as the sessions progressed. It is this latter result that is of theoretical interest and significance.

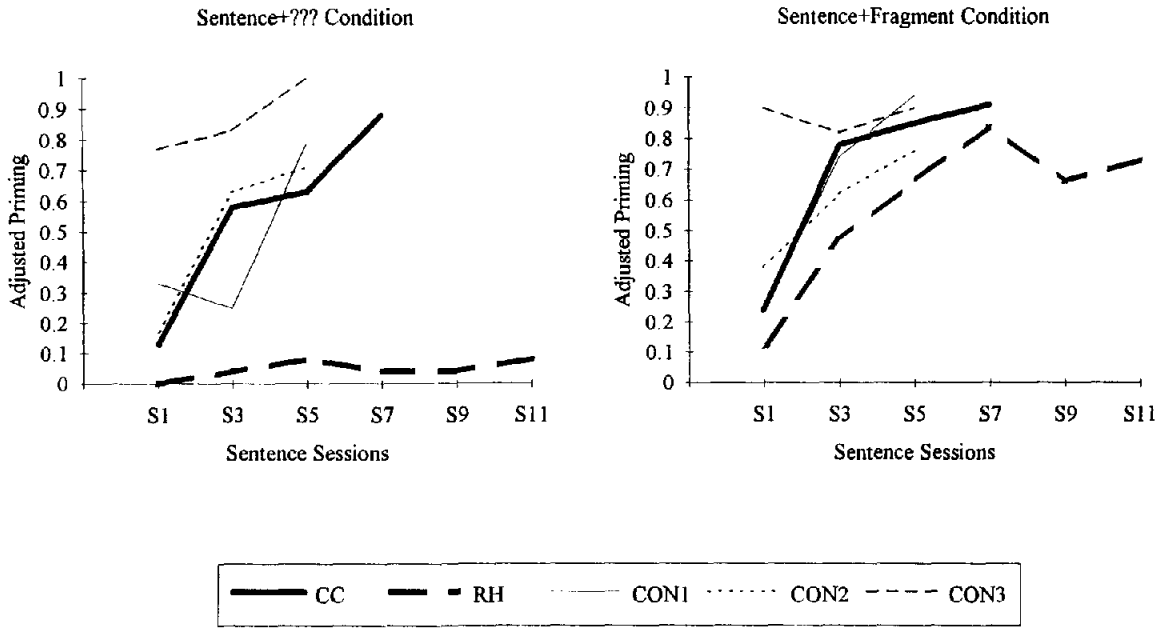

Figure 6. The adjusted priming scores from the 2 amnesic patients (C.C. and R.H.) and 3 control participants (CON1, CON2, and CON3) for the sentence cues in Experiment 1. S = session.

and R.H. performed comparably on explicit measures of memory for the newly acquired information and were notably impaired on this task relatively to control participants.

These data offer possible accounts of the conflicting findings reported in the past on associative learning of verbal information in amnesia. First, it appears that the retrieval conditions under which learning is measured are critical in yielding positive or negative evidence for new learning. Both C.C. and R.H. showed evidence of learning new information when the target production was constrained by perceptual cues (sentence+fragment cues), thereby reducing the response competition and interference

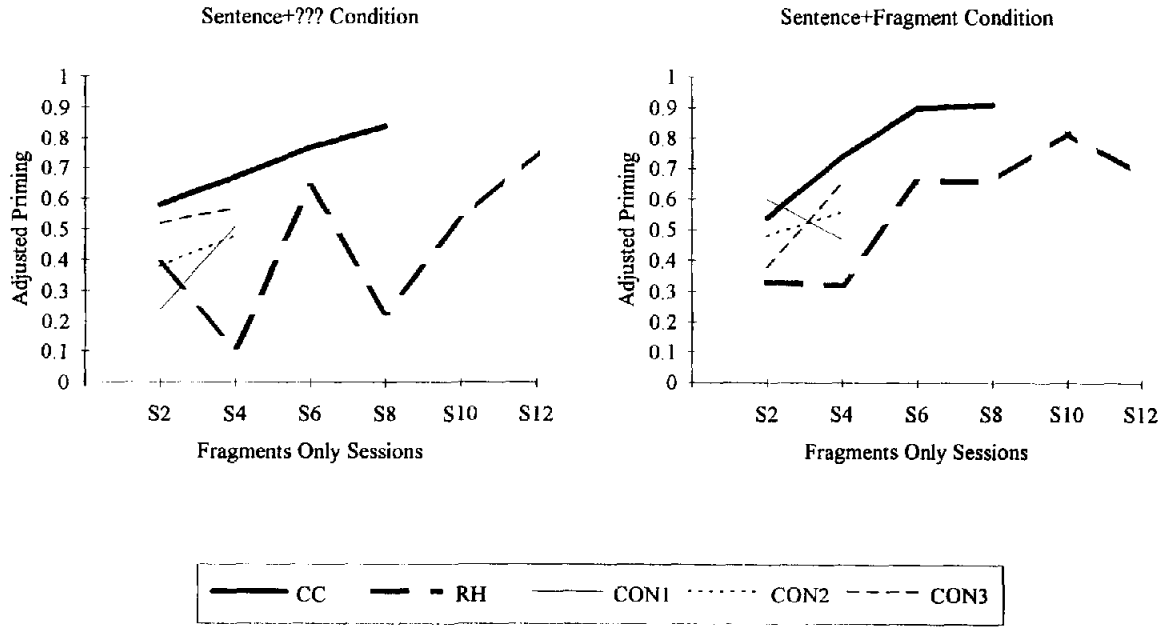

Figure 7. The adjusted priming scores from the 2 amnesic patients (C.C. and R.H.) and 3 control participants (CON1, CON2, and CON3) for the fragments-only cues in Experiment 1. S = session.

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from possible preexperimental associations that have been shown to impede learning in amnesia (Hayman et al., 1992). To be specific, across sessions priming scores for fragments dropped numerically for R.H. when the sentence context was removed (see Tables 1 and 2). This trend is not amenable to statistical analysis but supports the possibility that sentence and fragment pairing had a positive effect on R.H.'s performance compared with fragment-only cues. We investigated this issue further in Experiment 3 by designing a better comparison of sentence+fragment and fragment-only conditions.

As important as the factors affecting the conditions of learning are, they do not account for all the discrepancies in the evidence. This conclusion becomes evident when we contrast the performance of C.C. and R.H. in the sentence+??? condition. C.C., but not R.H., demonstrated robust learning in the absence of any perceptual cue for the target, whereas she performed at a level comparable to that of R.H. on the objective measure of explicit memory. Taken together, these findings suggest that new verbal learning is dependent on the learning conditions (Hayman et al., 1992; Tulving et al., 1991) as well as the locus of neurological damage mediating amnesia. An important observation in this regard is that within the context of this experiment, the differential learning in the two amnesic participants could not be attributed easily to differences in severity of amnesia because both amnesic participants produced equivalent levels of performance on the objective measures of explicit memory in both the neuropsychological examination and the recognition memory test administered in Experiment 1. We addressed this issue again in Experiment 3.

Experiment 2

Experiment 2 was designed to determine whether the newly acquired information could be used to learn related information. According to one view of new learning deficit in amnesia, any learning that could occur in amnesic individuals is inflexible in nature, particularly in amnesic individuals with hippocampal damage (Cohen et al., 1997; Squire, 1992). On this view, production of learned targets, thus, is dependent on the availability of the same cues that were present during learning. We took a different approach in Experiment 2 to determine amnesic individuals' ability to use learned information in novel situations under implicit retrieval instructions. Instead of presenting different cues for the previously learned targets, we changed the target itself to determine transfer of learning to new (related or unrelated) targets. To be more specific, we sought to determine the conditions, if any, under which new targets could be learned readily in response to old sentence cues. Thus, Experiment 2 was designed to test whether the newly acquired information could be used to achieve transfer to related situations.

Method

Materials. The materials in the study phase consisted of the same set of sentences as those used in Experiment 1, with one critical change. The targets in half of the study sentences (i.e., 24 sentences) were replaced by related words and in the other half by unrelated words. For example, *STAFF shot HIJACKER* and *MEDICINE cured HICCUP* were replaced with related sentences, such as *STAFF shot TERRORIST* and *MEDICINE cured BELCH*, respectively, and *TRAIN frightened KANGAROO* and *CORAL protected MOLLUSC* were replaced with unrelated sentences, such as *TRAIN frightened OFFICER* and *CORAL protected PLASTIC*, respectively. At test, these study sentences with related and unrelated targets were intermixed with the 32 nonstudied sentences used in Experiment 1, where the targets of half the nonstudied sentences (i.e., 16 sentences) were also replaced by related words and the targets of the remaining half of the sentences were replaced by unrelated words. As in Experiment 1, at test half of the studied items (i.e., 24 sentences) were presented in the sentence+fragment retrieval condition, and the remaining half were presented in the sentence+??? retrieval condition. Of the 24 study sentences in each of the two retrieval conditions described above, half of these sentences (i.e., 12 sentences) had been studied with a related target substitute and the other half with an unrelated target substitute. Once again, the same 12 studied sentences were presented in each condition in this experiment (i.e., sentences were nested within conditions.)

In a similar manner, for nonstudied sentences the targets of half the sentences presented in sentence+??? retrieval condition and in sentence+fragment condition were substituted with related words and the other half with unrelated words. Thus, the same eight sentences were presented within each nonstudied condition through all sessions (i.e., items were nested within conditions).

We carried out two norming studies to select related and unrelated target substitutes for the studied and nonstudied sentences in Experiment 2. In one study, 20 college undergraduates were presented with 240 pairs of target words. Eighty pairs consisted of the original target and its related target word, 80 other pairs consisted of the original target and its unrelated target word, and the last 80 pairs consisted of the related target and its unrelated counterpart. The undergraduates rated the pairs on a scale ranging from 1 (*highly related*) to 5 (*highly unrelated*). The average relatedness ratings given by the undergraduates to the pairs of the original and their related targets were 1.95 and 2.15, respectively, for studied and nonstudied sentences. The average relatedness ratings to the pairs of the original and their unrelated target counterparts were 4.59 and 4.47, respectively, for studied and nonstudied sentences. The high relatedness ratings given to original and related target pairs did not differ for the pairs to be used in the studied and nonstudied conditions, $t(78) = 1.59$. In a similar manner, the low relatedness ratings given to the original and unrelated target pairs did not differ for the studied and nonstudied items, $t(78) = 1.15$. As expected, for studied and nonstudied pairs taken together, the relatedness ratings for related pairs ($M = 2.01$) were significantly different from the ratings for the unrelated pairs ($M = 4.54$), $t(158) = 28.33$.

In the second norming study, fragmented versions of related and unrelated target substitutes for studied and nonstudied sentences selected for use in Experiment 2 were presented in the sentence context to a new group of 20 college undergraduates. These undergraduates were asked to complete the fragmented targets in the sentences with the first solution that came to mind. The mean proportion of targets accurately completed for the eight conditions ranged from .10 to .23 (related/studied/sentence+??? = .22, unrelated/studied/sentence+fragment = .15, related/studied/sentence+??? = .23, unrelated/studied/sentence+fragment = .10, related/nonstudied/sentence+??? = .18, unrelated/nonstudied/sentence+fragment = .20, related/nonstudied/sentence+??? =

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.16, unrelated/nonstudied/sentence+fragment = .22) and did not significantly differ from one another, $F(7, 72) = 0.57$, $MSE = .04$. Thus, the baseline probabilities of completion of the fragments to be presented in different encoding and retrieval conditions were found to be low and equivalent.

Design and procedure. As in Experiment 1, we conducted multiple sessions. Both amnesic participants (C.C. and R.H.) took part in six sessions, and each of the control participants took part in two sessions. For C.C. and control participants, the first session of Experiment 2 was administered 4 weeks, and for R.H. 1 week, after the conclusion of Experiment 1. The study sentences used in Experiment 1 were used in the present experiment with related or unrelated targets. Once again, the study phase was identical in all sessions. C.C., R.H., and control participants were presented with one sentence at a time on the computer screen (Macintosh SE), and as in Experiment 1, their task was to determine whether each sentence made sense to them. After the experimenter typed in the response (yes or no), the next sentence appeared on the screen.

Once again, the presentation of test items varied across sessions in the following manner. In Sessions 1, 3, and 5—called the sentence cues sessions—test items were presented in two retrieval formats. The same set of 24 studied sentences and 16 nonstudied sentences were presented in the sentence+fragment condition across all the above stated sessions for amnesic and control participants. The participants' task was to complete the fragment with the first word that came to mind. The same set of remaining 24 studied and 16 nonstudied sentences were presented in the sentence+??? condition in Sessions 1, 3, and 5. Now the task was to complete the sentence with the first word that came to mind. For control participants, both Sessions 1 and 2 consisted of sentence cues.

In Sessions 2, 4, and 6—called the fragments-only cues sessions—only the fragments of the targets from the studied and nonstudied sentences were presented. The patients were asked to complete the fragment with the first word that came to mind. The purpose of including these sessions was to determine whether perceptual priming could be obtained in the amnesic participants for target items when the experimentally associated cues (i.e., the sentence stems) were absent.

Results

Tables 3 and 4 present the sentence completion and fragment completion performance, respectively, of amnesic participants C.C. and R.H. for the studied and nonstudied and the related and unrelated items in different retrieval conditions across the six sessions in Experiment 2. The adjusted priming scores for each amnesic participant in each condition are also displayed in Tables 3 and 4. With C.C., evidence of transfer could potentially be observed in two retrieval conditions because she had demonstrated learning in sentence+??? and sentence+fragment conditions, whereas with R.H., any potential transfer could only be observed for the materials shown in the sentence+fragment condition because he failed to show any learning for targets in sentence+??? condition in Experiment 1.

For C.C., significant priming was obtained in only two retrieval conditions. First, significant and substantial transfer to related targets was obtained in the condition where the sentence cues and the fragments of the related words were presented, $t(18) = 8.37$. Second, when only the fragments cues of the related targets were presented, C.C. again showed substantial and significant perceptual priming, $t(18) = 5.54$. None of the remaining conditions yielded significant priming except for marginal perceptual priming for the fragments of the unrelated targets (in the fragments-only cues sessions) that were taken from the materials presented in the sentence+??? condition, $t(18) = 1.99$, $p = .06$. For R.H., numerical priming was observed for related items presented in sentence+fragment retrieval condition, but this effect failed to meet statistical significance, $t(18) = 1.64$, $p = .12$. None of the remaining conditions revealed significant priming. The adjusted priming data for control participants in the sentence cues condition are plotted in Figure 8 along with the adjusted priming scores of the amnesic participants in the sentence cues conditions.

Table 3
Performance of Participants C.C. (Basal Forebrain Amnesia) and R.H. (Medial Temporal Lobe Amnesia) in Experiment 2 When Sentence Cues Presented

Participant & session	Sentence cues															
	Related items								Unrelated items							
	Sentence+??? condition (e.g., *STAFF shot ???*)				Sentence+fragment condition (e.g., *MEDICINE cured BE__C__*)				Sentence+??? condition (e.g., *TRAIN frightened ???*)				Sentence+fragment condition (e.g., *CORAL protected P__A___IC*)			
	Old	New	AP	PI	Old	New	AP	PI	Old	New	AP	PI	Old	New	AP	PI
Participant C.C.																
Session 1	.08	.00	.08	0.42	0.75	.00	0.75	.08	.08	.00	.08	.25	.25	.25	.00	.16
Session 3	.00	.00	.00	1.00	1.00	.13	1.00		.00	.00	.00	.80	.33	.25	.11	.42
Session 5	.08	.00	.08	0.75	1.00	.38	1.00		.08	.00	.08	.66	.50	.38	.19	
Participant R.H.																
Session 1	.00	.00	.00		0.66	.25	0.55		.00	.00	.00		.33	.50	−.34	
Session 3	.00	.00	.00		0.66	.50	0.32		.00	.00	.00		.50	.38	.19	
Session 5	.00	.00	.00		0.92	.50	0.84		.00	.00	.00		.66	.63	.08	

Note. Old = studied items; New = nonstudied items; AP = adjusted priming scores; PI = proactive interference.

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Table 4
Performance of Participants C.C. (Basal Forebrain Amnesia) and R.H. (Medial Temporal Lobe Amnesia) in Experiment 2 When Only Fragments of Targets Presented

Participant & session	Fragment-only cues															
	Related items								Unrelated items							
	Sentence+??? condition (e.g., *_E___OR___T*)				Sentence+fragment condition (e.g., *BE__C__*)				Sentence+??? condition (e.g., *O_F___E__*)				Sentence+fragment condition (e.g., *P_A___IC*)			
	Old	New	AP	PI	Old	New	AP	PI	Old	New	AP	PI	Old	New	AP	PI
Participant C.C.																
Session 2	.25	.13	.14		0.83	.00	0.83		.25	.00	.25		.25	.00	.25	
Session 4	.33	.25	.11		1.00	.25	1.00		.58	.13	.52		.42	.25	.23	
Session 6	.58	.25	.44		0.83	.38	0.73		.42	.13	.38		.50	.25	.33	
Participant R.H.																
Session 2	.42	.25	.23		0.42	.50	−.16		.50	.38	.19		.66	.38	.45	
Session 4	.25	.25	.00		0.58	.50	.16		.42	.13	.33		.66	.63	.08	
Session 6	.25	.38	−.21		0.42	.50	−.16		.50	.13	.38		.50	.50	.00	

Note. Old = studied items; New = nonstudied items; AP = adjusted priming scores; PI = proactive interference.

These data show an interesting pattern: The control participants performed much better than both amnesic participants in all conditions except for the related items in the sentence+fragment condition. In other words, the sentence+??? cues were not as deleterious for control participants as they were for C.C. and R.H. Furthermore, in the sentence+fragment conditions, the relatedness variable greatly helped C.C.'s performance and, to some extent, R.H.'s performance. However, control participants showed substantial priming for related as well as unrelated fragments.

Finally, there was a noteworthy pattern in C.C.'s performance in addition to the significant priming scores obtained in the related conditions with fragment cues. In the sentence+??? retrieval conditions where no fragment cue was present to constrain the responses, substantial proactive interference were obtained (see Table 4, the column titled PI). As can be seen, the highest levels of proactive interference were obtained in the sentence+??? related and unrelated retrieval conditions. An interesting finding was that some proactive interference was also obtained in sentence+fragment retrieval condition for the unrelated

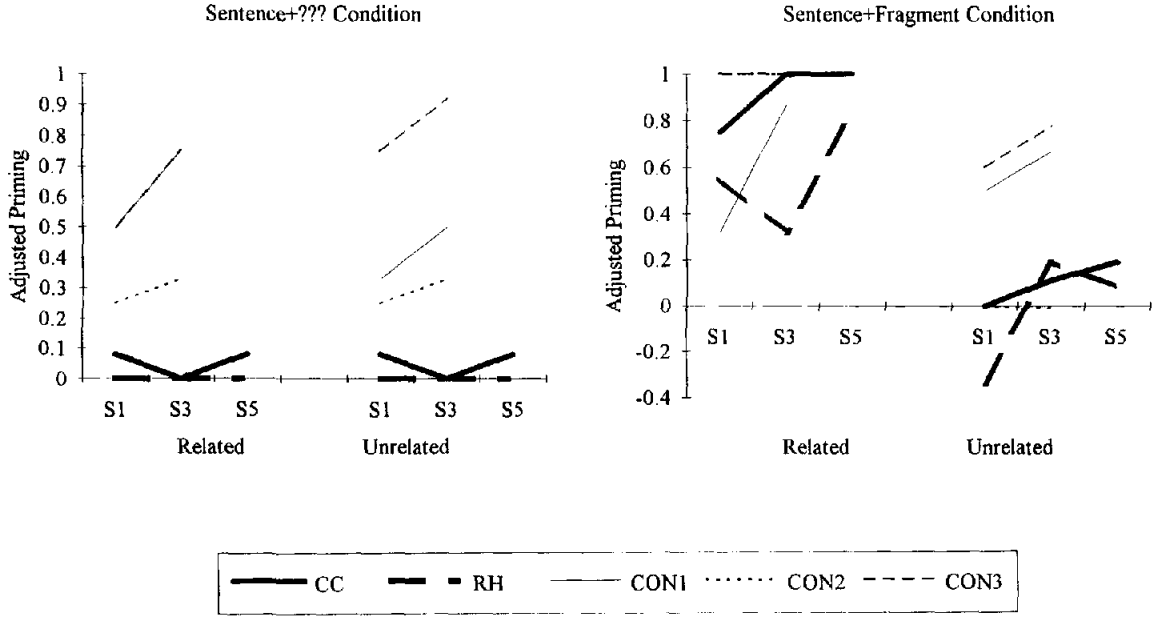

Figure 8. The adjusted priming scores from the 2 amnesic patients (C.C. and R.H.) and 3 control participants (CON1, CON2, and CON3) for the sentence cues in the related and unrelated conditions in Experiment 2. S1, S3, and S5 = Sessions 1, 3, and 5, respectively.

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items, whereas little interference was seen when the target fragment was a related one. In the unrelated sentence+fragment retrieval condition, C.C. expressed confusion when confronted with unrelated cues and remarked that the fragments looked "wrong." In contrast, for fragments in the related sentence+fragment retrieval condition, she did not report noticing anything unusual. No proactive interference was evident in R.H.'s performance. The control participants did not show any proactive interference in the sentence+fragment conditions, related or unrelated. In the sentence+??? conditions, the proactive interference for control participants was quite small and, furthermore, declined across Sessions 1 and 2 (see Figure 9).

Discussion

The results of Experiment 2 delineate the experimental conditions under which transfer can be obtained in amnesia from the newly acquired information. In the absence of perceptual cues (i.e., the sentence+??? condition), C.C. exhibited no transfer to related information and instead showed substantial proactive interference. As expected, R.H. showed little transfer in the sentence+??? condition because he had failed to learn the original targets in Experiment 1. When the retrieval cue at test constrained possible responses (i.e., the sentence+fragment related condition), C.C. showed robust transfer to related information. Transfer to semantically related information, particularly in C.C., can be contrasted with the lack of transfer to unrelated information (sentence+fragment retrieval condition for unrelated items) presented in the identical format as the related information across study and test. Converging evidence for the ability to use semantic relatedness in learning new information was obtained from C.C.'s proactive interference data. Although C.C. showed substantial proactive interference for new unrelated items even when the fragment cues were present, very little interference was observed for new related information.

In R.H.'s performance, a trend for transfer to related information was present but not reliable. Although these data do not permit any definitive conclusion regarding the transfer of information, they do hint that the sentence context modulated priming to some extent in R.H.'s performance. To be specific, the fact that R.H. showed a trend toward priming (p = .12) for related sentence+fragment cues (priming scores: Session 1 = .55, Session 2 = .32, Session 3 = .84) in Experiment 2 and not for unrelated sentence+fragment cues (priming scores: Session 1 = –.34, Session 2 = .19, Session 3 = .08) supports the notion that the context generated from the sentence+fragment pairing may have improved R.H.'s performance. No such beneficial effects of relatedness were found when fragments-only retrieval cues were presented to R.H.

C.C.'s performance in this experiment is particularly noteworthy in light of the control participants' data. Unlike C.C., the control participants showed substantial priming in all conditions regardless of the test format or relatedness, and they showed small effects of proactive interference. This divergence in the patterns of data between C.C. and control participants suggests that C.C.'s performance (to be specific, in the transfer observed for related information) was uncontaminated by explicit memory.

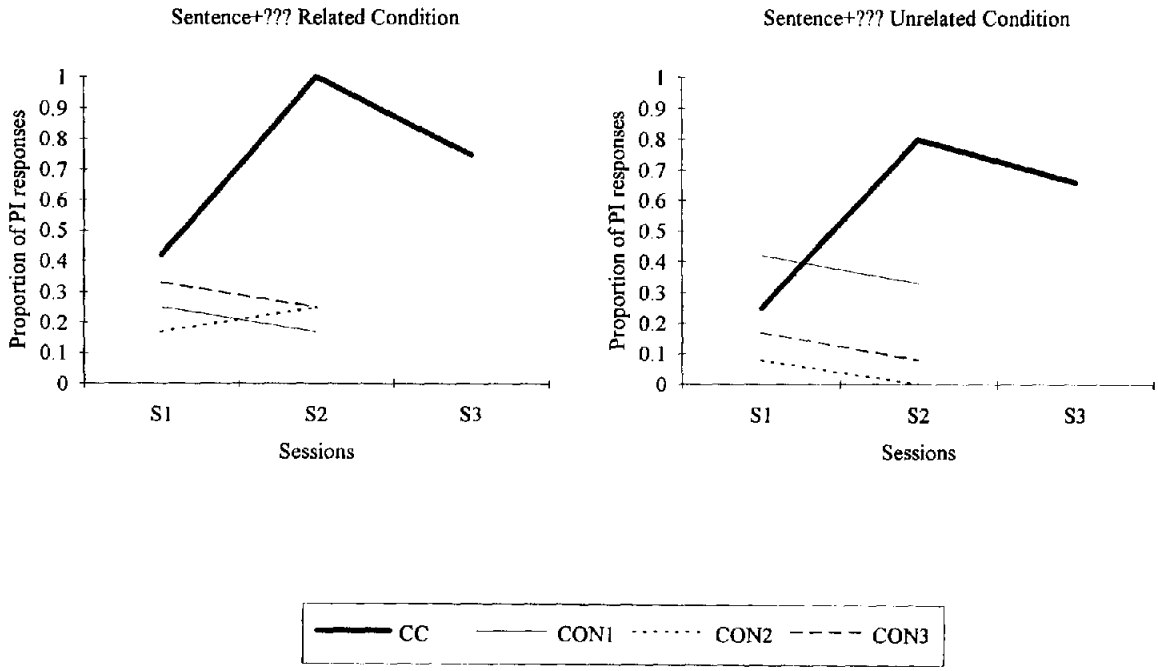

Figure 9. The proactive interference (PI) scores from patient C.C. and the 3 control participants (CON1, CON2, and CON3) in Experiment 2. S1, S2, and S3 = Sessions 1, 2, and 3, respectively.

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With respect to fragment-only cues retrieval conditions presented to the amnesic participants, most conditions revealed no significant priming. This result is somewhat surprising because both patients were presented with the new targets within the sentence contexts during the study phase of each session and had, therefore, been exposed to the physical information necessary for producing perceptual priming. These data suggest that perceptual priming for new associations can be disrupted by alterations in the conceptual encoding. The possible reasons for this anomalous finding are considered in the *Discussion* section of Experiment 4.

To summarize, in Experiments 1 and 2 evidence of new learning was observed in two amnesic individuals. These experiments specify the neuroanatomical and retrieval constraints in the acquisition of new information and the use of this information in learning conceptually related verbal information. To be specific, C.C. exhibited learning for target words in the context of the sentence structure both when the fragment of target word was present (e.g., *MEDICINE cured _ I _ C _ P*) and when it was absent (e.g., *STAFF shot ???*). R.H. exhibited learning only in the sentence+fragment retrieval condition. Furthermore, transfer to related information (e.g., *MEDICINE cured BELCH, STAFF shot TERRORIST*) was observed only when the fragmented form of the target in the sentence context was presented. Under such conditions, C.C. exhibited robust transfer and R.H. exhibited a trend for transfer.

Experiments 3 and 4 were designed to address several issues that emerged from the results of Experiments 1 and 2 as well as to replicate some of the core findings from Experiments 1 and 2. Experiment 3 was similar to Experiment 1 except for two principal changes in design. First, in Experiment 3, we trained C.C. and R.H. on an entirely new set of sentences. Recall that sentences in Experiment 1 were nested within each condition in order to hold constant the items that C.C. and R.H. saw in each condition. Therefore, a systematic replication of Experiment 1 findings with an entirely new set of materials was considered important for placing our findings on a firmer empirical ground. Furthermore, this goal was also considered important in light of the fact that the findings from Experiment 1 were based on two case studies. Second, in Experiment 3 we tested the amnesic participants in three different retrieval conditions within each session: sentence+???, sentence+fragment, and fragments-only. The purpose of this change was to enable a better assessment of the role of sentence cues in producing priming on fragments relative to a condition where only the fragments were presented at test. Finally, Experiment 3 provided us the opportunity to train the amnesic participants on an entirely new set of materials so that we could measure transfer to related material in Experiment 4 somewhat differently than in Experiment 2.

The rationale for conducting Experiment 4 was as follows: The learning and transfer observed in Experiments 1 and 2 could be based on two different mechanisms. One possibility is that the sentences in Experiment 1 were learned in a stimulus–response fashion such that the sentence cue (e.g., *MEDICINE cured ???*), produced the learned response (*HICCUP*). The second possibility is that not only were the physical format of the sentence cues and appropriate targets encoded, but also the concepts embodied in these sentences were. The results from Experiment 2 partially support the second mechanism because immediate and robust transfer to related (but not unrelated) targets was evident in the performance of one amnesic participant (C.C.) and hinted in the performance of the other amnesic participant (R.H.). We sought to devise a stronger test of this in Experiment 4.

The goal in Experiment 4 was to determine further whether successful verbal learning occurs at a conceptual level and as such is flexible. If such learning does occur at a conceptual level, transfer to related information should occur regardless of the physical similarity between the acquisition (Experiment 3) and transfer materials (Experiment 4). Recall that in Experiment 2, only the target word in the sentences from Experiment 1 was changed to related or unrelated words. In Experiment 4, we further reduced the perceptual overlap between the acquisition (Experiment 3) and the transfer (Experiment 4) materials by changing both the verb and the target (last) word of the sentences. Thus, in Experiment 3, amnesic and control participants were first trained on a new set of novel sentences. In Experiment 4, half of the transfer sentences contained both verbs and targets that were semantically similar and perceptually dissimilar to the original sentences (Experiment 3), and the remaining half of the transfer sentences contained both verbs and targets that were semantically and perceptually dissimilar to the original sentences. If new learning in amnesia has a reasonably strong conceptual basis, then we would observe transfer to semantically similar materials even though the perceptual overlap between the acquisition and transfer materials is considerably reduced.

Experiment 3

Method

Materials. We constructed 120 sentences following the same constraints used in Experiment 1; that is, the sentences were designed to be unfamiliar and yet plausible (see Table 5 for an example of materials used in Experiment 3). Sixty of these sentences served as studied sentences, and the remaining 60 sentences served as nonstudied sentences across sessions. The target words and their fragments were taken from the materials used by Blaxton (1989), who selected the targets on the basis of norming studies done for relatedness as well as base-rate fragment completion rates. We constructed an additional 30 new sentences that were similar in nature to the sentences described above to serve as nonstudied sentences in the recognition test described in the next section.

Design and procedure. This experiment was similar in design to Experiment 1, with one change to be described below. The amnesic participants C.C. and R.H. participated in 10 sessions, and the control participants took part in 5 sessions, which occurred at intervals from 1 to 3 weeks apart. As previously, each session consisted of a study phase, a retention interval of 5 min, and a test phase. In the study phase of each session, the same set of 60 sentences was presented visually, and the participants were asked to decide whether the sentences made sense. The remaining 60 sentences constituted the nonstudied sentences across all sessions. In the test phase, 20 studied and 20 nonstudied sen-

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Table 5
A Sample of Materials Used in Experiments 3 and 4 (Items in Parentheses Show the Format Used at Test)

Retrieval condition	Experiment 3	Experiment 4	Relatedness
	Studied items		
Sentence+???	*ZOOKEEPER traded AARDVARK.* (*ZOOKEEPER traded ???*)	*ZOOKEEPER exchanged ARMADILLO.* (*ZOOKEEPER exchanged ???*)	Related
Sentence+???	*PASSERBY fed PEACOCK.* (*PASSERBY fed ???*)	*PASSERBY hailed BEGGAR.* (*PASSERBY hailed ???*)	Unrelated
Sentence+fragment	*LIGHTNING torched JUNGLE.* (*LIGHTNING torched J___G___.*)	*LIGHTNING burned WILDERNESS.* (*LIGHTNING burned W__L_____N__S__.*)	Related
Sentence+fragment	*SCOUT visited RECLUSE.* (*SCOUT visited __EC___S__.*)	*SCOUT swept STADIUM.* (*SCOUT swept S__AD__U__.*)	Unrelated
Fragments-only cues	*AMENDMENT reinforced LIBERTY.* (*L___ER___*)	*AMENDMENT strengthened FREEDOM.* (*F__E__D__M*)	Related
Fragments-only cues	*HEIRS sued ASYLUM.* (*__S__LU__*)	*HEIRS met INVENTOR.* (*I___EN___R*)	Unrelated
	Nonstudied items		
Sentence+???	*APPEARANCE prompted RIDICULE.* (*APPEARANCE prompted ???*)	*APPEARANCE prompted SCORN.* (*APPEARANCE prompted ???*)	Related
Sentence+???	*FISHERMAN greeted DOLPHIN.* (*FISHERMAN greeted ???*)	*FISHERMAN billed JOGGER.* (*FISHERMAN billed ???*)	Unrelated
Sentence+fragment	*GRAPES tainted SALIVA.* (*GRAPES tainted __AL__V__.*)	*GRAPES stained SPIT.* (*GRAPES stained __PI__.*)	Related
Sentence+fragment	*DANCER offered COFFEE.* (*DANCER offered __O__F__E.*)	*DANCER evaluated SPACE.* (*DANCER evaluated __P__C__.*)	Unrelated
Fragments-only cues	*VEGETATION camouflaged PYTHON.* (*__YT___N*)	*VEGETATION disguised SNAKE.* (*__NA___*)	Related
Fragments-only cues	*SNIPER noticed AMBULANCE.* (*__MBU_____CE*)	*SNIPER erased TRADEMARK.* (*__RAD_____RK*)	Unrelated

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tences were presented nested within each of the following three implicit retrieval conditions across sessions: sentence+???, sentence+fragment, and fragments-only cues. The participants were asked to fill in the blank or complete the fragment with the first word that came to mind. Unlike in Experiment 1 in which perceptual priming was assessed in alternate sessions, a purer measure of perceptual priming was obtained here in the fragment-only cues condition because items from this condition were never presented at test along with the sentence context. The participants controlled the pace of study and test phases. In all the study and test phases, a new random order was used to present the materials, with the constraint that within a session the same random order was used for all participants.

In order to obtain a measure of explicit memory, we also conducted a recognition memory test after the completion of Session 10 for the amnesic participants (and Session 5 for the control participants). The recognition memory test was administered after the study, retention interval, and test phases were completed. The 60 studied sentences were randomly intermixed with 30 new sentences never shown in any other part of this or other experiments. The amnesic participants and control participants were asked to indicate which sentences looked familiar to them.

On the basis of the results of Experiment 1, we expected that in the absence of perceptual cues (i.e., the sentence+??? retrieval condition), only C.C., and not R.H., would exhibit learning of new information. In the sentence+fragment condition, both C.C. and R.H. were expected to show new learning across sessions as seen in Experiment 1. In the fragment-only cues condition, we expected that both C.C. and R.H. would exhibit perceptual priming. Finally, the recognition memory test was used to determine whether differential learning across patients would be accompanied by a concomitant difference in the explicit memory measure in each of the retrieval conditions. For the control participants, we expected that they would show substantial priming in all conditions and ceiling effects on the explicit memory measure.

Results

The proportion of studied and nonstudied items correctly produced across 10 sessions and the concomitant adjusted priming scores in each of the three retrieval conditions by each amnesic participant are presented in Table 6. In the sentence+??? retrieval condition, C.C. exhibited substantial learning across sessions, $t(38) = 9.44$. R.H., in contrast, failed to show any learning in this condition, $t(38) = 1.00$. This pattern for both amnesic participants replicates the results of Experiment 1 with a new set of materials. Evidence of learning in the sentence context with the aid of fragmented cues (i.e., in the sentence+fragment condition) was robust for C.C., $t(38) = 4.23$. R.H.'s performance reflected consistently high base-rates for nonstudied items, thereby yielding small priming effects. Therefore, although the difference was in the expected direction, it was not statistically significant, $t(38) = 0.57$. Finally, evidence for perceptual priming was measured in the fragment-only cues condition. For C.C., perceptual priming was found to be robust, $t(38) = 5.66$. For R.H., once again high base-rate performance led to small priming effects and, therefore, failed to reach statistical significance, $t(38) = 1.56$, $p = .13$.

Figure 10 presents the adjusted priming data from C.C., R.H., and the control participants in the three retrieval

Table 6
Performance of Participants C.C. (Basal Forebrain Amnesia) and R.H. (Medial Temporal Lobe Amnesia) in Experiment 3

Session no.	Patient C.C. Old	Patient C.C. New	Patient C.C. AP	Patient R.H. Old	Patient R.H. New	Patient R.H. AP
Sentence+??? condition						
1	.20	.00	.20	.00	.00	.00
2	.40	.00	.40	.00	.00	.00
3	.60	.00	.60	.00	.00	.00
4	.70	.00	.70	.00	.00	.00
5	.65	.00	.65	.00	.00	.00
6	.75	.00	.75	.05	.00	.05
7	.80	.00	.80	.00	.00	.00
8	.85	.00	.85	.00	.00	.00
9	.80	.00	.80	.05	.00	.05
10	.90	.00	.90	.05	.00	.05
Sentence+fragment condition						
1	.80	.30	.71	.65	.55	.18
2	.95	.40	.92	.65	.60	.13
3	.95	.40	.92	.70	.65	.14
4	.95	.45	.91	.75	.70	.17
5	.95	.40	.92	.75	.65	.29
6	.95	.45	.91	.80	.65	.43
7	.95	.45	.91	.80	.70	.33
8	.95	.45	.91	.75	.70	.17
9	.95	.45	.91	.75	.70	.17
10	.95	.45	.91	.80	.70	.33
Fragments-only cues condition						
1	.45	.05	.42	.60	.30	.43
2	.45	.05	.42	.60	.30	.43
3	.55	.10	.50	.55	.35	.31
4	.75	.10	.72	.65	.50	.30
5	.75	.15	.71	.70	.45	.45
6	.75	.10	.72	.65	.40	.42
7	.85	.15	.82	.60	.55	.11
8	.80	.10	.77	.75	.50	.50
9	.80	.15	.76	.75	.50	.50
10	.80	.15	.76	.60	.55	.11

Note. Old = studied items; New = nonstudied items; AP = adjusted priming scores.

conditions. As expected, the control participants showed consistently high priming scores in the sentence+??? and sentence+fragment conditions. Inexplicably, CON3 produced poor priming scores in the fragments-only cues condition even though his performance was found to be at a consistently high level in all the conditions of all the experiments. One reason for poor priming score may have been higher base-rates for CON3 (average for fragments-only sessions = .41) compared with the other two control participants (CON1 = .29, CON2 = .19).

Given that robust learning was obtained for C.C. whereas such learning was either absent (in the sentence+??? condition) or small and subject to ceiling effects (in the sentence+fragment condition) for R.H., we needed to determine whether C.C.'s performance reflected contamination from explicit memory. Table 7 displays the hits and false alarm rates for C.C. and R.H. C.C. and R.H. exhibited nearly identical d' and β values. This result is noteworthy because by the end of Session 10, C.C. could produce most of the target words in all three retrieval conditions whereas R.H. could not reliably produce any target items in the sentence+??? condition. In fact, an inspection of the hit rates for studied sentences from each of the three retrieval conditions revealed that the explicit memory of C.C. and R.H. was nearly identical across all three conditions. In summary, these findings indicated that differential learning by C.C. and R.H. in the sentence+??? condition could not simply be attributed to differential levels of explicit memory. This conclusion is further supported by the near ceiling performance of control participants (for the 3 control participants, average hits = .95, average false alarms = .01). Note that control participants' recognition memory with 5 training sessions exceeded the performance of both amnesic participants in recognition memory after 10 training sessions.

Discussion

In Experiment 3, we replicated with a new set of materials the central finding of new verbal learning from Exper-

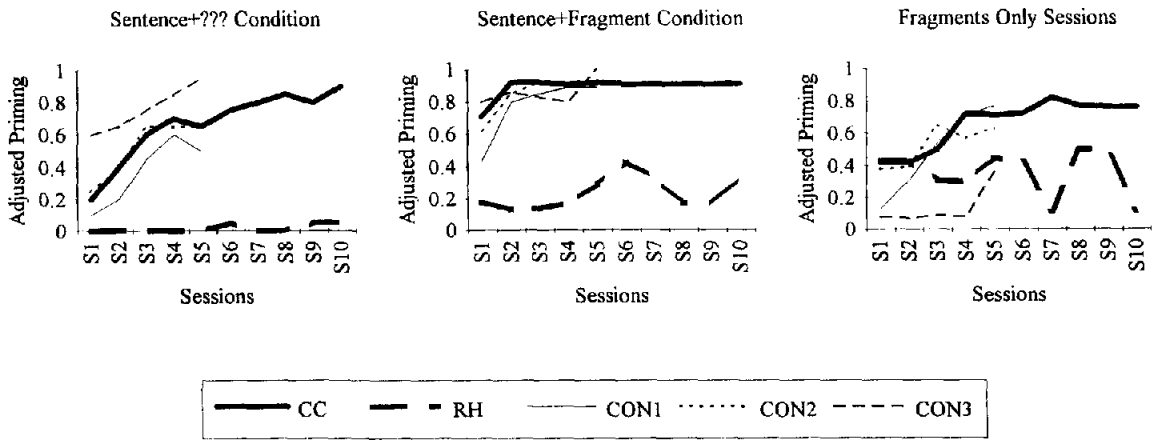

Figure 10. The adjusted priming scores from the 2 amnesic patients (C.C. and R.H.) and 3 control participants (CON1, CON2, and CON3) in Experiment 3. S = session.

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Table 7
Results From the Recognition Memory Task in Experiment 3

Participant	Hits	False alarms	d'	β
C.C.	.75	.07	2.15	2.39
R.H.	.73	.07	2.09	2.48
	Sentence + ???	Sentence + fragment	Fragments only	
C.C.	.75	.80	.70	
R.H.	.80	.75	.65	

Note. Bottom half of the table represents proportion hits across the three conditions.

iment 1. The results support the previous reports in the literature (e.g., Tulving et al., 1991) that new learning can be obtained in severe amnesic patients even when no perceptual cue for the target is provided (i.e., sentence+??? retrieval cues). However, the results from Experiments 1 and 3 also show that such learning can be obtained in some but not all amnesic individuals. The data suggest that even when explicit memory deficits are comparable, medial temporal lobe damage appears to hinder this type of learning.

As in Experiment 1, C.C. showed robust learning in the sentence+fragment condition and showed robust perceptual priming in the fragments-only cues condition. R.H.'s performance in the sentence+fragment condition and the fragment-only cues condition requires some explanation. In both these conditions, we failed to find significant priming because of ceiling effects, although consistent numerical trends in the right direction were present. These fragments were taken from Blaxton (1989), who developed the completion norms on college undergraduates. In order to keep as many experimental details equated between C.C. and R.H. as possible, we used the same fragments for C.C. and R.H. (and, of course, the control participants). The difficulty level of these fragments worked well with C.C., but R.H., who was adept at crossword puzzles and fond of word games in general, found these fragments too easy.

Two consequences of this pattern of base-rates were as follows. First, these base-rates and priming rates precluded an assessment of any potential benefit in R.H.'s performance from use of sentence cues in solving the fragments. Two, we performed an additional word fragment completion task and a word stem completion task with a new set of materials in order to rule out the unlikely possibility that R.H.'s performance in the sentence+fragment and fragments-only conditions reflected impaired perceptual priming. One hundred and twenty high-frequency words ranging in length from five to seven letters were selected for these two tasks. Sixty words were used in each of the tasks. Sixty words (mean frequency = 54.83, Kucera & Francis, 1967) were used in the word stem completion task in which both amnesic participants were asked to study the same subset of 30 words. After a 5-min retention period, both patients participated in an implicit word stem completion task where three-letter stems of studied words were randomly intermixed with three-letter stems of 30 nonstudied words, and the participants' task was to complete the stem with the first solution that came to mind. Both patients showed substantial priming: C.C. produced 43% studied and 23% nonstudied correct completions for a priming score of 20%, and R.H. produced 50% of studied and 17% of nonstudied solutions for a priming score of 33%. These scores were comparable to the significant priming scores we obtained from 10 college undergraduates for the same study list (mean studied completion = 54%, mean nonstudied completion = 26.3%), $t(9) = 7.87$. It should be noted that another group of 10 college undergraduates were tested on the counterbalanced second study list that also yielded significant priming (mean studied completion = 47%, mean nonstudied completion = 30%), $t(9) = 5.38$.

The remaining 60 words (mean frequency = 45.35, Kucera & Francis, 1967) were used in the implicit word fragment completion task. At study, C.C. and R.H. performed an incidental encoding task by rating 30 words for the pleasantness of meaning on a 5-point scale. A 5-min retention interval followed this incidental encoding task. At test, fragments of studied and an additional 30 nonstudied (previously not shown) words were presented in a random order, and the two participants with amnesia were asked to complete the fragments with the first word that came to mind. Both participants exhibited priming: C.C. produced 23% priming (studied = 43% and nonstudied = 20% correct completions), and R.H. produced 13% priming (studied = 50% and nonstudied = 37% correct completions; note the higher base-rate completion for R.H. again). The important point to note is that the priming scores of both of these participants with amnesia were comparable to those of 10 undergraduates (mean priming = 14%) tested on the same study and test lists (mean studied completion = 36%, mean nonstudied completion = 22%), $t(9) = 5.36$. Also note that significant perceptual priming was obtained with an additional 10 undergraduates for the counterbalanced second study list (studied = 34%, nonstudied = 27%), $t(9) = 2.37$.

The results of these two additional implicit memory tasks clearly show that R.H. exhibited normal levels of perceptual priming with different sets of materials and support our conclusion that a lack of significant priming in Experiment 3 for fragments is attributable to high base-rate performance. The important point to note is that the overall pattern of R.H.'s performance across the three retrieval conditions was similar across Experiments 1 and 3. Furthermore, because R.H. had received at least 10 exposures to the studied items in Experiment 3, we included him also in Experiment 4.

The goal of Experiment 4 was to determine whether the learning exhibited by the two amnesic participants in Experiment 3 included a conceptual component. In order to examine the nature of this learning, in Experiment 4 we uniformly reduced the perceptual overlap between the acquisition sentences (Experiment 3) and the transfer sentences (Experiment 4) while we manipulated the semantic overlap (related vs. unrelated). On the basis of the results of Experiment 2, we predicted that both C.C. and R.H. would exhibit transfer to related but not unrelated sentences. To be

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specific, this transfer was expected to occur when the required responses were constrained by the fragmented cues (i.e., in the sentence+fragment condition).

With respect to the sentence+??? retrieval condition, recall that proactive interference was obtained from C.C. in Experiment 2. The sentence+??? retrieval condition in the present experiment permitted us to determine whether such interference could be reduced by decreasing the perceptual overlap between the training and transfer materials. To be specific, in the present experiment, we substituted not only the target words, but also the verbs of the sentences across study and test (see Table 5). Because the training and transfer materials across Experiments 3 and 4 contained less perceptual overlap than before, a reduction in proactive interference in Experiment 4 would demonstrate a greater role of perceptual similarity in giving rise to proactive interference. Furthermore, if a reduction in proactive interference occurred in conjunction with significant transfer to related targets in the sentence+??? condition, such a pattern would constitute strong evidence for a conceptual basis of learning in amnesia.

Experiment 4

Method

Materials. The same set of 120 sentences as those in Experiment 3 were used in this experiment, with one change. For half of the studied sentences from Experiment 3 (e.g., *ZOOKEEPER traded AARDVARK*), we replaced the verbs and targets with related words in Experiment 4 (e.g., *ZOOKEEPER exchanged ARMADILLO*). For the remaining half of the studied sentences from Experiment 3 (e.g., *PASSERBY fed PEACOCK*), we replaced the verbs and targets with unrelated words in Experiment 4 (e.g., *PASSERBY hailed BEGGAR*). In a similar manner, related verb and target substitutes were used for half of the nonstudied sentences and unrelated verbs and targets were used for the remaining half of the nonstudied sentences in all the retrieval conditions (see Table 5 for an example of materials and design).

The relatedness and unrelatedness of verbs and targets across the materials from Experiment 3 and Experiment 4 were determined by carrying out a norming study; the results are shown in Table 8. Eighteen college undergraduates were presented with 360 randomly arranged pairs of sentences. Of these pairs, 120 consisted of the original sentences (from Experiment 3) with their related counterparts, another 120 consisted of original sentences with their unrelated counterparts, and the remaining 120 consisted of the related and unrelated sentences. Participants were asked to rate on a scale from 1 (*unrelated*) to 5 (*highly related*) how well the two sentences related in meaning. The results indicated that the relatedness ratings for the original and related sentences (Table 8, left side of top panel) did not differ from each other across the three retrieval conditions ($F < 1$). In a similar manner, the relatedness ratings for the original and unrelated sentences (Table 8, right side of top panel) did not differ from one another across the three retrieval conditions ($F < 1$). Finally, we found that the specific sentences to be used in the related conditions (collapsing across the studied–nonstudied status and the three retrieval conditions) received significantly higher relatedness ratings ($M = 4.4$) than sentences to be used in the unrelated conditions ($M = 1.39$), unpaired $t(118) = 47.38$.

We carried out another norming study by presenting the related and unrelated target substitutes within the sentence frames to establish preexperimental fragment completion rates. We presented a new group of 16 college undergraduates with fragments of the related word substitutes, and we presented another group of 16 college undergraduates with the fragments of the unrelated word substitutes. The completion rates for the fragments that were to be presented within the related and unrelated sentence+fragment and fragments-only conditions for both studied and nonstudied items are presented in Table 8. These completion rates for items in the eight conditions did not differ from one another in an item analysis, $F(7, 72) = 0.26$, $MSE = .03$.

Design and procedure. Both C.C. and R.H. participated in three sessions, and the control participants participated in two sessions, held 1 week apart. The study sentences used in Experiment 3 were used in the present experiment with related or unrelated verbs and targets. Once again, the study phase was identical in both sessions—participants were presented with one sentence at a time on the computer screen (Macintosh SE), and, as in previous experiments, their task was to determine whether each sentence made sense to them. After the experimenter typed in the response (yes or no), the next sentence appeared on the screen. After a 5-min retention interval, the test phase was presented. In the test phase of each session, the cues were presented in three retrieval conditions, sentence+???, sentence+fragment, and fragment-only cues, with implicit retrieval instructions.

Table 8
Results of Norming for Relatedness of Targets and Baseline Fragment Completion Rates for Stimuli Used in Experiment 4

Item	Related targets			Unrelated targets		
	Sentence+??? condition	Sentence+fragment condition	Fragments-only condition	Sentence+??? condition	Sentence+fragment condition	Fragments-only condition
Norming results for relatedness of sentences from Experiments 3 and 4[a]						
Studied	4.31	4.32	4.47	1.45	1.45	1.32
Nonstudied	4.57	4.44	4.30	1.31	1.27	1.54
Norming results for baseline fragment completion rates in Experiment 4						
Studied		.14	.16		.13	.15
Nonstudied		.09	.13		.18	.13

[a] Scale ranged from 1 (*highly unrelated*) to 5 (*highly related*).

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Table 9
Performance of Participants C.C. and R.H. in Experiment 4

Condition and session no.	Patient C.C. Old	New	AP	PI	Patient R.H. Old	New	AP	PI
Related items								
Sentence+???								
Session 1	.40	.00	.40		.00	.00	.00	
Session 2	.70	.00	.70	.10	.00	.00	.00	
Session 3	.50	.00	.50	.10	.00	.00	.00	
Sentence+ fragment								
Session 1	.90	.10	.89		.70	.30	.57	
Session 2	.80	.20	.75		.80	.40	.67	
Session 3	.90	.30	.86		.60	.40	.33	
Fragments-only								
Session 1	.60	.10	.56		.60	.10	.55	
Session 2	.50	.20	.38		.60	.20	.50	
Session 3	.60	.20	.50		.50	.30	.29	
Unrelated items								
Sentence+???								
Session 1	.00	.00	.00		.00	.00	.00	
Session 2	.10	.00	.10		.00	.00	.00	
Session 3	.20	.00	.20	.20	.00	.00	.00	
Sentence+ fragment								
Session 1	.40	.50	−.20		.40	.30	.14	
Session 2	.60	.60	.00		.40	.40	.00	
Session 3	.70	.70	.00		.70	.40	.50	
Fragments-only								
Session 1	.20	.20	.00		.50	.10	.44	
Session 2	.20	.10	.11		.30	.10	.25	
Session 3	.50	.20	.38		.30	.30	.00	

Note. Old = studied items; New = nonstudied items; AP = adjusted priming scores; PI = proactive interference.

Results

Table 9 presents the sentence completion and fragment completion performance of C.C. and R.H. for the studied and nonstudied related and unrelated items in the three retrieval conditions in Experiment 4. The adjusted priming scores for each amnesic participant in each condition are also shown in Table 9. Recall from the findings of Experiment 3 that with C.C., evidence of transfer could potentially be observed in all three retrieval conditions because she had demonstrated learning in the sentence+??? , sentence+fragment, and fragments-only conditions, whereas with R.H., any potential transfer could be observed only for the materials shown in the sentence+fragment and fragments-only conditions because he failed to show any learning for targets in sentence+??? condition in Experiment 3.

For C.C., significant priming for related (but not unrelated) targets was obtained in all three retrieval conditions. As in Experiment 2, significant transfer to related targets was obtained in the condition where the sentence cues and the fragments of the related words were presented, $t(18) = 4.38$. In a similar manner, when only the fragment cues of the related targets were presented, C.C. again showed substantial perceptual priming, $t(18) = 2.06$. An interesting finding was that in this experiment, C.C. was able to show transfer to related targets even when no perceptual cue for the target (i.e., the sentence+??? condition) was present, $t(18) = 4.31$. C.C. also produced very few proactive interference errors. These two findings are strikingly different from the findings in Experiment 2 where very little transfer and large proactive interference were observed in the sentence+??? retrieval condition. In addition, unlike Experiment 2, C.C. did not report noticing anything unusual in the stimuli presented to her in both the study and the test phases. The present results can be attributed to the fact that both the verb and the target of the sentences were changed to related words, thereby reducing the perceptual similarity between the materials in Experiments 3 and 4. These results clearly suggest that perceptual similarity plays a stronger role in creating proactive interference in amnesia, and conceptual similarity can facilitate learning at least in some forms of amnesia.

For C.C., a small and marginally significant amount of learning was obtained for unrelated items in the sentence+??? condition as well, $t(18) = 1.96$, $p = .07$. However, a direct comparison of the studied items in the related and unrelated conditions revealed that this effect was considerably and significantly smaller than the one observed for related items (see Table 8), $t(18) = 3.24$.[3] The lack of significant priming for C.C. for unrelated fragments in the fragment-only cues condition was similar to the pattern seen in Experiment 1 and was surprising. The possible reasons for this result are discussed in the *Discussion* section.

For R.H., once again, the trends for evidence of transfer were in the expected direction but were statistically marginal. For the sentence+fragment related condition, the numerical trend in priming failed to reach statistical significance, $t(18) = 1.65$, $p = .12$. For the fragments-only related condition, the priming effect was significant, $t(18) = 2.3$. Taken together, the results from Experiment 2 and Experiment 4 provide some, though not strong, evidence of transfer in R.H. None of the remaining priming effects were significant, and, as expected, R.H. exhibited no transfer in the sentence+??? condition.

As in Experiment 2, the control participants did not show substantial effects of relatedness in their priming scores (see Figure 11) in the sentence+??? condition. In the sentence+fragment and fragments-only conditions, the effect of relatedness was more apparent in the control data. As in Experiment 2, the control participants once again produced negligible proactive interference responses in this experiment (average = .06).

Discussion

The results from Experiment 4 provide strong evidence for transfer to related information subsequent to new learning in some types of amnesia. These data indicate that

[3] Such a comparison was made possible by the fact that for both related and unrelated conditions, C.C.'s scored zero for the nonstudied items in all sessions.

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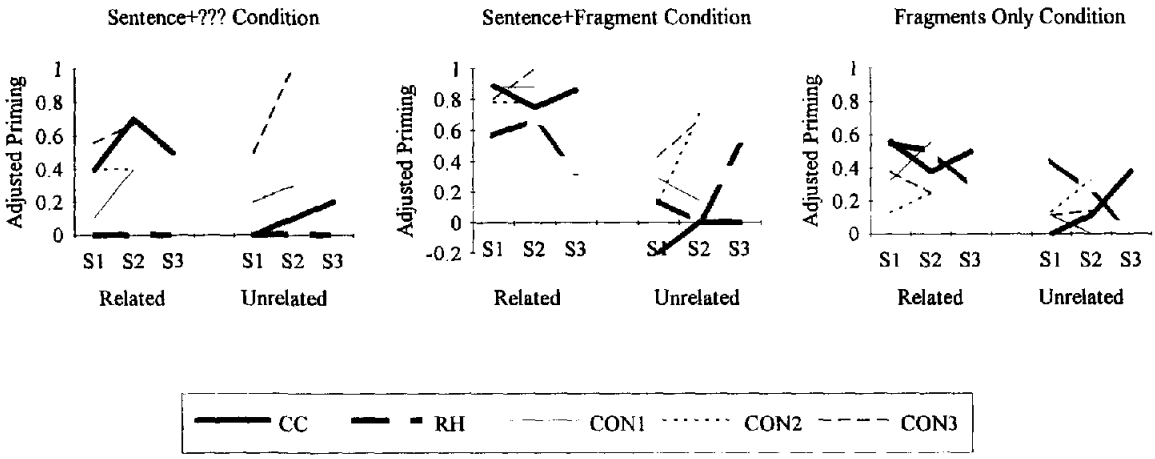

Figure 11. The adjusted priming scores from the 2 amnesic patients (C.C. and R.H.) and 3 control participants (CON1, CON2, and CON3) for the related and unrelated conditions in Experiment 4. S1, S2, and S3 = Sessions 1, 2, and 3, respectively.

learning related information is facilitated by the reduction in perceptual overlap between the original and transfer materials. For example, in the case of C.C., this pattern was evident not only in substantial priming for related verbs and targets, but also in the reduction of the proactive interference that was earlier observed in Experiment 2. The reduction in proactive interference also suggests that such interference arose from perceptual, and not conceptual, similarity in Experiment 2. In the case of R.H., the reduction in perceptual overlap neither reduced nor bolstered the weak transfer to related materials observed in Experiment 2

There is one set of data in Experiments 2 and 4 that warrants explanation. In both experiments, little evidence of perceptual priming was obtained for unrelated target items for both C.C. and R.H. even though these target words were exposed within the sentence context during study. Lack of priming cannot simply be attributed to the specific items that were used, because this null effect was obtained across different sets of items in the two experiments. A possible explanation for this null result may be that for new associations, conceptual encoding can interfere with perceptual priming under certain experimental conditions.

The role of conceptual encoding in mediating perceptual priming of target words (e.g., *reason*) in newly associated pairs (e.g., *window–reason*) is well-documented both in normal and amnesic populations (Graf & Schacter, 1985; Micco & Masson, 1991). For example, priming for new associations has been reported for unrelated word pairs encoded under elaborative and conceptual encoding conditions but not shallow encoding conditions (Graf & Schacter, 1985; Schacter & Graf, 1986; but see Masson & Freedman, 1990). Furthermore, there is a reduction in priming for targets in these unrelated pairs when the cue word (e.g., *window*) changes from study to test (say, *pencil–rea*_____) in contrast to a condition where the cue is constant across study and test (i.e., *window–rea*_____; Graf & Schacter, 1985). This finding suggests that the perceptual fragment of the target itself is not sufficient to produce comparable levels of priming in the two cueing conditions for the targets in newly associated pairs.

In a study that directly examined the effects of interference on perceptual priming of targets in newly associated pairs (Graf & Schacter, 1987), college undergraduates were shown an unrelated A–B pair once (e.g., *shirt–finger*), followed by a single exposure to an unrelated A–C pair (e.g., *shirt–energy*), and then were tested on the A–C pair to measure perceptual priming for the stem of the target word C (i.e., *ene*_____). Under such conditions, no effect of proactive interference on perceptual priming was reported relative to control conditions. However, the conditions in our experiments were different in two important ways. First, the first set of encoded associations in our Experiments 1 and 3 were presented repeatedly as opposed to only once as in Graf and Schacter's (1987) study. Second, the first set of encoded associations in our Experiments 1 and 3 were presented in a sentence format as opposed to word pairs. The sentence format presumably engenders stronger conceptual processing of the target than the word pair format (see MacLeod, 1989).

This second possibility receives support from a study using college undergraduates where deleterious effects of change in the conceptual context across study and test for new associations were reported when sentence structures constituted the encoding materials (Micco & Masson, 1991). Participants were presented with homographs at study such that within the study list, both interpretations of a homograph were presented for study in a spaced fashion (e.g., *The electric FAN was placed on a large desert STONE*, and *The starry eyed FAN waited for hours at the record STORE*). At test, participants were presented with probe items, such as *cooling FAN–STO*_____, where the same-context response was *STONE* and the different-context response was *STORE*. Even though comparable (though not identical) levels of perceptual information were presented at study for both completions (*cooling FAN–STONE* or *sports FAN–STORE*), the interpretation of meaning (of

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FAN) was different in the two cases. The results showed that priming for targets (e.g., *STONE*) was greater in the same-context test condition compared with the different-context test condition.

Thus, repetition and the use of sentence structures could have resulted in stronger conceptual unitization of the sentences, thereby reducing the perceptual processing of the individual words within the sentences. In fact, the reduced priming scores of control participants in Experiment 4 for the unrelated targets in the sentence+fragments and fragments-only conditions support this explanation and also Micco and Masson's (1991) general findings.

The remarkable aspect of these interference effects for new associations in our study is that these effects were obtained in densely amnesic participants in whom significant contributions of explicit memory were unlikely. Our data also suggest that conceptual interference may have affected the processing of unrelated items at the encoding stage because little perceptual priming was found in the fragments-only cues test condition as well. It is important to note that the explanations and speculations detailed here require further empirical substantiation in future studies to clearly understand the role of conceptual interference on perceptual implicit memory for new associations.

General Discussion

The results of the four experiments can be summarized as follows. In Experiments 1 and 3, new verbal learning (measured with sentence+??? retrieval cues) occurred following basal forebrain amnesia, but such learning was not found following medial temporal lobe amnesia even though the experimental conditions were identical. However, substantial learning was obtained in both types of amnesia when both conceptual and perceptual cues (measured by sentence+fragment retrieval cues) were provided. As would be expected, perceptual priming (measured with fragments-only retrieval cues) was also found to be intact.

The results of Experiment 2 revealed robust priming in basal forebrain amnesia for related but not unrelated information when both conceptual and perceptual cues were provided to constrain the possible responses; in the absence of perceptual cues, strong proactive interference from previous materials impaired transfer to related information. This transfer to related (but not unrelated) information was not reliable in medial temporal lobe amnesia.

Experiment 4 replicated the patterns of transfer to related information obtained in Experiment 2 despite a reduction in the perceptual overlap between the training and transfer materials. In addition, these results showed that such reduction in perceptual overlap reduced proactive interference and created a better condition for transfer of learning to occur in C.C. Finally, the effects of proactive interference on unrelated information were not completely eliminated even under conditions of reduced perceptual overlap (Experiment 4) because perceptual priming was adversely affected for unrelated (though not related) targets. Taken together, findings from these four experiments delineate several determinants of new associative learning in amnesia. We discuss these findings in the context of several factors proposed in the beginning of the article as critical for new verbal learning in the absence of episodic memory.

The critical question addressed was whether amnesic individuals can exhibit new associative learning in the verbal domain. C.C.'s performance in Experiments 1 and 3 demonstrates that the verbal learning in amnesia reported by Hayman et al. (1992) and Tulving et al. (1991) may be found in other severely amnesic patients as well. However, data from R.H., who was tested under identical experimental conditions, clearly demonstrate that such learning is not observed in all amnesic individuals. There are a number of potential explanations for the differences in performance exhibited by our patients and other amnesic participants reported in the literature (Gabrieli et al., 1988; see also Verfaellie et al., 1995).

One factor that may account in part for discrepancies in reports of new verbal learning in amnesia is differences in experimental methodology. The present experiments provide strong support for the claim that learning of new associations in amnesia is highly dependent on the encoding and retrieval conditions under which learning is measured (Hayman et al., 1992; Hamann & Squire, 1995; Tulving et al., 1991). Robust learning was obtained in both amnesic participants when maximal cues (sentence+fragment retrieval condition) were provided, whereas only one amnesic participant showed learning in the absence of perceptual cues for the target (sentence+??? retrieval condition). Furthermore, in Experiments 2 and 4, the exact arrangement of retrieval conditions was shown to be important to observe transfer to related information and reduce the proactive interference.

Within the context of experimental methodology, another methodological issue that warrants discussion is the possible role of interference in our experiments. One might argue that R.H.'s failure to learn new targets in the absence of perceptual cues is attributable to the intraexperimental associative interference (Hayman et al., 1992) created by the study–test format we used. For instance, Hamann and Squire (1995) recently reported that learning of factual knowledge (e.g., statements such as *TOURIST wanted SNAPSHOT*) in a group of amnesic participants was poorer when the training sessions involved both study and test within each session compared with a situation where amnesic participants repeatedly only studied the material and were tested on them after several sessions.

However, substantial differences in methodology between Hamann and Squire's (1995) experiments and our work render the outcome of a direct comparison unclear. Thus, in every session, Hamann and Squire presented the cue first and the patients produced a response before the correct target word appeared. In our Experiments 1 and 3, in every session the correct, complete sentences were first presented for study and were subsequently tested. Thus, the level of interference in our experiments was not as high as for the study–test format used by Hamann and Squire, although it was also not as low as the study-only format used by them. Also, a more important difference between the two investigations is the instructions given to the pa-

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tients for retrieval. Hamann and Squire gave explicit retrieval instructions to the patients in the test of both fact learning (presumed to measure semantic memory) and event memory (presumed to measure episodic memory). In contrast, we used implicit instructions to measure new learning and explicit instructions to assess recognition memory.

Additional relevant evidence on this issue comes from Hayman et al.'s (1992) work. Even under the highest interference condition of study–test format described above, Hayman et al. reported some learning in the severely amnesic patient K.C. (M = .38 after 10 sessions). K.C.'s level of learning appears to be substantially greater than R.H.'s best performance (.08 after 12 sessions in Experiment 1 and after 10 sessions in Experiment 3) in our lower interference study–test format condition.

A second factor that should be considered in accounting for differences in performance between C.C. and R.H. is severity of amnesia. One might suggest that R.H.'s failure to learn new information in the sentence+??? condition was attributable to the fact that R.H. suffered from a more severe memory deficit. Although such an account cannot be definitely excluded, we believe this to be an unlikely explanation for the dramatic differences in performance exhibited by R.H. and C.C. in light of their comparable levels of impairment on explicit memory measures. For example, C.C. and R.H. were equally impaired on the logical memory subtest of WMS, recalling 4.5 out of 23 concepts initially and, after 10 min, failing to remember being presented with a story. In addition, in Experiment 1 both participants were comparably impaired in recognizing the studied sentences even after multiple exposures. Finally, in Experiment 3, the recognition memory for sentences tested in different retrieval conditions was virtually identical for both amnesic participants even though their implicit learning in a critical condition (sentence+???) was strikingly different. Thus, although it is possible that subtle but important differences in the severity of amnesia between the two patients may not have been captured in the clinical observations and on the existing measures of explicit memory, there are little definable differences in amnesia severity that could readily explain the striking differences in their performance. A review of the literature also suggests that performance on verbal associative learning tasks is not clearly predicted by amnesia severity (Hayman et al., 1992; Tulving et al., 1991). For instance, Tulving et al.'s (1991) patient K.C. performed extremely poorly on a test of recognition memory for repeatedly studied sentences where he failed to recognize any of the repeatedly studied sentences. Yet he was able to exhibit learning of these new associations, whereas in the present experiments R.H. failed to show such learning in two experiments.

As described in the beginning of the article, an alternate account of the differences in new learning exhibited by C.C. and R.H. as well as other amnesic participants appeals not only to differences in amnesia severity, but also to the locus of lesion causing the amnesia. Thus, one possible account of these data is that new associative learning in amnesia depends on the integrity of the medial temporal lobe structures. This hypothesis is consistent with reports of Gabrieli et al. (1988) and Verfaellie et al. (1995) of a failure in learning in amnesic patients with medial temporal lobe damage. For example, Verfaellie et al. (1995) failed to find any evidence of postmorbid vocabulary acquisition across a number of sensitive tests, including the lexical decision task and the sentence verification paradigm, in an amnesic participant with presumed medial temporal pathology. In addition, Blaxton (1992) reported impaired conceptual priming in a series of experiments in memory-impaired patients with the etiology of temporal lobe epilepsy. Finally, it has also been reported that H.M. (a well-known medial temporal lobe amnesic participant) failed to show new associative learning under experimental conditions similar to those under which patient K.C. (Tulving et al., 1991) showed such learning (cited in Squire & Knowlton, 1995).

Thus, these findings do suggest a special role of the medial temporal lobes in facilitating postmorbid learning of verbal associations in amnesia (see also Moscovitch, 1994a, 1994b; Moscovitch & Umilta, 1990, 1991; Squire, 1992). The proposal that medial temporal lobe structures play a special role in mediating such learning offers a possible explanation for the inconsistencies in the literature regarding verbal learning in amnesia. To be specific, although acquisition of knowledge is indeed possible after the onset of severe amnesia (Kinsbourne & Wood, 1975; Tulving et al., 1991), such learning is not always possible following extensive damage to the hippocampus and related structures (Gabrieli et al., 1988; Squire, 1992; Verfaellie et al., 1995).[4]

Using the positron emission tomography (PET) technique, one study recently reported that the entorhinal cortex within the medial temporal lobes is specifically involved in mediating the recall of newly learned paired associates in memory-intact, healthy humans (Klingberg, Roland, & Kawashima, 1994). In another study that used functional magnetic resonance imaging (fMRI), significant activation was reported in the hippocampal regions in normal humans when they were engaged in memory tasks that required binding of various associations into novel configurations (Cohen et al., 1994).

Several lines of evidence from the animal literature also suggest that the hippocampus and likely other medial temporal lobe structures are involved in the formation of new associations and configurations (Eichenbaum, 1994; Moscovitch, 1994a, 1994b; Rudy & Sutherland, 1994). Recent lesion and single-cell recording research with the rat and monkey models of amnesia continue to refine our knowledge of the specific and differential roles of the medial temporal lobe structures, such as the hippocampus, the entorhinal, and the perirhinal cortex in mediating memory for novel information (see Eichenbaum, Otto, & Cohen, 1994). There is also growing evidence that damage to the hippocampus per se (Area CA1) leads to less severe mem-

[4] Evidence also exists for new learning in a young girl who became amnesic following an episode of herpes simplex encephalitis (Wood, Brown, & Fulton, 1989). However, it has been argued that her learning was mediated by residual episodic memory (see Ostergaard & Squire, 1989).

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ory impairments than damage that includes the related structures, such as the parahippocampal gyrus, both in humans and in monkeys (see Squire, 1992; Zola-Morgan et al., 1986).

Our findings point to the role of the medial temporal lobes in mediating new verbal learning but do not specify the particular structures within the medial temporal lobe region that might be involved in this function because of the extensive medial temporal lobe damage exhibited by R.H. A recent report of three amnesic individuals with developmental brain injuries limited to the hippocampi bilaterally with the sparing of the perirhinal and entorhinal cortices near the hippocampi is relevant in this regard (Vargha-Khadem et al., 1997). Despite their developmental injuries, these amnesic individuals appear to have acquired language competence and factual knowledge within low-average to average range. It is interesting that despite such acquisitions, these individuals were impaired on laboratory tasks that required the development of some associations in multitrial associative recognition tasks. Although new verbal associative learning and transfer investigated in our study were not examined in Vargha-Khadem et al.'s study, their findings demonstrate that associative learning is particularly sensitive to damage to the medial temporal lobes. On the basis of prior lesion studies with monkeys and the results of these human case studies, these investigators concluded that the cortices adjacent to the hippocampi are critical for large-scale acquisition of new verbal information. Our findings support this claim because the cortical damage in our patient R.H. included the hippocampi as well as the adjacent cortices, and this patient failed to show any evidence of learning and little evidence of conceptual transfer in our study.

As illustrated by the striking amnesia exhibited by C.C., basal forebrain structures also play a critical role in human memory (Damasio, Eslinger, Damasio, Van Hoesen, & Cornell, 1985; Damasio, Graff-Radford, Eslinger, Damasio, & Kassell, 1985; DeLuca, 1993; Mayes, 1991; Phillips, Sangalang, & Sterns, 1987). In most cases, these structures are damaged as a result of the rupture of the aneurysm of the ACoA or from the atrophy of the basal forebrain cells in Alzheimer's disease.

As indicated by the performance of C.C. and R.H., amnesia resulting from basal forebrain damage is in many ways similar to medial temporal lobe amnesia (see Rajaram, 1997). For example, we found that perceptual implicit memory (as measured by word fragment completion) is intact in basal forebrain amnesia, and explicit memory (as measured by the recognition memory task) is impaired. This dissociation between implicit and explicit memory performance has also been reported by others in ACoA amnesic individuals in tasks such as implicit skill learning, picture fragment completion, and explicit free recall (e.g., Bondi, Kaszniak, Rapcsak, & Butters, 1993). Similar patterns of performance between ACoA patients and amnesic patients with other etiologies have also been reported in measures of retrograde amnesia (Gade & Mortensen, 1990) and in the differences between recall and recognition memory (Volpe & Hirst, 1983). These functional similarities are, perhaps, not surprising in light of the anatomical interconnections between basal forebrain and medial temporal lobe structures, specifically the hippocampus (Damasio et al., 1985; Mayes, 1991; Zola-Morgan & Squire, 1993).

However, we found that important differences may also exist between medial temporal lobe amnesia and basal forebrain amnesia. To be specific, new verbal learning and robust transfer to related information was possible following basal forebrain but not medial temporal damage. The status of new learning and conceptual priming in basal forebrain amnesia has received little attention. Recently, one study reported that word stem completion performance, now considered to involve more conceptual components than word fragment completion or picture fragment completion tasks (see Keane, Gabrieli, Fennema, Growdon, & Corkin, 1991), was found to be intact in ACoA amnesic patients (Bondi et al., 1993). Anatomically, there is evidence reported from PET studies that damage to the basal forebrain disrupts the hippocampal functions but only partially (Damasio et al., 1985). These reports, in conjunction with our robust empirical findings with C.C., suggest that partial disruption in the hippocampal activity may not be sufficient to eliminate conceptual priming and new verbal learning in basal forebrain amnesia.

Our in-depth investigation of two case studies has revealed theoretically significant similarities and differences across different forms of amnesia. The case study nature of our report necessarily limits the matching of etiology as well as pathology across the two patients, although this limitation is difficult to overcome in human studies. Furthermore, better anatomical resolution obtained through brain imaging than we report here will undoubtedly further improve our understanding of the differential roles of the basal forebrain region and the medial temporal lobe region in mediating new verbal learning in amnesia. Our findings also do not address the status of new learning in amnesia resulting from the third well-identified neural structure, the diencephalic circuits. The current evidence on this issue is based on studies with Korsakoff's patients, and the findings are mixed (Dopkins et al., 1994; Grossman, 1987; Van der Linden et al., 1994). Given the differences documented between diencephalic amnesia and medial temporal lobe amnesia, an investigation of this issue in diencephalic amnesia is timely.

Finally, our findings have implications not only for the question of learning new associations in amnesia, but also for the issue of transfer of learned information to other situations. With respect to this issue, there is some evidence both from rats (Eichenbaum, 1994) and humans (Glisky et al., 1986a) that learning in amnesia is marked by inflexibility of use. However, our findings of successful transfer (particularly in the participant with basal forebrain amnesia) are consistent with the recent observations that transfer to related information in persons with amnesia can sometimes occur at levels that are similar to those observed in normal controls. For example, Hamann and Squire (1995) found comparable levels of transfer in amnesic participants and normal controls when they used a different method to measure transfer. Sentences from the training sessions (e.g., *TOURIST wanted SNAPSHOT*) were replaced by either one

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or two words (e.g., *TOURIST desired ???* or *SIGHTSEER desired ???*) such that the target word to be produced was always the same in both the training and transfer sessions. In our experiments, one or two words were changed such that the target word (i.e., the last word) to be learned was always different in the training and the transfer sessions. Thus, the experimental conditions in our study required the transfer to not only a different context (e.g., Experiment 4) as in Hamann and Squire's study, but also to a completely different, albeit related, target (Experiments 2 and 4). Thus, our experiments delineate additional conditions under which transfer can be obtained in some forms of amnesia.

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