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New Conceptual Associative Learning in Amnesia: A Case Study

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We report two experiments in this article that were designed to investigate the role of retrieval constraints and interference in implicit learning of new verbal associations in a densely amnesic participant, C.V., who had presumably sustained medial temporal lobe damage secondary to an anoxic episode. In Experiment 1, repeatedly studied novel sentences produced significant priming with Sentence+Fragment retrieval cues that provided maximal perceptual support as well as perceptual priming for the single-word targets. However, little learning was observed when no perceptual cues were provided for the target itself with the Sentence+??? retrieval cues. In Experiment 2, the effects of intraexperimental interference were measured by examining new verbal learning under the Study-Only, Study-Immediate test, Test-Study training conditions. Unlike in the findings reported in prior studies, C.V. showed little learning with the Sentence+??? retrieval cues even under the minimal interference, Study-Only, condition. Together, these results demonstrate that implicit access to novel verbal associations at a level more abstract than their perceptual configurations is not ubiquitously observed in dense amnesia even when the learning conditions are optimized. These results provide a window into the processes that mediate implicit learning of novel verbal associations when the explicit memory contribution is minimized.

In recent years, empirical studies involving memory-intact as well as memory-impaired (or amnesic) participants have informed theories of memory functions and processes. Investigations involving memory-intact participants have demonstrated that repetition, interference, and retrieval cues play a large role in modulating memory performance. In the present article, we examine the role of these variables on the acquisition of new information in a densely amnesic individual. The purpose of our investigation is to isolate the role of implicit processes in the acquisition and retrieval of new verbal information.

The amnesic syndrome is characterized by the selective loss of memory for events subsequent to the onset of amnesia (also known as anterograde amnesia) while other cognitive functions such as language, perception, attention, reasoning, problem solving, intelligence, and short-term memory are relatively intact. A loss of memory for events immediately preceding the onset of amnesia, or retrograde amnesia, is also commonly reported.

The classic studies by Warrington and Weiskrantz (1968, 1970) demonstrated that despite grossly impaired explicit memory functions, as those involved in recall and recognition, implicit memory functions, as those involved in word fragment completion, may be

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largely intact in amnesia (Diamond & Rozin, 1984; Graf & Schacter, 1985). In the word fragment completion task, participants are shown a list of words at study (e.g., elephant) and are later given fragmented versions of the studied (_ l _ p _ a n _; solution: elephant) and nonstudied words, and they are asked to complete the fragments with the first word that comes to mind. The advantage in completing studied fragments over nonstudied fragments constitutes the measure of implicit memory, or priming (Tulving et al., 1982). Such implicit memory tasks are largely data-driven such that changes in modality across study and test reduce priming (Blaxton, 1989; Rajaram & Roediger, 1993; Srinivas & Roediger, 1990), but meaningful encoding does not necessarily increase priming relative to surface-level analysis of study material (see review by Roediger & McDermott, 1995).

Priming is also observed in implicit memory tasks when the task relies on conceptual, and not perceptual, processes. For example, in a conceptual implicit task such as category production, participants study exemplar names (e.g., elephant) of various categories. At test, only the category names are provided (e.g., animals), and participants are asked to write down the first few exemplars of that category that come to mind. This task is considered to be conceptual in nature because the exemplars and category names are conceptually related, and no perceptual overlap exists between study and test stimuli. Predictably, modality changes do not impair such priming whereas manipulation of meaningful encoding enhances such priming (e.g., Blaxton, 1989; Hamann, 1990; Srinivas & Roediger, 1990).

Both perceptual and conceptual forms of priming, or implicit memory, have been extensively examined in amnesia and found to be generally preserved (see Moscovitch et al., 1993, for a review), although the evidence for preserved conceptual priming is somewhat mixed. Many studies have shown preserved conceptual priming in amnesia across a variety of conceptual implicit tasks (Gardner et al., 1973; Hamann, 1990; Keane et al., 1997; Schacter, 1985; Shimamura & Squire, 1984; Vaidya et al., 1995; Warrington & Weiskrantz, 1982; Winocur & Weiskrantz, 1976). Yet, others have reported impairment on conceptual priming in amnesia on a similar group of tasks (Blaxton, 1992; Cermak et al., 1998; Keane et al., 1997). The reasons for these discrepancies are not clear, but one possibility may be the differences in procedure and different groups of amnesic participants employed across these studies.

The database on the perceptual and conceptual priming effects in amnesia has informed and refined our theories of intact memory functions by providing a window into the operation of implicit memory when the contribution of explicit memory is minimized (Blaxton, 1995; Cohen & Squire, 1980; Gabrieli, 1995; Moscovitch, 1992, 1994a; Roediger et al., in press; Schacter, 1990; Tulving & Schacter, 1990). The studies reviewed thus far reveal both the processing and neural requirements for the reactivation of *learned information* under different retrieval conditions. Specifically, the perceptual, lexical, and conceptual representations of words such as “elephant” exist in the cognitive system prior to the experimental context.

A key question that has concerned researchers in recent years is the role of implicit memory in mediating the learning of *new* verbal information. It is obvious that explicit memory or conscious awareness plays a vital role in the acquisition of new information, as evidenced by the performance of memory-intact individuals in the laboratory and in the real world. Whether implicit memory also supports the acquisition of new verbal information, and if it does, what the nature of such learning might be, constitute the questions examined in the present article. We investigated these questions in a densely amnesic individual because the minimal operations of explicit memory may help isolate the implicit processes that mediate new verbal learning.

Recent studies have investigated the role of implicit processes in mediating new verbal learning in the memory-intact as well as the amnesic populations. The latter set of studies is directly relevant here, and these studies fall into three general categories. In one set of studies, the acquisition of hitherto unknown words was examined in the amnesic population. The results of these studies are mixed. Some studies have shown little, if any, evidence of acquisition of new vocabulary in the medial temporal lobe patient H.M. (Gabrieli et al., 1988) or in Korsakoff's patients (Grossman, 1987). In contrast, positive evidence of new learning has been reported in amnesics in some studies. For example, there have been reports of progress in the academic training of a young amnesic girl (Wood et al., 1989), normal acquisition of new French vocabulary (Hirst et al., 1988), learning of single-word interpretations of ambiguous descriptions (McAndrews et al., 1987), and learning of implicit frequency judgments (Dopkins et al., 1994). The reasons for these discrepancies once again are not clear, but they may arise from differences in tasks and procedures and differences in the severity and etiology of amnesia among the participants.

In a second set of studies, new learning in amnesia has been examined for individual novel items such as nonwords and novel shapes in priming tasks such as perceptual identification, word reading, and lexical decision. By and large, there appears to be preserved priming for nonwords (Cermak et al., 1991; Gabrieli & Keane, 1988; Musen & Squire, 1991) as well as novel shapes (e.g., Gabrieli et al., 1990; Musen & Squire, 1992a; Schacter et al., 1993; Verfaellie et al., 1992). However, in some studies such priming is found to be at subnormal levels (e.g., Diamond & Rozin, 1984; Gordon, 1988), raising the concern that evidence for normal levels of priming for novel information may sometimes be contaminated by residual explicit memory in some amnesics (see Bowers & Schacter, 1993).

In the third set of studies, new learning has been assessed for verbal associative information; these studies are directly relevant for the present purposes because we used novel sentences as the stimuli in our study. Although associative learning has been examined with different types of stimuli such as learning computer vocabulary and programming commands (Glisky & Schacter, 1988; Glisky et al., 1986a, 1986b), simple facts (Shimamura & Squire, 1987), and name–face associations (Thoene & Glisky, 1995), the most extensively studied paradigm in this domain involves the learning of novel word associations. In a typical experiment of this sort, participants are presented with unrelated word pairs (window–reason, march–shave) and are later presented with intact pairs (window–rea_____) or recombined pairs (march–rea_____) during the stem completion task. The advantage in stem completion priming for intact pairs over recombined pairs provides the measure of new learning. The evidence with amnesic participants on this task has been mixed (Graf & Schacter, 1985; Schacter & Graf, 1986) such that new associative learning reliably occurred only in mild to moderate amnesics and not severe amnesics (but see Tulving et al., 1991). However, recent studies have demonstrated normal levels of priming in amnesics for new associations when rapid word identification (Gabrieli et al., 1997; but see Paller & Mayes, 1994), reading time (Moscovitch et al., 1986, but see Musen & Squire, 1992b), or the lexical decision task (Goshen-Gottstein & Moscovitch, 1992) were used as the dependent measures. Once again, the discrepancies in the implicit acquisition of new associations appear to be due to changes in tasks as well as to severity of amnesia.

Together, the following conclusions may be drawn from these mixed findings on the acquisition of new verbal information in the amnesic population. One, the positive evidence of new learning is often not purely implicit in nature and may be mediated by residual episodic memory. If the explicit memory involvement complicates the interpretation of the data in the moderately amnesic participants, this problem may become exaggerated in the memory-intact population. Thus, in order to understand the unique contribution of implicit memory to new verbal learning in the normal cognition of memory, it is critical to examine these processes under conditions where the operations of explicit memory are minimized. An effective way to achieve this goal is by examining the implicit learning processes in severely amnesic participants. To this end, we tested a severely amnesic participant in the present experiments. Two, the variations in tasks and procedures across laboratories may be partly responsible for the mixed findings. Thus, the selection of the critical tasks and procedures used in other laboratories with dense amnesic participants is necessary to effectively address this problem with different patient samples. For this reason, our experiments were closely modeled after the tasks and procedures used in recent studies that investigated related issues (Hayman et al., 1992; Rajaram & Coslett, in press; Tulving et al., 1991). Three, the reviewed studies also indicate that acquisition of individual, novel perceptual units (such as nonwords and novel shapes) is observed more reliably in amnesics, but new learning that involves an associative component is often impaired (see also Curran & Schacter, 1997). We focused on the latter outcome in the present investigation because the associative component of learning may be fundamental to most verbal learning (see Rajaram & Coslett, in press). For instance, learning new vocabulary (Gabrieli et al., 1988) also requires the development of an association between a new word and its meaning. Thus, the role of implicit memory in mediating new verbal learning in general may be best understood by examining the mechanisms that govern new *associative* learning.

Associative learning may occur either only at the perceptual/lexical level, as measured by the perceptual identification, lexical decision, or the reading tasks (Gabrieli et al., 1997; Goshen-Gottstein & Moscovitch, 1992; Moscovitch et al., 1986), or at a higher conceptual or semantic level where some of the perceptual/lexical parts of the cue are not provided to the participants (Hayman et al., 1992; Tulving et al., 1991). In the present study, we focus on the latter, relatively more conceptual, level of associations to examine whether successful new learning can occur beyond the level where the participants could simply rely on the perceptual gestalt of the stimuli (see also Goshen-Gottstein & Moscovitch, 1995).

The selection of the particular amnesic participant (C.V.) in this study also permitted us to collect evidence pertaining to a related issue, the possible neuroanatomical basis of new conceptual associative learning. A number of theories have recently proposed a special role of the medial temporal lobe structures in facilitating the binding of various elements of new information (Cohen & Eichenbaum, 1993; Cohen et al., 1997; Cohen et al., 1994; Johnson & Chalfonte, 1994; McClelland et al., 1995; Moscovitch, 1994b; O'Reilly & McClelland, 1994). According to these proposals, one may predict impairment in the binding of new associations when damage is sustained to the medial temporal lobe structures. Evidence from rodent studies supports this prediction (see Eichenbaum et al., 1994). In humans, the preliminary evidence from recent neuroimaging studies (Cohen et al., 1994; Klingberg et al., 1994) as well as data from some of the amnesic case studies support this prediction (Gabrieli et al., 1988; Rajaram & Coslett, in press; Verfaellie et al., 1995; see also Squire & Knowlton, 1995; but also see Hayman et al., 1992; Tulving et al., 1991). However, the specific conditions under which acquisition and testing take place have often varied across studies, and the exact nature of learning impairment is not clearly understood.

In summary, our central goal was to examine whether implicit memory processes can support the acquisition of new, conceptual associative learning in a densely amnesic individual. The recruitment of a densely amnesic individual was expected to provide a window into the operations of implicit memory that cannot be isolated easily in memory-intact individuals in whom it is often difficult to rule out the contributions of explicit memory. We systematically examined the effects of interference and types of retrieval cues on new verbal associative learning. The selection of specific manipulations was motivated by the findings from previous studies (Hamann & Squire, 1995; Hayman et al., 1992; Tulving et al., 1991; Rajaram & Coslett, in press). The specific goals and manipulations of each of the two experiments are presented separately in the forthcoming sections.

In addition to this primary aim, our study also provides suggestive data that speak to the possible role of medial temporal lobe structures in mediating the learning of new associations, and by inference, in the binding of different elements of the associative stimuli (i.e., sentences) presented to the amnesic participant. We note that findings from our study provide suggestive insights into, and not a direct assessment of, this relationship.

PARTICIPANT DESCRIPTION

C.V.

C.V. was a 50-year-old college-educated man who suffered a cardiac arrest, perhaps as a consequence of a sustained seizure (status epilepticus), approximately 4 years prior to the testing reported here. After the cardiac arrest, C.V. noted profound memory impairment but was otherwise asymptomatic. Unable to return to his work in computer programming and international sales, he devoted his time to volunteer work and golf. C.V.'s wife stated that his personality and social interactions had not been altered by the cardiac arrest. Neurologic examination revealed C.V. to be alert, pleasant, and cooperative. He exhibited a severe amnesia but the examination was otherwise normal.

MRI of the brain demonstrated no abnormalities. Although we do not have pathologic confirmation of the lesion site in C.V., neuropathologic investigations of patients with status epilepticus have consistently demonstrated the hippocampus to be the most severely affected brain region (e.g, Corsellis & Bruton, 1983; Cendes et al., 1995; Hopkins et al., 1995). Patchy areas of laminar neuronal loss in the cortex and death of Purkinje cells in the cerebellum are less consistently observed. Furthermore, several studies have reported quantitative MRI analyses of the hippocampus in anoxic patients where significant reduction in the hippocampal region was noted in patients compared to controls (Press et al., 1989; Squire et al., 1990; Kesner et al., 1992; Hopkins et al., 1995). In light of these and other neuropathologic findings (e.g., Graham and Lantos, 1997), as well as C.V.'s strikingly preserved intellect, we suggest that his amnesia is attributable to hippocampal disruption and its connections.

Neuropsychological examination revealed that C.V. functioned in the superior range on many tasks despite his severe memory disorder. On the Wechsler Adult Intelligence Test-Revised (WAIS-R), C.V. obtained a full scale IQ of 130 (verbal = 139, performance = 113), with high-scaled scores of 17 on the vocabulary as well as arithmetic sections. These scores corroborate the clinical impression of intelligence in the superior range. C.V. scored 58/60 on the Boston naming test; he successfully named the remaining 2 items with the use of phonemic cues. In stark contrast, on the Wechsler Memory Scale – Revised (WMS-R), C.V. obtained a remarkably impaired score of 86 for general memory and scored below 50 on the delayed recall. His impairment was evident on memory-loaded subtests of the scale; for example, he was unable to recall any details from the logical memory subtest 10 min after presentation. At the same time, his performance on the attention/concentration section of the WMS-R was in the high range (125). This last score is consistent with his outstanding digit span performance on the WAIS-R (forward = 9, backward = 7). Altogether, C.V.'s profound amnesia was confirmed on these neuropsychological tests as the differential between his WAIS-R full scale IQ score (130) and the General Memory score on WMS-R (86) was more than 2 *SD* apart by normative standards (mean = 100, *SD* = 15). This pattern was further substantiated by the large differential between C.V.'s score on the attention/concentration section of the WMS-R (125) and the delayed recall section of the WMS-R (below 50). On the Warrington forced-choice recognition test, C.V. scored below the first percentile for his age group (faces = 34/50, names = 34/50).

Control Participants

Four control participants (henceforth called Matched Controls), matched for age (mean = 50.5 years, *SD* = 2.38) and education (mean = 15.5 years, *SD* = 1), were tested so as to counterbalance materials across conditions at least once.[1] Another group of nine control participants (henceforth called Young Controls) with

[1] Two matched control participants were tested in List 1 of the materials for reasons described under Results for Experiment 2.

mean age of 21.56 years (*SD* = 3.78) and mean education of 15.11 years (*SD* = 1.96) was also tested in Experiment 2 to fully counterbalance materials across conditions. Control participants were treated identically to the amnesic participant except when noted otherwise.

EXPERIMENT 1

The motivation for Experiment 1 came from recent reports of the learning of new verbal associations in densely amnesic participants K.C. (Tulving et al., 1991) and C.C. (Rajaram & Coslett, in press) and from mixed evidence of learning in another densely amnesic participant R.H. (Rajaram & Coslett, in press). In their study, Tulving et al. (1991) focused on the importance of experimental factors in producing long-lasting learning of new associations in amnesia. Amnesic participant K.C. exhibited profound memory loss following extensive head injury from a motorcycle accident in 1980. Tulving et al. (1991) presented K.C. with a number of novel but plausible sentences (e.g., MEDICINE cured HICCUP) at study across a number of sessions conducted at least one week apart. At test, implicit retrieval instructions were given to assess the retention of these associations, and the retrieval cues varied across sessions in the amount of perceptual information they contained. As has been reported in numerous studies, perceptual priming for the target words (e.g., _ I _ C _ P) was found to be intact in K.C. Interestingly, K.C. also showed substantial retention for the target item when no perceptual cue for the target itself was provided (MEDICINE cured ???) even though he was unable to recognize any of the studied sentences when explicit memory instructions were given. This finding was taken as evidence for new semantic learning in dense amnesia. Tulving et al. (1991) concluded from their data that new learning of this kind is slow and laborious in amnesia, but is long lasting.

We became particularly interested in the findings from the Sentence+??? retrieval condition because performance under this condition requires the binding of new associations at a relatively more conceptual level than in the tasks such as perceptual identification and reading, where all of the perceptual information about the new associations is provided to the participants. Consequently, in a recent study, we (Rajaram and Coslett, in press) attempted to replicate Tulving et al.'s findings with two densely amnesic participants, C.C. and R.H. Amnesic participant C.C. developed profound memory loss after the resection of a meningioma arising in the olfactory groove that created focal encephalomalacia bilaterally in the gyri recti and inferior portions of the cingulate gyri as well as the basal forebrain and other subfrontal structures. Postoperatively, C.C. exhibited normal intelligence but grossly impaired memory functions. R.H. became profoundly amnesic following a period of seizures in his early twenties. MRI scans at the time of testing revealed extensive but focal damage bilaterally in the medial temporal lobe regions, including the hippocampus, and some atrophy of the left lateral temporal lobe. R.H. exhibited superior levels of intelligence, with an IQ of 121, but dramatically impaired memory functions.

The comparison of these two amnesic participants in our study provided the opportunity to determine whether the findings reported by Tulving et al. (1991) generalize to other densely amnesic participants. To this end, we used the same set of materials that Tulving et al. used and adopted the critical features of the methodology from their study. Furthermore, the comparison of C.C.'s and R.H.'s performances where all the materials and experimental procedures were matched for the two participants provided the opportunity to delineate the possible, differential roles of the underlying neural structures involved in new associative learning. In particular, based on the theories of amnesia that posit a specialized function of binding information to the medial temporal lobe structures (Cohen & Eichenbaum, 1993; Cohen et al., 1997; Cohen et al., 1994; Johnson & Chalfonte, 1994; McClelland et al., 1995; Moscovitch, 1994b; O'Reilly & McClelland, 1994), we predicted that conceptual learning of new associative information, as measured by the Sentence+??? retrieval cues, would be impaired in the medial temporal lobe participant R.H.

For present purposes, the methodological details and results of Experiment 1 are relevant. This experiment included many sessions (8 for C.C., 12 for R.H., and 5 for the three matched control participants). Each session was conducted from 1–3 weeks apart and contained a study phase, a brief retention interval, and a test phase. In all sessions, participants studied novel and unfamiliar sentences at study (e.g., MEDICINE cured HICCUP, STAFF shot HIJACKER). In sessions 1, 3, 5, 7, 9, and 11, two types of retrieval cues were provided, Sentence+Fragment (MEDICINE cured _I _ C _ P) and Sentence +??? (STAFF shot ???). The Sentence+??? retrieval condition provides a strong test of new associative learning because participants have to develop links between hitherto unassociated words and these links have to be strong enough for the participants to generate the target word in the absence of any perceptual support for that word. The Sentence+Fragment condition provided maximal cues and was expected to produce considerable priming for the target words. Sessions 2, 4, 6, 8, 10, and 12 presented only the fragments of all target words (_I _ C _ P, _ I J _ _ K _ R) to assess the status of perceptual priming in these two amnesic participants.

We replicated Tulving et al.'s (1991) finding of new learning under the Sentence+Fragment as well as under the Sentence+??? conditions, but only in the performance of our basal forebrain amnesic participant C.C. We failed to find the evidence of new learning with the relatively more conceptual cues of Sentence+???, even after 12 sessions of study and test, in our medial temporal amnesic participant R.H. These data stand in sharp contrast with the findings of Tulving et al. (1991). Notably, R.H. showed preserved perceptual priming with the Fragments Only cues (_ I J _ _ K _ R) for the same set of target words (HIJACKER) that he failed to produce with the Sentence+??? cues (STAFF shot ???). We further replicated this pattern of performance for C.C. and R.H. with an entirely new set of materials (Rajaram & Coslett, in press, Experiment 3). Together, these findings have two important implications. One, learning of new verbal associations can occur at a relatively conceptual level even when the operations of explicit memory are minimized. However, such learning appears to be slow and laborious, depends on repeated trials, and is not observed in all amnesics. Two, these findings constitute initial but strong evidence from human studies for the proposal that medial temporal lobes may be specifically involved in the learning of new verbal associations. It should be noted, however, that Tulving et al's amnesic patient K.C. had also sustained medial temporal lobe damage but did exhibit semantic learning. Thus, we need more empirical information that can provide us with further insights into the possible role of the medial temporal lobes in mediating new associative learning. We discuss this issue further in the General Discussion section.

At the cognitive level, the absence of new associative learning as measured by the Sentence+??? retrieval cues in our amnesic participant R.H. (Rajaram & Coslett, in press) may be attributable to two different sources. One, new learning may not occur because the amnesic participant fails to develop the association between different words in the sentence, or fails to bind the information. Two, it is possible that some associative learning does occur with repeated trials, but this learning may be tenuous and susceptible to rapid forgetting. In our experiment with R.H. (Rajaram & Coslett, in press), the study-test sessions were held 1–3 weeks apart. This extended delay between sessions may have led to forgetting between sessions.

We tested this latter hypothesis in Experiment 1 here. To do so, we performed an experiment similar to the investigation described above (Experiment 1, Rajaram and Coslett, 1991) but with one critical change. We reduced the interval between sessions from 1–3 weeks to 10 min–17 h. We reasoned that if a relatively accelerated presentation of sessions can counteract the forgetting process, then amnesic participant C.V. may exhibit some learning of new associations in the Sentence+??? retrieval condition. This outcome will further delineate the mechanisms (forgetting versus failure to initially bind associations) that mediate implicit verbal associative learning. Thus, if such acceleration were not sufficient to attenuate the forgetting process, then our findings would demonstrate that the binding of new associations at a relatively conceptual level is severely limited when explicit memory is suspended.

Method

Materials. Eighty three-word sentences used by Tulving et al. (1991) and Rajaram and Coslett (1999, Experiment 1) were used as the critical stimuli in this experiment. Each sentence consisted of three words that together made sense but also constituted a novel, hitherto unknown, configuration. Of these 80 critical sentences, 48 were presented for study, and 32 were used as nonstudied sentences to assess priming. At test, 24 studied and 16 nonstudied sentences were presented under the Sentence+Fragment retrieval condition and the remaining 24 studied and 16 nonstudied sentences were presented under the Sentence+??? retrieval condition. In some sessions (specified later), the fragments of all the studied and nonstudied targets (the last word of each sentence) were presented to assess perceptual priming. Across sessions (from 1–9), the specific sentences were nested within each condition such that a given sentence always appeared under the same condition in all sessions. In the study list, in addition to the 48 study sentences, 12 buffer sentences, 8 at the beginning of the study list and 4 at the end of the study list, were included to eliminate primacy and recency effects. At test, in addition to the 80 critical sentences (of which 48 were studied and 32 were nonstudied), 8 nonstudied buffer sentences (not used anywhere in the experiment) were presented at the start of the test list under different retrieval conditions. The presentation of all critical sentences within each study and test list was randomly arranged with respect to conditions and with the restriction that the order for C.V. was identical to the order used for C.C. and R.H. in Rajaram and Coslett's (1999, Experiment 1) study.

As in the Rajaram and Coslett (1991, Experiment 1) study, a recognition memory task was administered at the end of the ninth session. The recognition task in this experiment consisted of a booklet containing all 48 study sentences and a new set of 48 nonstudied (buffer) sentences (not used for any other purpose in this or the next experiment) arranged in a new random order.

The selection and assignment of materials to different conditions as described, and all the critical details of the design and procedure to be described shortly, were identical to those used in the Rajaram and Coslett (1991, Experiment 1) study. The only change in the procedure was the reduction in the intersession interval from 1–3 weeks (Rajaram & Coslett, in press, Experiment 1) to 10 min–17 h. These steps were taken to ensure that the treatment of the present amnesic participant C.V. was identical in all respects to that of amnesic participants C.C. and R.H., as well as to that of matched control participants tested in our prior study, except for the intended manipulation of accelerated study and test cycles.

Design and procedure. Nine sessions were conducted with each session containing a study phase, a 5-min retention interval, and a test phase. Each session was conducted from 10 min–17 h apart. In the study phase, C.V. was presented with one sentence at a time on a Macintosh computer and was asked to decide whether the sentence made sense to him. C.V.'s responses included both "yes" and "no," particularly in the initial sessions. Following a 5-min break, the test phase was conducted. In the odd-numbered sessions 1, 3, 5, 7, and 9, to be designated the Sentence Cues sessions, the retrieval cues consisted of Sentence+Fragment (MEDICINE cured _ I _ C _ P) and Sentence+??? (STAFF shot ???). C.V. was instructed to provide the first solution or the first word that came to mind. In sessions 2, 4, 6, and 8, to be designated Fragments Only Cues sessions, the fragmented versions of all the studied and nonstudied target words were presented, and C.V. was asked to complete the fragments with the first solution that came to mind.

One hour after the completion of nine study-test sessions, a recognition memory test was administered to C.V. All 48 studied and 48 nonstudied sentences were presented in a booklet, and C.V. was asked to check all the sentences that looked familiar to him.

TABLE 1

Response Probabilities of Amnesic Participant C.V. in Experiment 1

Sentence cues sessions	Sentence+??? (e.g., STAFF shot ???) Studied	Sentence+??? Nonstudied	Sentence+fragment (e.g., MEDICINE cued _I_C_P) Studied	Sentence+fragment Nonstudied
1	0.04	0	0.67	0.38
3	0.04	0	0.88	0.50
5	0	0	0.88	0.69
7	0.08	0	0.92	0.63
9	0.13	0	0.88	0.63
Fragments only cues sessions	**Targets from sentence+??? (e.g., _IJ__K_R) Studied**	**Targets from sentence+??? Nonstudied**	**Targets from sentence+fragment (e.g., _I_C_P) Studied**	**Targets from sentence+fragment Nonstudied**
2	0.67	0.44	0.63	0.31
4	0.63	0.31	0.50	0.38
6	0.79	0.50	0.67	0.56
8	0.79	0.50	0.92	0.50

Results

New learning was measured by subtracting the proportion of correctly completed nonstudied items from the proportion of correctly completed studied items under all three retrieval conditions, Sentence+Fragment, Sentence+???, and Fragments Only. The mean completion performance under various conditions is presented in Table 1. The standard priming data were analyzed in the following way. Within each retrieval condition, the total number of correct responses across sessions was computed for each studied and nonstudied item. An independent *t* test by item was conducted to determine the advantage for studied over nonstudied items within each retrieval condition. In addition, an adjusted priming measure (Snodgrass, 1989) was also derived under each condition for each session. To derive this measure, the standard priming score (studied − nonstudied) was divided by (1 − nonstudied) in order to adjust for baseline differences that often complicate the comparison of different conditions in case studies. This measure is commonly used in priming studies and was also used by Tulving et al. (1991) and Rajaram and Coslett (1999). The adjusted priming scores across sessions for the Sentence Cues conditions and Fragment Only Cues conditions are displayed in Fig. 1 in the left and right panels, respectively. Note, however, that the statistical analyses reported below were conducted on the more conservative, standard, priming scores.

The critical question in this experiment was whether the amnesic participant C.V. would exhibit learning of new verbal associations when the intersession intervals were shortened in duration. As Fig. 1 shows, despite this manipulation, C.V. exhibited little learning of new associations under the Sentence+??? retrieval condition, $t\ (38) = 1.55$, $SE = 0.23$. The highest level of performance under this condition was found in Session 9, where C.V. produced 3 out of 24 correct responses. This performance is quite similar to R.H.'s performance in Rajaram and Coslett's study (1999, Experiment 1), in which R.H.'s best performance in the Sentence+??? condition consisted of 2 out of 24 correct responses and was dramatically different from C.C.'s, who produced 21 out of 24 correct responses. Thus, we failed to find evidence of new associative learning in C.V. despite arranging relatively optimal conditions of learning.

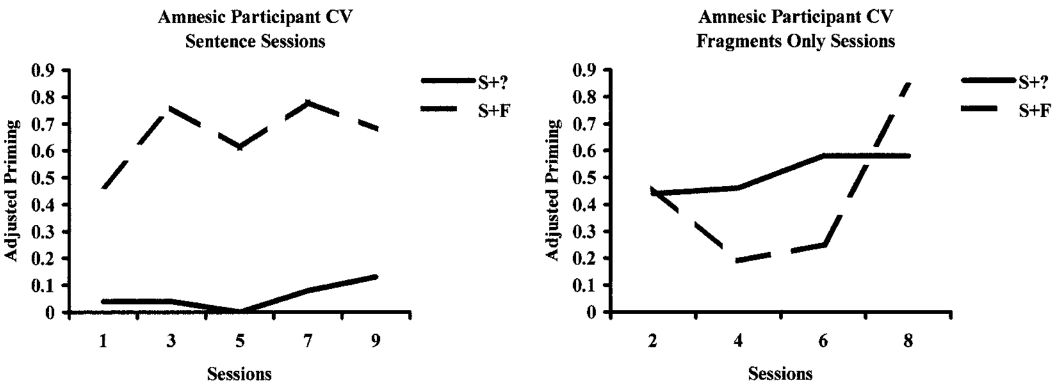

FIG. 1. The data from Experiment 1 for amnesic participant C.V. are displayed. The left panel displays the adjusted priming scores for the sessions where the sentence cues were presented either with the target word missing (Sentence+??? retrieval cue condition, labeled as S+? here) or with the fragmented version of the target word (Sentence+Fragment retrieval cue condition, labeled as S+F here). The right panel displays perceptual priming scores with the adjusted priming measure for only the fragments of the targets from both the Sentence+??? (S+? here) and the Sentence+Fragment (S+F here) retrieval cue conditions.

Priming performance under the second condition of Sentence+Fragment cues yielded significant priming, $t(38) = 2.44$, $SE = 0.52$, demonstrating the effectiveness of perceptual constraints in C.V.'s performance. Priming scores were also analyzed for the Fragment Only cues (Sessions 2, 4, 6, and 8) for the target words of sentences that belonged to the Sentence+Fragment and Sentence+??? conditions. Perceptual priming scores for targets that belonged to the sentences in the Sentence+??? conditions (e.g., _ I J _ _ K _ R) were found to be significant, $t(38) = 2.42$, $SE = 0.44$. This finding is notable in that these were the very targets that C.V. failed to produce in response to the Sentence+??? cues. In other words, this finding diminishes the concern that possible peculiarities in the target word in the Sentence+??? items might have resulted in a lack of learning. These data also mimic the pattern reported for the medial temporal lobe amnesic R.H. who exhibited robust perceptual priming for targets that he failed to produce under the Sentence+??? condition (Rajaram & Coslett, in press, Experiment 1). Finally, perceptual priming for targets that belonged to the Sentence+Fragment condition was also almost significant, $t(38) = 1.92$, $SE = 0.47$ ($p = .06$, two-tailed).[2]

On the recognition memory task, C.V. recognized 42 out of 48 studied sentences correctly and did not false alarm to any of the 48 nonstudied sentences. Thus, C.V. exhibited reasonably good recognition memory for studied information that was exposed to him nine times. He also admitted to the recognition task being "less threatening" than the other tasks he had to do, although he could not quite describe the other tasks he had been asked to do.

[2] We also compared priming across the Sentence+Fragment retrieval condition and the Fragments Only retrieval condition for the same set of items to determine whether priming levels increased as a function of the sentence cues. This comparison showed a trend for better standard priming under the Sentence+Fragment condition compared to under the Fragments Only condition, as also indicated by the adjusted priming scores displayed in Fig. 1, but this did not meet significance, $t(38) = 1.63$, $p = .11$ (two-tailed), $SE = 0.33$. This comparison should be viewed with caution because the same items served under the Sentence+Fragment and Fragments Only conditions across sessions. It should also be noted that because our focus was on the measure of associative learning under the relatively more conceptual, Sentence+??? condition, the comparison presented here was not critical with respect to the question we addressed in this series of experiments.

Discussion

Three main findings of this experiment are noteworthy. One, C.V. showed little evidence for the learning of new verbal associations when no perceptual cues for the targets were provided to aid the target production. This pattern of performance is similar to the pattern reported for the medial temporal lobe amnesic, R.H., but different from the pattern reported for the basal forebrain amnesic, C.C., and the head injury amnesic, K.C. (Rajaram & Coslett, in press; Tulving et al., 1991). Two, in contrast to his poor performance under the Sentence+??? condition, C.V. showed significant priming when the retrieval cues of Sentence+Fragment provided maximal support to aid retrieval. This finding, albeit with a different task, is similar to the reports of successful associative learning by amnesics in perceptual identification and reading tasks that also provide all of the perceptual information at test (Gabrieli et al., 1995; Goshen-Gottstein & Moscovitch, 1992; Moscovitch et al., 1986). Three, C.V. also showed significant perceptual priming when fragments of the targets were presented in isolation (Fragments Only cues). Perceptual priming for such fragments was obtained even for the set of targets that C.V. failed to produce under the Sentence+??? condition. Overall, C.V.'s performance bears a striking similarity to R.H.'s performance reported in our previous study (Rajaram & Coslett, in press, Experiment 1).

It is important to note that C.V.'s (and R.H.'s) performance cannot readily be attributed to severity of amnesia alone. Both these amnesic participants did exhibit profound amnesia on both clinical and neuropsychological assessment. However, C.V.'s recognition performance was considerably better than that reported for either R.H. (16/48 correct) or C.C. (24/48 correct). Alternately, Tulving et al. reported that K.C. failed to recognize any of the studied sentences after multiple study-test sessions, and yet unlike C.V., Tulving et al.'s amnesic K.C. did show substantial learning under the Sentence+??? condition. Furthermore, in the present experiment, C.V.'s feedback suggested that his recognition performance may simply be based on a vague sense of familiarity. But this sense of familiarity, even though superior to that seen in the other amnesics described above, was clearly not sufficient to support even the implicit production of correct targets.

In Experiment 2, we examined the role of interference in mediating implicit learning of new verbal associations. In memory research, the deleterious role of interference has long been noted both in studies of memory-intact (Martin, 1971; Postman, 1971; Runquist, 1975; Underwood & Postman, 1973) and amnesic participants (Cermak & Butters, 1972; Cermak et al., 1974; Mayes et al., 1987; Warrington & Weiskrantz, 1973, 1974; Winocur & Weiskrantz, 1976). Some theories of amnesia postulate that the mechanism by which medial temporal lobe structures facilitate the binding of various elements in new stimuli is by suppressing interference from other stimuli (Shapiro & Olton, 1994). In a recent study, Hayman et al. (1992) and Hamann and Squire (1995) examined new verbal, associative learning under study-test conditions that varied in the amount of interference they created. We reasoned that if C.V.'s failure to show poor new associative learning is attributable to possible interference effects in Experiment 1, then under conditions that minimize interference (Hayman et al., 1992), C.V. should exhibit better learning even when retrieval cues are perceptually impoverished.

EXPERIMENT 2

The design and procedure of this experiment were adopted from Hayman et al.'s (1992) and Hamann and Squire's (1995) procedures but were modified to suit the particular hypotheses tested in this experiment. One possible reason for poor new learning in the absence of perceptual cues may be that the test cue format (Sentence+???) creates a high-interference situation. That is, when the amnesic participant fails to produce the correct (studied) target, some other answer is produced to complete the sentence because of the implicit retrieval instructions given to the participant. This spontaneously produced (incorrect) response may interfere with the learning of the correct (studied) target, thereby resulting in little new learning.

In support of this argument, recently Hayman et al. (1992) reported that amnesic participant K.C. learned the correct target responses much faster under the Study Only condition compared to the Study-Test condition. Specifically, under the Study Only condition, the entire study item (e.g., a talkative featherbrain-parakeet) was presented repeatedly without any testing until the last session. In their Study-Test condition, K.C. was presented with definition cues (e.g., a talkative featherbrain-???) and was asked to generate the target word. Following his spontaneous response, the correct target (parakeet) appeared on the screen. (Note here that because of the order in which the events occurred under this retrieval condition, it is more appropriate to label this condition as Test-Study, and therefore, this condition will henceforth be referred to as the Test-Study retrieval condition.) The generation of a response prior to the presentation of the target within each session led to the production of incorrect targets, thereby leading to high interference. Under our Sentence+??? retrieval condition in Experiment 1, amnesic participant C.V. was asked to produce responses in every session. Thus, one might argue that the failure of R.H. in the previous study (Rajaram & Coslett, in press) and that of C.V. in the present study to learn the appropriate target sentences may be attributable to the high-interference learning condition used in our experiments.

It is important to note that the Sentence+??? retrieval condition used in our experiments (Experiment 1 in the present study, and Experiment 1 in Rajaram and Coslett's (1999) study) is somewhat different from the Test-Study retrieval condition just described. Under the Sentence+??? retrieval condition, the correct and complete sentences were always presented first (at study) within a session. Subsequently, within the same session the Sentence+??? cues were provided for implicit retrieval of the studied targets. Thus, the amnesic participants in our studies did not first generate a response after which the correct target was presented, as was the case under the Test-Study condition used by Hayman et al. (1992). Therefore, although the Sentence+??? condition in our study did not eliminate interference to the extent possible under the Study Only retrieval condition, it also did not create levels of interference as high as those that occur under the Test-Study condition. Because of the order of events under our Sentence+??? retrieval condition, this condition will henceforth be referred to as the Study-Immediate Test condition.

The present experiment was designed to obtain direct empirical evidence for these differential levels of interference. Specifically, the implicit new learning of amnesic participant C.V. was directly compared across three conditions—the Study Only, the Test-Study, and the Study-Immediate Test conditions. The first two conditions were selected to adopt the procedure used by Hayman et al. (1992) for manipulating "intraexperimental" interference. Specifically, intraexperimental interference arises from the conditions of the experiment that generate interference effects rather than from preexperimental associations known to participants. The third, Study-Immediate Test, condition was included to obtain a direct replication of the results of Experiment 1 with a new set of materials. This comparison of three conditions was expected to demonstrate whether differential amounts of interference in the learning and testing situations lead to differential levels of new, and relatively conceptual, associative learning. We predicted little new learning under the Test-Study learning condition because this condition has been shown to produce the highest level of interference for other amnesics (Hayman et al., 1992; Hamann & Squire, 1995). With respect to the Study-Immediate Test condition, we previously found minimal new learning (present Experiment 1), and we expected to replicate those findings. The most interesting learning condition in the present experiment was the Study Only condition. Hayman et al. found that learning under this condition was greatly facilitated in a severely amnesic participant K.C. Positive evidence of new learning under this condition by our amnesic participant C.V. would delineate at least one experimental condition under which new verbal, associative learning can ubiquitously occur in cases of severe amnesia.

Method

Materials. A new set of 174 sentences was constructed for this study. These sentences were similar to those used in Experiment 1 in that they were unfamiliar and yet plausible in nature (e.g., MACHINE refined COPPER, COUNTRY exported PEPPERMINT). Of these, 120 sentences were taken from the materials used by Rajaram and Coslett (1999, Experiment 3). Of these 120 sentences, 72 served as critical stimuli in this experiment. These 72 sentences were randomly divided into three sets of 24 sentences, each to appear under three conditions of the experiment (Study Only, Test-Study, Study-Immediate Test). We constructed three such lists to completely counterbalance the sets of sentences across conditions for both Matched and Young Control participants.[3]

Of the remaining 102 sentences from the overall set of sentences, 6 were used to serve as primacy and recency buffers in the three study lists just described with one each appearing at the beginning and end of each of the three lists. Of the remaining 96 sentences, 24 served as fillers in the test (described shortly) for the Study-Immediate Test condition. The remaining 72 sentences served as fillers in a recognition task that was conducted at the end to obtain one of several measures of explicit memory. In addition to these 174 sentence stimuli, 72 additional words were selected to serve as foils in a forced-choice recognition task that served as one of several measures of explicit memory.

Design and procedure. Each participant was tested over three days in this experiment. Participants (amnesic participant C.V., four Matched Controls, and nine Young Controls) were tested individually. The design and procedure were adopted (and modified where necessary) from Hayman et al.'s (1992) and Hamann and Squire's (1995) studies. Day 1 consisted of baseline measurements for target completion for the 72 critical stimuli. The first baseline task consisted of Sentence+??? cues for the 72 critical stimuli.[4] The participants' task was to complete the sentence cues with the first word that came to mind. The second baseline measure consisted of fragmented versions of the target words (presented in isolation) from the 72 critical sentences, and the participants were asked to complete the fragment with the first word that came to mind. In both baseline tasks, participants were given a maximum of 15 s for each completion.

A gap of at least 1 day (6 days in the case of amnesic participant C.V.) intervened between the baseline measurement and the next, acquisition, phase of the experiment. The entire acquisition phase was carried out within 1 day, with a gap of 30 min to 3 h between sessions. A total of six sessions was conducted during the acquisition phase. Each session included the three learning conditions described below. The presentation of conditions within each session was blocked and was counterbalanced for order across sessions with a Latin Square design. Across sessions, each set of 24 sentences was nested within each condition such that the same set of 24 sentences was presented within a given condition in all six sessions for amnesic participant C.V. For the Matched and Young Control participants, sentences were counterbalanced across learning conditions but were nested within the condition in all six sessions for a given participant. Following Hamann and Squire's (1995) encoding instructions, under all three conditions, participants were asked to in-

[3] Two Matched Control participants were tested on List 1 for reasons described in footnote 5. One Matched Control participant each was tested in Lists 2 and 3.

[4] Note that according to Hayman et al.'s (1992) definitions, this procedure may create an interference situation because participants are asked to produce spontaneous answers that may be incorrect. However, Hamann and Squire (1995) used this procedure to obtain the baseline completion measure and subsequently found sizeable learning under the minimal interference condition, i.e., Study Only, in their group of amnesic participants. Thus, precedence for this method already exists in this literature. Because the baseline measurement in our experiment required spontaneous production of responses only once, and was collected six days prior to the learning phase for C.V., the influence of interference from the baseline procedure, if any, may have dissipated. The baseline intrusion rates for C.V. described in footnote 5 confirm this prediction. Finally, our selection of this baseline measure was also guided by the fact that this measure has the obvious advantage of providing clean priming measures in our small-*N* design.

dicate on a scale from 1–5 how much sense each sentence made to them on a 5-point scale of (1) very little, (2) a little, (3) some (average), (4) a fair amount, (5) a lot. A maximum of 15 s was allowed for each decision. Participants completed the task quickly and efficiently.

—*Study Only* condition: This condition contained 24 of the 72 critical sentences. Each sentence was presented one at a time for the rating task. No intervening test was conducted on these materials until Day 3. This condition was assumed to create minimal intraexperimental interference.

—*Test-Study* condition: This condition included another set of 24 of the 72 critical sentences. For each item, participants were first presented with the Sentence+??? cue and were asked to guess the target. After the participants provided the response, the intended target was presented with the sentence cue for the rating task. This condition was assumed to create maximal intraexperimental interference.

—*Study-Immediate Test* condition: The remaining set of 24 of the 72 critical sentences was presented under this condition. This condition is the same as the Sentence+??? condition used in Experiment 1. Participants were presented with the entire sentence for the rating task. After the presentation of three study blocks, the 24 sentences from this condition were once again presented in the Sentence+??? format to measure new learning. These 24 studied sentences were intermixed with 24 filler, nonstudied sentences (the same set in every session) in order to simulate the interference C.V. experienced in Experiment 1.

After the acquisition phase, tests of implicit and explicit memory were conducted on the following day. The participants were tested on 5 measures presented *in the following order.*

—*Implicit production:* This test consisted of 72 studied items from all three learning conditions described above presented in a random order. In addition, four buffer cues not used anywhere else in the experiment were presented at the beginning of this list. These stimuli were presented in the Sentence+??? format and participants were asked to write down for each cue the first response that came to mind.

—*Explicit recall:* This test was identical to the implicit production test except that the stimuli were presented in a new random order and different retrieval instructions were given. Participants were asked to complete each Sentence+??? cue with the studied target word.

—*Recognition test for studied items.* Participants were presented with all 72 studied sentences in a new random order and were asked to circle YES for the items they believed to be studied. This test was conducted to maximize the familiarity of the stimuli for the amnesic participant.

—*Two-alternative forced-choice recognition:* Each of the 72 sentences from the three studied conditions was presented in the following fashion. The sentence cue of the test was presented with the target as well as an unrelated foil. The two alternatives were arranged above and below, and to the right of, the sentence cue. The position of the target was randomly selected across stimuli. The foils were derived from a different pool of items and were not used anywhere else in this experiment or in Experiment 1. These foils were normed on a group of 10 college undergraduates to ensure that the targets and foils were equally likely to be selected as targets prior to study (selection of targets versus foils, $t(9) = 1.14$, $SE = 1.67$). In the forced-choice recognition task, C.V. and control participants were asked to pick the studied target that matched with the sentence. This test is similar to the recognition memory test used by Hamann and Squire (1995).

—*Yes/No recognition:* The 72 studied sentences were intermixed with a new set of 72 filler, nonstudied sentences (not used anywhere else in the experiment), and participants were asked to select the sentences they had studied earlier.

Explicit memory was tested in the four different ways just described in order to explore various aspects of C.V.'s performance. It was expected that explicit recall would be the most difficult task for C.V. The recognition tasks, particularly the forced-choice recognition task, were considered to be easier than the other explicit tasks (Freed & Corkin, 1988; Freed et al., 1987), and the forced-choice recognition task was expected to show some memory for the newly learned stimuli.

—*Implicit word fragment completion test:* This test was conducted 4 h after the preceding series of tests were completed by C.V. as well as the control participants. The fragmented versions of target words from the 72 studied sentences were intermixed with filler fragments, and participants were asked to complete each fragment with the first solution that came to mind. No sentence cues were included in this test, and participants were given a maximum of 15 s to complete each fragment.

TABLE 2

Mean Response Probabilities of Amnesic Participant C.V. and Mean Response Probabilities of Young Controls (N = 9) and Matched Controls (N = 4) in the Word Fragment Completion Task in Experiment 2 (The Standard Deviations Are Presented in Parentheses)

	Young controls	Matched controls	C.V.
Study only			
Studied	0.29	0.26	0.46
Nonstudied	0.07	0.10	0.08
Study-Immediate Test			
Studied	0.33	0.27	0.38
Nonstudied	0.08	0.07	0.17
Test-Study			
Studied	0.24	0.28	0.50
Nonstudied	0.05	0.07	0.13

Results and Discussion

In the implicit production task, the proportion of correct targets produced in the baseline phase served as the nonstudied items and were subtracted from the proportion of studied targets produced in the test phase on Day 3. Neither the amnesic participant C.V. nor the Matched Controls produced any of the correct responses during the baseline period. Among the Young Controls, only two participants produced 1 out of 72 correct completion each in the baseline measure. Thus, the baseline completion rate for all participants taken together was close to zero. For the implicit word fragment completion test, the baseline completion rate was assessed on Day 1 for the targets that were subsequently studied in the sentence context (on Day 2) under the three conditions just described. The baseline completion rate was subtracted from the proportions of fragments completed on Day 3 to obtain the measure of standard priming. Because the same set of items served as nonstudied and studied items in this experiment, we did not adjust for baseline differences with adjusted priming as in Experiment 1. Thus, we present the data only for the more conservative, standard, priming measure in this experiment. The mean fragment completion rates for C.V., Matched Controls, and Young Controls across different conditions are displayed in Table 2.

The implicit new learning test was designed to measure the extent of implicit new verbal, associative learning under three learning conditions that varied in the amount of intraexperimental interference. The data from the amnesic participant C.V., the Matched Controls, and Young Controls are displayed in the left panel of Fig. 2. Amnesic participant C.V. showed poor learning under all three conditions, including the Study Only condition that was presumed to create the lowest amount of interference. In fact, C.V.'s production of correct targets was equivalent under the Study Only (0.08) and Test-Study conditions (0.08). This pattern is quite different from the advantage in priming reported by Hayman et al. (1992) for their amnesic participant K.C. and by Hamann and Squire (1995) for their group of nine amnesic participants. C.V.'s performance appeared to be numerically higher under the Study-Immediate Test condition (0.17) that is most comparable to the new verbal learning condition of Experiment 1 and is presumed to be the condition of moderate (not high) interference in the present experiment. However, this level of performance was still quite low such that standard priming scores (studied − nonstudied) across the three learning conditions, Study Only, Study-Immediate Test, and Test-Study did not differ from one another, X^2 = 0.99. Predictably, amnesic participant C.V.'s implicit new learning was

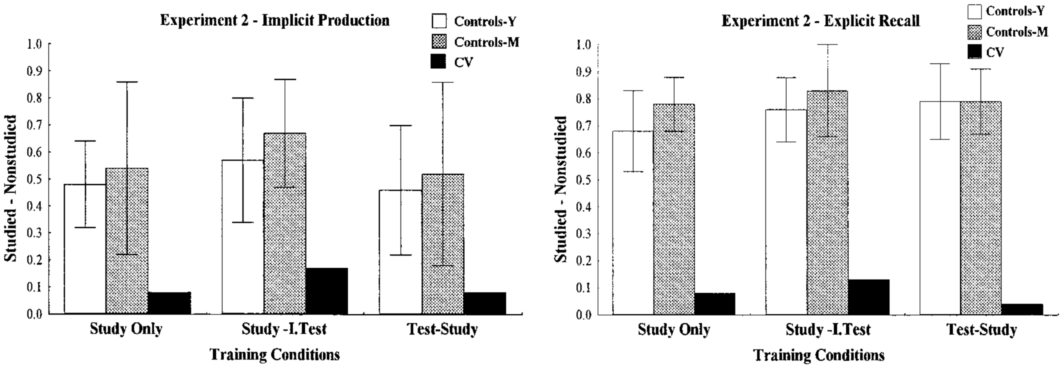

FIG. 2. The correct target production in Experiment 2 is displayed for amnesic participant C.V. and the two control groups. The left panel presents the data for the implicit production task as proportions of priming (studied–nonstudied) for the three learning conditions with varying amounts of interference. The right panel presents the explicit recall data as the proportions of corrected recall (studied–nonstudied) for the three learning conditions with varying amounts of interference. (Control-Y, Young Controls; Control-M, Matched Controls).

substantially lower than the learning exhibited by the control participants, both Matched and Young, such that C.V.'s performance fell below the 95% confidence intervals for each of the control groups under all of the training conditions in the implicit production task (see Fig. 2, left panel).

As expected, the data from the explicit recall test (Fig. 2, right panel) revealed grossly impaired performance from amnesic participant C.V. under all three learning conditions, and they fell outside the range of the explicit recall performance of Young Controls as well as that of Matched Controls. Also, it took C.V. nearly 15 min to perform this explicit recall task whereas the control participants took an average of 9 min and 40 s (Young Controls average = 9 min, 20 s; Matched Controls average = 10 min) to complete this task. This difference is particularly striking in light of the duration data for the previous, implicit production, task where C.V. took 7 min and 30 s to complete the task and control participants took an average of 8 min and 38 s (Young Controls average = 8 min and 26 s; Matched Controls average = 8 min 50 s).

The data from the control participants for the Study Only and Test-Study conditions were compared to determine whether these two conditions led to differential performance in the implicit production and explicit recall tasks. In the implicit production task, performance did not differ for either the Young Controls (Study Only = 0.48; Test-Study = 0.46) or the Matched Controls (Study Only = 0.54, Test-Study = 0.52) across the two conditions, $t < 1$ (for both groups collapsed).[5] These data are

[5] The performance of one Matched Control participant requires some explanation. This participant performed poorly in the implicit production task, particularly under the Study Only (0.13) and Test-Study (0.17) conditions. At first glance, these data are problematic. However, during the debriefing session, this participant explained the strategy she used in the implicit production task. She explained that she liked some other completions better than the ones provided in the learning sessions. At test, when she saw the sentence cue, both the studied response as well as her preferred response came to mind simultaneously. She often chose her preferred response over the studied response. Therefore, her production of studied responses was lower than expected. This explanation predicts a much higher level of performance in the explicit recall task because in this test participants were asked to complete the sentence stems with the studied responses. Results confirmed this prediction as this Matched Control participant performed near ceiling in the explicit recall task (Study Only = 0.88, Study-Immediate Test = 0.96, and Test-Study = 0.83). It should be noted that none of the results reported for the control participants, either averaged across all controls participants or averaged only for the Matched Control participants, change when the data from this participant are removed from the analyses. Therefore, we took the more conservative approach of including this participant's data in the analyses.

An additional concern pertaining to this Matched Control participant's performance may be that amnesic participant similar to those reported by Hayman et al. (1992) for their four control participants who also exhibited equivalent performance in the implicit production of correct targets under the Study Only and Test-Study conditions (0.85 and 0.83, respectively). In contrast, Hamann and Squire (1995) reported that their control participants produced more targets under the Test-Study condition compared to the Study Only condition (0.77 and 0.61, respectively, derived from their graph). Hamann and Squire's (1995) results showing an advantage for Test-Study condition in memory-intact participants replicate prior findings with memory-intact participants (e.g., Carrier & Pashler, 1992; Darley & Murdock, 1971; Runquist, 1986; Wenger et al., 1980). The apparent discrepancy between our findings and Tulving et al.'s findings, on one hand, and those of Hamann and Squire's, on the other, can be resolved by considering the retrieval instructions given to all participants. In Hayman et al.'s study and our present experiment, participants were asked to produce the first word that came to mind, whereas in the Hamann and Squire study, participants were asked to "produce the target words they had studied on previous sessions" (p. 1032). Together, two implications can be derived from this overall pattern of findings. One, superior memory in memory-intact participants under the Test-Study condition in previous reports is attributable to the explicit retrieval instructions given to participants, and it does not generalize to implicit production in memory-intact participants. Two, this pattern predicts that in our subsequent explicit recall task, we should expect to obtain an advantage for the Test-Study items over Study Only items. Consistent with this prediction, in the Explicit Recall task, the control participants exhibited significantly better recall for targets learned under the Test-Study training condition than under the Study Only training condition, $t(12) = 2.53$, $SE = 0.03$. This pattern is similar to the findings of Hamann and Squire (1995) and suggests that the advantage for the Test-Study training procedure in memory-intact participants may be more easily obtained in explicit memory tasks than in implicit tasks.

One possible reason that the advantage for the Study Only procedure is seen in many cases of amnesia (though not ours) but not under the implicit retrieval condition for memory-intact participants may partially be attributable to the use of explicit memory access used by memory-intact participants even in the implicit tasks. Specifically, with multiple training sessions, memory-intact participants may more easily invoke explicit access to study materials than may the amnesic participants. Although this explicit access may only be partial and not as willful as in the explicit recall task, it may be sufficient to eliminate the Study Only advantage observed in amnesic participants by other researchers (Hamann and Squire, 1995; Hayman et al., 1992). Our own results with control participants in the implicit production task may be susceptible to this possibility, but we do note that such explicit access in our implicit production task was not complete because the overall level of memory performance improved significantly for the control participants across the implicit production and explicit recall tasks, $t(12) = 3.38$, $SE = 0.07$.

On the three recognition memory tasks that followed, C.V.'s performance was expected to improve because of the familiarity component of recognition. The data from the three recognition tasks are displayed in Fig. 3. In the first recognition task, where all 72 studied sentences were presented to provide maximum familiarity for performance (the left-most of the bars in Fig. 3), C.V. recognized 69% studied sentences correctly. Although C.V.'s performance was reasonably good, it still fell outside the range of

C.V. also had preferred responses that blocked his production of correct responses in the implicit production task. This concern is allayed by the examination of amnesic participant C.V.'s intrusion rates from the baseline measure. C.V. produced 14% baseline intrusions in the implicit production task (Study Only = 17%, Study-Immediate Test = 8%, Test-Study = 17%), and 19% baseline intrusions in the explicit recall task (Study Only = 25%, Study-Immediate Test = 21%, Test-Study = 12%). Thus, there were large proportions of items in the implicit production task (86%) and the explicit recall task (81%) in which new learning could have taken place without the interference of intrusions from preexperimental associations.

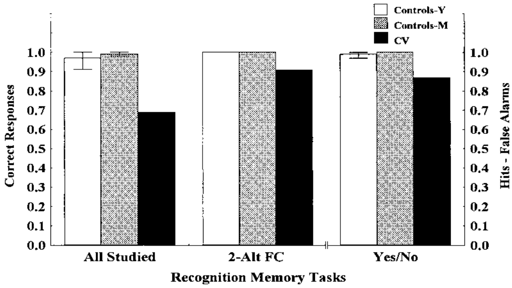

FIG. 3. The recognition memory performance of amnesic participant C.V. and two control groups across three different measures of recognition memory in Experiment 2 is displayed. The left-most panel presents the correct recognition of the 72 studied sentences. The middle panel presents the correct recognition of the sentences where participants had to choose between the correct target and a foil placed in front of the sentence cue. The right-most panel presents the hits–false alarm data collapsed across the three learning conditions from the yes/no recognition task. (Control-Y, Young Controls; Control-M, Matched Controls).

recognition performance of Young Controls (97% correct) and Matched Controls (99% correct), who performed at ceiling. Furthermore, it is interesting to note that it took C.V. over 7 min to complete this task, whereas the control participants took an average of 3 min and 26 s (Young Controls average = 3 min 33 s; Matched Controls average = 3 min 20 s) for completion.

On the second recognition task of two-alternative forced-choice recognition (the middle set of bars in Fig. 3), C.V. showed remarkably good recognition memory (91% correct), supporting the extant data that amnesic participants show improved performance on forced choice recognition memory tasks (Freed & Corkin, 1988; Freed et al., 1987). But C.V.'s performance was somewhat below that of controls, who obtained perfect scores on this task. Once again, the time taken to complete the task reflected poorer performance on C.V.'s part (18 min) compared to control participants, who took an average of 4 min (Young Controls average = 3 min, 40 s; Matched Controls average = 4 min, 20 s). C.V.'s report following this test was also revealing regarding his level of conscious awareness of the study materials. C.V. remarked at the end of the forced-choice recognition test that he found this task easy because *he* had earlier constructed logical sentence completions such as "the rabbi and the turkey" (studied sentence presented to C.V., "Rabbi requested turkey").

On the third recognition memory task of yes/no recognition (the right-most set of bars in Fig. 3), amnesic participant C.V. correctly recognized 70 out of 72 sentences, and he produced 7 out of 72 false alarms, yielding a d' value of 3.16 and a B of 1.47, and demonstrating good recognition memory. Control participants showed nearly perfect recognition memory (Young Controls, hits = 100%, false alarms = 1%; Matched Controls, hits = 100%, false alarms = 0). The time taken to complete this task showed the same pattern as the earlier tasks such that C.V. took 8 min and 50 s to complete the tasks whereas the control participants took an average of 5 min 41 s (Young Controls = 5 min 53 s; Matched Controls = 5 min 30 s).

The status of perceptual priming was measured with a word fragment completion task by obtaining the standard priming scores (studied–nonstudied). Collapsed across three study conditions, amnesic participant C.V. produced substantial priming for the studied targets (studied = 32, nonstudied = 9). C.V.'s performance either was within the range of the control participants or even exceeded that of control participants across different conditions (see Fig. 4). It is also relevant to note that C.V. exhibited perceptual priming for learned targets even when he failed to produce them in response to

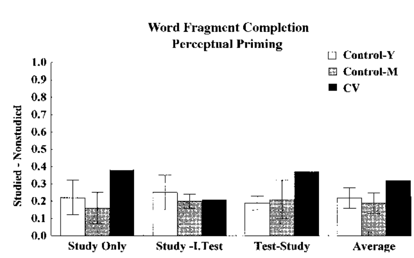

FIG. 4. The perceptual priming data in the form of adjusted priming scores from the word fragment completion task in Experiment 2 are displayed for the amnesic participant C.V. and the two control groups. The fourth set of bars present the average adjusted priming scores across all stimuli from all three learning conditions. (Control-Y, Young controls; Control-M, Matched Controls).

sentence cues in the implicit production task and explicit recall tasks.

Taken together, C.V.'s performance did not improve under the Study Only learning condition compared to under the Test-Study condition even though the former condition was shown to be more beneficial for learning in another densely amnesic participant (Hayman et al., 1992) and a group of amnesic participants (Hamann and Squire, 1995). Predictably, C.V.'s explicit recall was also found to be grossly impaired. C.V.'s recognition memory performance was found to be reasonably good although it took C.V. much longer to perform this task compared to control participants. C.V.'s contrasting pattern of performance across the implicit production and explicit recall tasks, on one hand, and the recognition tasks, on the other, is similar to the pattern of performance recently reported by Isaac and Mayes (1999a, 1999b) in a group of amnesics for the forgetting rates in free recall and cued recall tasks, on one hand, and the recognition task, on the other. Finally, C.V. exhibited normal levels of perceptual priming for the studied targets.

GENERAL DISCUSSION

Two experiments were conducted to examine the role of different retrieval cues and types of interference in new conceptual associative learning in a severely amnesic participant, C.V. Experiment 1 revealed substantial priming for repeated, novel sentences when the retrieval cues either provided perceptual information only for the targets (perceptual priming) or provided the sentence frames as well as perceptual information for the targets (Sentence+Fragment cues). These findings are similar to the priming data obtained from the performance of a basal forebrain amnesic participant, C.C. and a medial temporal lobe amnesic participant, R.H. (Rajaram & Coslett, in press), as well as from a densely amnesic participant, K.C. (Tulving et al., 1991). Critically, C.V.'s performance under the Sentence+??? retrieval cue condition was grossly impaired. This pattern of impairment is similar to the impaired performance observed for the medial temporal lobe amnesic participant R.H. (Rajaram & Coslett, in press, Experiments 1 and 3) and quite different from the substantial priming produced by the basal forebrain amnesic participant C.C. (Rajaram & Coslett, in press) and the amnesic participant K.C. (Tulving et al., 1991) with the Sentence+??? retrieval cues. C.V.'s poor performance under the Sentence+??? retrieval condition is particularly remarkable because the Study-Test sessions in the present Experiment 1 were presented in quick succession, unlike in the previous studies described here.

In Experiment 2, the role of interference in new conceptual associative learning was tested by manipulating the levels of intraexperimental interference across three learning conditions, Study Only, Study-Immediate test, and Test-Study. Unlike previous studies, in the present experiment we failed to find improved learning in C.V.'s performance even under the condition that presumably created the least amount of intraexperimental interference, i.e., the Study Only learning condition.

An obvious and reasonable interpretation of the present data pertains to the role of severity of amnesia in mediating learning of new verbal associations. Previous studies on priming of new associations with unrelated word-pairs (Graf & Schacter, 1985) showed that new association priming could be obtained in mildly and moderately amnesic participants but not in severely amnesic participants (Schacter & Graf, 1986). One possibility may be that gross impairments in priming with the Sentence+??? retrieval cues for the amnesic participants R.H. (Rajaram & Coslett, in press) and C.V. (the present experiments) may be attributable to their severe amnesia. Similarly, C.V.'s inability to benefit from the Study Only learning method may also be attributable to his severe amnesia.

Undoubtedly, new verbal learning, particularly at the conceptual and semantic level, would be impaired more in severe amnesia than in moderate amnesia. However, several aspects of the data from these and other studies strongly suggest that differences in severity of amnesia can not solely account for the patterns of performance exhibited by amnesic participants. For instance, the first evidence of positive learning under the Sentence+??? retrieval condition was reported for a severely amnesic participant, K.C., who failed to recognize any of the studied sentences after several trials of learning (Tulving et al., 1991). Similarly, basal forebrain amnesic participant C.C. showed substantial learning under the Sentence+??? retrieval condition even though her recognition memory for the same sentences was poor and comparable to that of the medial temporal lobe amnesic participant R.H., who failed to show such learning (Rajaram & Coslett, in press). Finally, in Experiment 2 in the present series, C.V. exhibited poor learning in response to Sentence+??? retrieval cues, but his recognition memory was reasonably good for the same set of stimuli. In sum, although severity of amnesia may account in large part for the failure of new verbal, associative learning, as measured by the Sentence+??? retrieval cues, this explanation does not account for all of the data in the literature.

An alternate interpretation may be that the medial temporal lobes including the hippocampal system may be heavily involved in mediating new verbal, associative learning where perceptual support at test is limited. The failure of medial temporal lobe amnesic participant R.H. supports this interpretation. Because C.V.'s amnesia also appears to be a result of presumed hippocampal damage, the results from the present study also support this interpretation. Similarly, medial temporal lobe amnesic participant H.M.'s failure to produce the correct targets under the Sentence+??? conditions also favors this notion (in Squire & Knowlton, 1995). Recently, Isaac and Mayes (1999a, 1999b) and Aggelton and Brown (1999) have also proposed that damage to the extended hippocampal system disrupts the consolidation of complex associations.

However, three lines of evidence complicate the interpretation that the medial temporal lobe regions play a large role in the formation of new verbal associations. One, densely amnesic participant, K.C., who did show successful semantic learning under conditions very similar to those tested here, reportedly sustained extensive brain injury that also included some of the medial temporal lobe regions bilaterally (Hayman et al., 1992; Kohler et al., 1997; Tulving et al., 1991). Two, in a recent study, Vargha-Khadem et al. (1997) reported three case studies where the participants exhibited amnesia resulting from bilateral hippocampal pathology sustained in early childhood. In all three cases, the amnesic participants displayed debilitating episodic memory deficits but had acquired speech and language skills, literacy, and factual knowledge within the low-average to average range. These findings suggest that semantic memories can be acquired despite hippocampal damage. However, it is also relevant to note that in laboratory tests of multitrial (10 trials in each task) recognition tasks of novel associations (faces with voices, objects with places), these amnesic participants performed poorly relative to controls. Thus, the learning achieved in the real world may be attributable to multiple sources of rich encoding that may have far exceeded the number of repetitions typically tested in the laboratory settings. Three, in Experiment 2 reported here, we found that C.V. failed to acquire novel verbal associations even under the minimal interference condition. This finding is problematic at least for the strong version of the claim that the hippocampus and the related structures enable learning of novel associations by suppressing interfering stimuli.

A possible resolution of these findings may emerge with a more precise consideration in human participants of different substructures within the medial temporal lobes that may subserve different cognitive components that underlie new learning (see also Mishkin et al., 1998). At the cognitive level, the streamlining across laboratories of acquisition and retention tasks, and the putative processes tapped by these tasks, will greatly facilitate such analysis and provide a better assessment of the structure–function mappings of implicit learning of novel verbal information in the human cognitive system.

Implications for Normal Cognition

The results from the present series of experiments provide a window into the contributions of the implicit memory processes in mediating new verbal associative learning in a memory-intact cognitive system. As demonstrated by the extant data, new associative learning at a conceptual or semantic level (as required by the Sentence+??? retrieval cues) requires multitrial training. Multiple trials in memory-intact participants present the danger of explicit access to the learned material. Such contamination complicates our understanding of the exact role of implicit memory in supporting new learning, and the exact conditions under which such learning may occur. These problems may be circumvented by assessing the effects of implicit learning in cases of severe amnesia.

The findings with dense amnesics from other studies (Hamann & Squire, 1995; Hayman et al., 1992; Rajaram & Coslett, 1991; Tulving et al., 1991; see also Van der Linden et al., 1994; Verfaellie, et al., 1995) and our findings here demonstrate that new verbal associative learning is slow and laborious in amnesia. Interestingly, this pattern in the amnesic performance for verbal learning bears a strong resemblance to the pattern observed in the memory-intact population in studies of implicit learning for rule-governed sequences of stimuli such as artificial grammar learning and probability learning (Reber, 1989), the serial reaction time task (Stadler, 1989), and the choice reaction time task (Lewicki et al., 1987). In these studies with the memory-intact population, learning is found to occur without any conscious awareness of the rules and typically requires several (sometimes hundreds) of trials. In studies of new verbal learning in the memory-intact population, including the control data in the present series of experiments, learning seems to occur at a more rapid rate and with some awareness, indicating that it is much more difficult to eliminate the use of explicit memory in new learning of verbal stimuli. Our comparison of new implicit and explicit learning in memory-intact participants provided the first direct comparison within one study of performance under the Test-Study and Study Only conditions in Experiment 2. These findings revealed likely effects of explicit contamination on implicit learning. Specifically, the memory-intact participants did not demonstrate the Study Only advantage exhibited by other amnesics (Hamann & Squire, 1995; Hayman et al., 1995) in the implicit production task even though they did exhibit the predicted Test-Study advantage in the explicit recall task. Presumably, the advantage amnesics show for the Study Only condition dissipates in memory-intact participants because of explicit access in multitrial learning situations. Together, these findings underscore the contribution of the amnesic data toward understanding the normal cognitive functions.

Our findings reported in this manuscript also delineate the differences between implicit learning of new associations at a perceptual level and a conceptual level. Amnesic participant C.V. (as well as another severely amnesic participant, R.H., we reported earlier, Rajaram & Coslett, in press) failed to show any learning with retrieval cues that provided only partial perceptual support and required access to learned information at the conceptual or semantic level. In contrast, these participants exhibited substantial perceptual priming for single words as well as for novel associative stimuli when perceptual support for the to-be-retrieved item was available. These results suggest a dissociation between perceptual and conceptual binding of verbal associations. Because perceptual binding does not seem to guarantee conceptual binding as well, an understanding of implicit acquisition of new information in normal cognition will require a systematic analysis of these separable cognitive components and mechanisms.

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