Neuropsychology
2000, Vol. 14, No. 1, 3–15

0894-4105/00/$5.00 DOI: 10.1037//0894-4105.14.1.3

Latent Learning in Medial Temporal Amnesia: Evidence for Disrupted Representational but Preserved Attentional Processes

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Damage to the hippocampus and medial temporal (MT) structures can lead to anterograde amnesia and may also impair latent learning, in which prior exposure to cues affects their subsequent associability. Normally, latent learning may reflect both representational and attentional mechanisms. Prior work has suggested that individuals with MT amnesia have specific deficits in representational processing; thus, latent learning that invokes primarily representational mechanisms might be especially impaired in MT amnesia. The current results provide preliminary confirmation of this prediction. In Experiment 1, a latent learning paradigm expected to invoke representational mechanisms was impaired in individuals with MT amnesia, whereas in Experiment 2, a paradigm expected to invoke other attentional mechanisms was spared in individuals with MT amnesia. This suggests the representational and attentional components of latent learning are dissociable and differentially affected in anterograde amnesia.

Damage to the medial temporal (MT) lobe, including hippocampus and related structures, leads to a characteristic anterograde amnesic syndrome in humans in which acquisition of new declarative or fact-based knowledge is impaired (e.g., Squire, 1987). For many years, the common wisdom was that learning of procedural or nondeclarative information, such as classical conditioning or skill learning, was spared in MT amnesia. For example, in classical conditioning, a previously neutral cue (the conditioned stimulus or CS) is repeatedly paired with a response-evoking stimulus (the unconditioned stimulus or US) until presentation of the CS alone evokes a protective, anticipatory conditioned response. Such simple CS–US association is not disrupted in MT amnesia (e.g., Daum, Channon, & Canavan, 1989; Gabrieli et al., 1995; Weiskrantz & Warrington, 1979) or in animal models of amnesia involving hippocampal-region damage (e.g., Port, Mikhail, & Patterson, 1985; Schmaltz & Theios, 1972). However, if the conditioning paradigm involves more complex contextual, spatial, temporal, or configural relationships, there may indeed be an impairment after hippocampal-region damage (e.g., Clark & Squire, 1998; Hirsh, 1974; McGlinchey-Berroth, Brawn, & Disterhoft, 1999; McGlinchey-Berroth, Carrillo, Gabrieli, Brawn, & Disterhoft, 1997; Nadel & Willner, 1980; Sutherland & Rudy, 1989). One class of conditioning behaviors affected by hippocampal-region damage is latent learning, in which prior unreinforced exposure to stimuli affects the speed of later learning associations involving those stimuli. One example is latent inhibition, in which prior exposure to the CS retards later CS–US association (Lubow, 1973). Another example is learned irrelevance, in which prior exposure to both the CS and the US, uncorrelated with each other, retards their subsequent association (Rescorla, 1966). In classical conditioning tasks, damage to the hippocampal region in animals impairs both latent inhibition (Kaye & Pearce, 1987; Solomon & Moore, 1975) and learned irrelevance (Allen, Chelius, & Gluck, 1998).

In light of these and related findings, several theories have proposed that hippocampal-region function is better described in terms of information-processing approaches than in terms of what classes of learning are impaired and spared after hippocampal-region damage. Many theories agree that

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This research was supported by National Institute of Neurological Disorders and Stroke Grant 1P50NS26985 and by grants from the McDonnell-Pew Foundation and the Alzheimer's Association. We thank John Gabrieli for his help and support.

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simple association does not require the hippocampal region but that the hippocampal region is essential for learning arbitrary relationships between stimuli. Thus, the hippocampal region has been variously implicated in learning flexible relationships between stimuli (Eichenbaum, 1992), in forming cognitive maps (Nadel & Willner, 1980), in processing background contextual information (Hirsh, 1974), and so on.

A recent computational theory (Gluck & Myers, 1993; Myers & Gluck, 1994) has suggested that one function of the hippocampal region is the formation of new stimulus representations that encode environmental regularities. A *stimulus representation* is defined simply as a recoding of information (Shepard, 1958); in the brain, information is represented as the pattern of activities it evokes over a given set of neurons. Learning that a CS predicts a US involves mapping from the representation of that CS to output that (directly or indirectly) gives rise to a conditioned response. If two stimuli have similar or overlapping representations, mappings learned to one stimulus tend to generalize easily to the other stimulus. This is beneficial if the two stimuli are to be associated with similar future events (e.g., USs) but problematic if the two stimuli predict different future events. Thus, learning can be facilitated by choosing stimulus representations that allow for the appropriate degree of generalization. The Gluck–Myers theory suggests that the hippocampal region can selectively compress (or make more similar) the representations of stimuli that reliably co-occur or predict similar future events while at the same time differentiating (or making less similar) the representations of stimuli that never co-occur or that predict different future events.

This theory, implemented as a connectionist network model, has had some success in accounting for a range of behavioral data in hippocampal-lesioned animals (Gluck & Myers, 1993; Myers & Gluck, 1994, 1996) and in humans with amnesia resulting from MT damage that includes the hippocampus or the parahippocampal region (Gluck, Ermita, Oliver, & Myers, 1997; Gluck, Oliver, & Myers, 1996). More recently, it has provided an account of the effects of selective hippocampal lesions that spare surrounding hippocampal-region structures (Myers, Gluck, & Granger, 1995) and of the modulatory effects of septohippocampal projections and their disruption through anticholinergic drugs (Myers et al., 1996; Myers, Ermita, Hasselmo, & Gluck, 1998).

The computational theory has also made several predictions about the effects of hippocampal-region damage on latent learning paradigms such as latent inhibition and learned irrelevance (Myers et al., 1998; Myers & Gluck, 1994). It stresses representational processes in latent learning. For example, in latent inhibition, unreinforced exposure to the CS in the experimental context results in representational compression of the CS with the context—because the two co-occur and neither makes any prediction about US arrival. Later, when the CS predicts the US, this representational compression makes it hard to learn one response to the CS but a different response to the context alone. This slows learning relative to a control condition in which there was no CS exposure and hence no representational compression. Similar representational explanations of latent learning have been proposed by Mackintosh (1973), Hirsh (1974), Levy (1989), and Eichenbaum (1992). Because this explanation of latent learning depends on representational processes putatively mediated by the hippocampal region, it accounts for the fact that latent learning is disrupted after hippocampal-region damage.

There is an alternate class of explanation for latent learning that invokes attentional processes (e.g., Lubow, 1989; Mackintosh, 1975; Pearce & Hall, 1980). According to this view, unreinforced exposure to the CS results in the CS being tuned out of attention; this reduced attention impedes the CS from entering into subsequent associations. Consistent with this interpretation, latent inhibition is disrupted in individuals with attentional impairments, such as acute schizophrenia (Baruch, Hemsley, & Gray, 1988).

The attentional and representational accounts of latent learning are not necessarily in conflict; ordinarily, in the intact brains of animals and people, both attentional and representational processes may contribute to produce latent learning effects. However, a particular latent learning paradigm that invokes attentional processes more than representational processes, or vice versa, could be designed. In this case, individuals with representational disruptions due to MT damage might show disrupted latent learning in paradigms that primarily invoke representational processes—but they might show spared latent learning in paradigms that primarily invoke attentional processes.

The current studies test this proposed dissociation between representational and attentional mechanisms in latent learning. In Experiment 1, we consider a computer-based procedure that was previously used to demonstrate learned irrelevance in normal human participants (Myers et al., 1998). This task appears to emphasize representational processes and, therefore, should be disrupted in MT amnesia. In Experiment 2, we consider a procedure for demonstrating latent inhibition (Lubow, Ingberg-Sachs, Zalstein-Orda, & Gerwitz, 1992). This task appears to emphasize attentional processes, and, indeed, it is disrupted in individuals with impaired attention (e.g., Baruch et al., 1988); however, it does not appear to emphasize representational processes. Thus, we hypothesize that individuals with MT amnesia should show preserved latent learning in this paradigm.

Experiment 1

In classical conditioning, learned irrelevance refers to a slower CS–US association following prior exposure to the CS and the US, uncorrelated with each other (Rescorla, 1966). Learned irrelevance still occurs even if the US is signaled by a different neutral cue during the exposure phase (Baker & Mackintosh, 1979; Matzel, Schachtman, & Miller, 1988). Studies with normal animals have established that the critical basis of learned irrelevance is the absence of a correlation between the CS and the US in the exposure phase (Baker & Mackintosh, 1979; Matzel et al., 1988; Overmier & Wielkiewicz, 1983). This should result in exactly the kind of representational learning that the Gluck–Myers theory predicts should depend on the hippocampal region: Specifi-

cally, because the CS does not predict the US during the exposure phase, its representation should be compressed together with the context. Consistent with this interpretation, hippocampal-region damage does disrupt learned irrelevance in animal conditioning (Allen et al., 1998).

Myers, Oliver, Warren, & Gluck (in press) demonstrated a learned irrelevance effect in normal humans. This task embedded the logical structure of learned irrelevance within a computer-based task. Specifically, participants were shown a picture of a magician and were told that the magician was trying to produce a rabbit under his hat; participants were required to learn that a color change predicted whether the rabbit would appear. It may be useful to note that the predictive color change was broadly analogous to a CS, the to-be-predicted rabbit was broadly analogous to a US, and the task was thus analogous to learning a CS–US association. It is convenient to use these terms for simplicity in discussion, without necessarily implying that the participants' responses have been classically conditioned. Learning the color–rabbit (CS–US) association was significantly slowed in participants who had received prior uncorrelated exposure to the color CS and rabbit US (Myers et al.).

Experiment 1 applied this learned irrelevance paradigm to a group of amnesic individuals. We expected that in the nonexposed condition, amnesic participants would learn the association between color (CS) and rabbit (US) as quickly as control participants. However, we expected that amnesic participants in the exposed condition would not show retarded learning. That is, amnesic participants should not show latent learning in this paradigm.

Method

Participants. Six individuals with severe anterograde amnesia served as the amnesic group (A1–A6); Table 1 shows demographic, etiologic, and neuroimaging–pathological information for this group. Five of the participants had confirmed abnormalities in areas including the medial temporal lobes. One participant (A4) declined to undergo imaging; her etiology is consistent with presumed medial temporal lobe damage, although her behavior suggests possible additional damage (see below).

A battery of neuropsychological tests was given to assess intelligence, memory, and attention; these results are also summarized in Table 1. General cognitive function was assessed by the Wechsler Adult Intelligence Scale—Revised (WAIS–R; Wechsler, 1981), which generates age-normed means of 100 and a standard deviation of 15 (Lezak, 1995). With the exception of 1 amnesic participant (A4), all amnesic participants scored within the normal range on all WAIS–R subtests. Amnesic participants were also given the Wechsler Memory Scale—Revised (WMS–R; Wechsler, 1987) to assess memory function. This test also generates age-normed means of 100 and a standard deviation of 15 (Lezak, 1995). The amnesic participants all scored well below normal on the delay memory (Del.) component, and most scored below normal on the general memory (GM) index. By contrast, the amnesic participants generally scored within the normal range on the attention–concentration (Attn) index of the WMS–R, with the exception of participant A4, whose score falls somewhat below the normal range. In summary, with the exception of participant A4, the amnesic individuals showed normal cognition and attention–concentration, with strongly impaired memory.

We also tested twelve control participants and assigned them equally to two conditions (exposed and nonexposed). Within each condition, the control participants were matched to the 6 amnesic participants for age, gender, and WAIS–R Verbal IQ (VIQ). In the exposed control condition, the average age was 46.7 years (SD = 13.9) and the average Verbal IQ was 100.0 (SD = 5.1). In the nonexposed control condition, the average age was 43.0 years (SD = 11.5) and the average Verbal IQ was 117.0 (SD = 13.9). Neither the age nor Verbal IQ for either control group differed significantly from the amnesic group (t tests, all $ps > .05$).

Amnesic participants were tested at the Boston University Memory Disorders Research Center (MDRC) and at Rush-Presbyterian-St. Luke's Medical Center. Control participants were tested at the MDRC and at Rutgers University. All participants were offered compensation for their participation at a rate of $10 per hour plus $5 for travel expenses.

Apparatus. The experiment was automated on a Macintosh LC, PowerBook, or equivalent computer programmed in the SuperCard (Allegiant Technologies, San Diego, CA) language, with a color screen. Responses were recorded by pressing one of two labeled computer keys; except for these keys, the remainder of the keyboard was masked.

Stimuli. On each trial, the computer screen showed a drawing of a magician waving a wand at a large hat (see Figure 1A). A "magic word" was printed in large black lowercase letters inside a cartoon balloon above the magician. These magic words were taken from a set of 30 monosyllabic nonwords (Myers et al., in press); for each participant, 15 were used in Phase 1 and the remaining 15 were used in Phase 2. One of the Phase 1 magic words was randomly selected to be the signal word, *W*, which would predict the rabbit. The cartoon balloon above the magician could be red, green, or uncolored (gray). One of the colors (either red or green) was randomly selected to be the stimulus CS+ that would predict the rabbit in Phase 2, and the other color was selected to be stimulus CS–.

Procedure. Each amnesic participant was tested twice, once in the exposed and once in the nonexposed condition, with at least 1 month elapsing between sessions. Session order was counterbalanced between participants. The participant sat in front of the computer. The following instructions appeared: "Welcome. You will see a magician. He is trying to make a rabbit appear under his hat. Sometimes he succeeds, and sometimes he fails. Try to predict when the rabbit appears." The experimenter read these instructions aloud and then demonstrated the two keys, labeled "yes" and "no," with which the participant would enter responses.

On each trial, the magician and hat appeared, together with a magic word inside the word balloon (see Figure 1A). The prompt, "Is there a rabbit under the hat?" appeared. The participant then pressed one of the response keys, and the hat was raised to reveal whether or not the rabbit had appeared (see Figure 1, Panels B and C). Corrective feedback was given along with a computer beep in the case of incorrect responding.

Phase 1 consisted of 30 trials. During 15 randomly selected trials, the signal word *W* was presented and the rabbit appeared. On the remaining trials, other words were presented and no rabbit appeared. Thus, magic word *W* was perfectly predictive of the rabbit in Phase 1. In addition, for participants in the exposed condition, the cartoon balloon appeared in color CS+ on 10 trials and in color CS– on the remaining trials, with the constraint that CS+ and the rabbit were uncorrelated; that is, the probability of the rabbit's appearance was the same given color CS+ or CS–. For participants in the nonexposed condition, the cartoon balloon was always uncolored (gray). After Phase 1, the following instructions appeared and were read aloud by the experimenter, "Good! The magician is still trying to predict the rabbit, but now the rules of magic may have changed. Try to predict when the rabbit appears."

Table 1
Demographic, Etiologic, and Neuroimaging–Pathological Data for the Amnesic Participants in Experiments 1 and 2

Participant	Age (years)	Education (years)	Sex	Etiology	Neuroimaging–pathology summary	WAIS–R			WMS–R			Experiment	
						VIQ	PIQ	FSIQ	GM	Attn	Del.	1	2
A1	37	12	Male	Hypoxia post status epilepticus	Left temporal lobectomy; removal confirmed by surgical notes.	99	107	102	81	124	57	Y	Y
A2	38	14	Female	Anoxia	MRI: atrophy of cerebrum involving limbic system; hippocampi are atrophic.	95	87	90	90	115	50	Y	Y
A3	68	18	Male	Encephalitis	CT: bilateral lesions in anterior and medial temporal lobes, insular and putamen. Left frontal lobe lesion secondary to shunt.	126	126	130	102	114	50	Y	Y
A4	26	12	Female	Status epilepticus	N/A (Patient declines to undergo MRI.)	79	79	77	50	74	50	Y	Y
A5	37	12	Female	Anoxia	CT: increased volume in temporal horns of lateral ventricles. MRI: increased signal in medial temporal bilaterally.	104	117	110	88	108	71	Y	
A6	56	16	Male	Anoxia	MRI: mild general cerebral volume loss prominent in medial temporal lobe.	105	110	108	76	92	51	Y	
A7	46	16	Female	Anoxia	MRI: bilateral abnormalities in temporal lobes.	111	109	111	81	107	69		Y
A8	59	20	Male	Anoxia	MRI: diffuse cortical atrophy including temporal lobes.	109	100	105	65	89	61		Y
M (Experiment 1)	43.7	14.0				101.3	104.3	102.8	81.17	104.5	54.8		
SD	15.3	2.5				15.3	18.0	18.2	17.6	18.3	8.4		
M (Experiment 2)	45.7	15.3				103.2	101.3	102.5	78.2	103.8	56.2		
SD	15.5	3.3				16.0	16.8	18.1	18.4	18.7	7.8		

Note. WAIS–R = Wechsler Adult Intelligence Scale—Revised (Wechsler, 1981); WMS–R = Wechsler Memory Scale—Revised (Wechsler, 1987); VIQ = verbal IQ; PIQ = performance IQ; FSIQ = full scale IQ; GM = general memory index; Attn = attention–concentration index; Del. = delay memory index; MRI = magnetic resonance imaging; CT = computerized tomography; Y = yes.

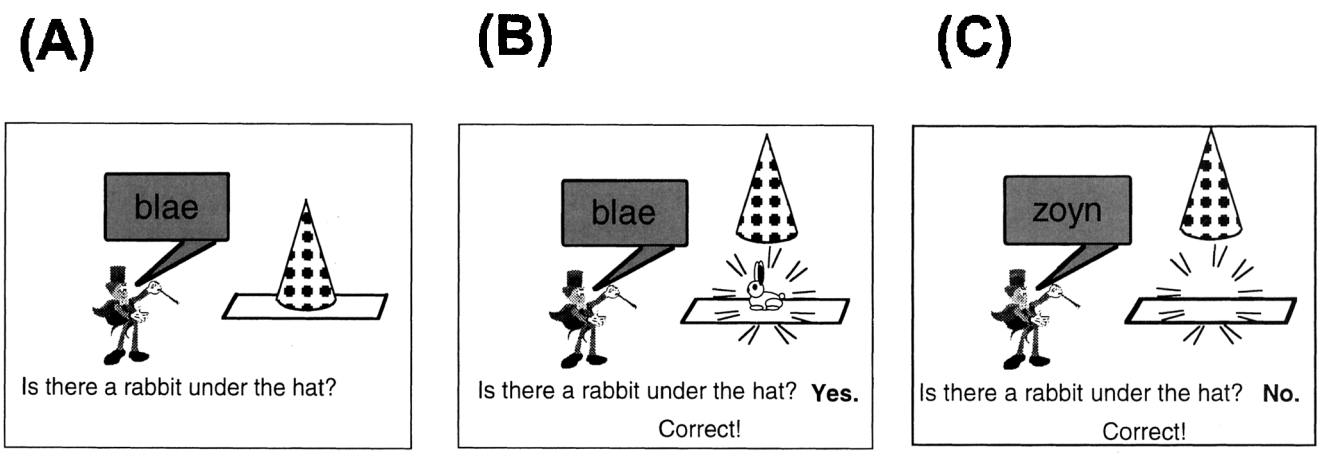

Figure 1. Screen events in the learned irrelevance paradigm. A: On each trial, the magician appears together with a "magic word" printed on a background that may be colored (red or green) or colorless (gray). The participant is asked to predict whether or not the rabbit will appear on the current trial. B and C: The hat is then raised to reveal whether the rabbit is present and corrective feedback appears.

Phase 2 consisted of 60 trials. On each trial, a magic word appeared, but these words were uncorrelated with the appearance of the rabbit. Instead, color CS+ occurred randomly five times in each block of 15 trials, along with the rabbit. Color CS– occurred on the remaining trials. Thus, participants were expected to learn that color CS+ always predicted the rabbit would appear, and color CS– predicted the rabbit would not appear. It is important to note that the magic words were now irrelevant with respect to predicting the rabbit and that no magic word appeared in both Phases 1 and 2. Phase 2 continued for a maximum of 60 trials or until the participant made 15 consecutive correct responses.

Data collection. For Phase 1, the total errors out of 30 trials were recorded for each participant. We defined criterion performance as eight consecutive correct responses. For phase 2, total errors to criterion, or to the maximum 60 trials, were calculated for each participant. For each participant, the computer recorded errors and correct responses in the presence and absence of the rabbit. The overall response rate was calculated as the percentage of trials on which the participant predicted the rabbit (whether this response was right or wrong). Two additional measures were computed, percentage CS+ (%CS+) and percentage CS– (%CS–), each indicating the percentage of correct responses on all rabbit-present (CS+) trials and rabbit-absent (CS–) trials.

Results

Figure 2A shows the total Phase 1 errors for each participant group and condition. One control participant in the exposed condition failed to reach criterion performance in Phase 1, as did 2 amnesic participants (A1 and A2) in the nonexposed condition. Both A1 and A2 did reach criterion

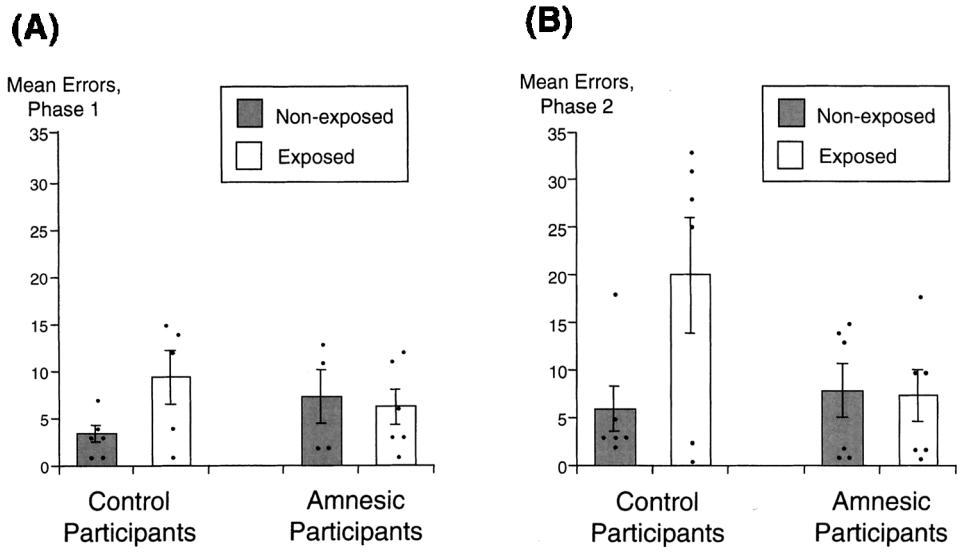

Figure 2. Results from Experiment 1. A: Total Phase 1 errors. B: Total Phase 2 errors.

performance in the exposed condition, indicating that they were able to master the task demands; furthermore, whereas A1 did the nonexposed condition first, A2 did the exposed condition first, suggesting that A2 could master the Phase 1 task on her first session. One control participant in the exposed condition also failed to reach criterion performance within the maximum 30 trials.

Of the remaining participants, Figure 2A shows a slight tendency for fewer mean errors among control participants in the nonexposed condition than the exposed condition, but an analysis of variance (ANOVA) confirmed that there was no significant effect of participant group, exposure condition, participant age, or gender on Phase 1 performance (ANOVA, all $ps > .05$). Figure 2B shows the mean Phase 2 errors for each participant group. Control participants showed a strong learned irrelevance effect, with fewer errors in the nonexposed condition than the exposed condition, but this effect was not evident among the amnesic participants. An ANOVA confirmed a significant effect of participant group, $F(1, 20) = 5.33$, $p < .05$, exposure condition, $F(1, 20) = 7.65$, $p < .05$, and Group × Exposure interaction, $F(1, 20) = 8.51$, $p < .05$. There was no significant effect of age, Verbal IQ, or Phase 1 performance (in terms of total errors) on Phase 2 performance (all $ps > .05$). Planned post hoc comparisons revealed that there was a significant difference between the control exposed and nonexposed conditions ($p < .05$) but that the amnesic participants in the exposed and nonexposed conditions did not differ from each other nor from the nonexposed control participants (all $ps > .05$). Thus, the effect of uncorrelated exposure in Phase 1 was to delay Phase 2 learning in control but not amnesic participants.

Notably, the 2 amnesic participants (A1 and A2) who failed to reach criterion performance in Phase 1 did reach criterion in Phase 2. The control participant who failed to reach criterion performance in Phase 1 did not reach criterion in Phase 2, but his Phase 2 performance was comparable with others in the exposed condition in terms of total errors.

Because the amnesic participants were tested twice, once within each condition, it is also possible to examine within-subject effects. Figure 3 (A and B) shows the performance for each amnesic participant in each exposure condition. Among those participants given the exposed session first, 1 participant (A3) showed better performance on the exposed than nonexposed session, and 1 participant (A2) showed better performance on the nonexposed session. None of the other participants showed strongly differing performance across sessions. Notably, participant A4, the amnesic individual whose cognitive and attentional scores fall somewhat below the normal range (refer to Table 1), was able to solve Phase 2 quickly in both sessions. Overall, there is no clear tendency toward reduced errors on the second session and no clear evidence of a savings effect. There is also no clear evidence of fewer errors on the nonexposed condition (regardless of session order). This is in contrast to the control participants (compare with Figure 2B), in which all but 1 nonexposed participant made five or fewer errors, whereas all but 2 exposed participants made 25 or more errors.

Finally, although the overall error rates do not differ for the amnesic participants in the exposed and nonexposed condition, it is possible that this score masked some subtle differences. Specifically, Phase 2 involved learning two different subtasks: generating a *yes* response in the presence of color CS+ and generating a *no* response in the presence of color CS–. To investigate this, we analyzed correct responses to the two colors separately. On trials with the CS+, both control and amnesic participants in the exposed and nonexposed conditions performed similarly in terms of percentage correct (see Figure 4A; ANOVA, all $ps > .05$). On trials with the CS–, there was a slight tendency for the control participants in the exposed condition to make more

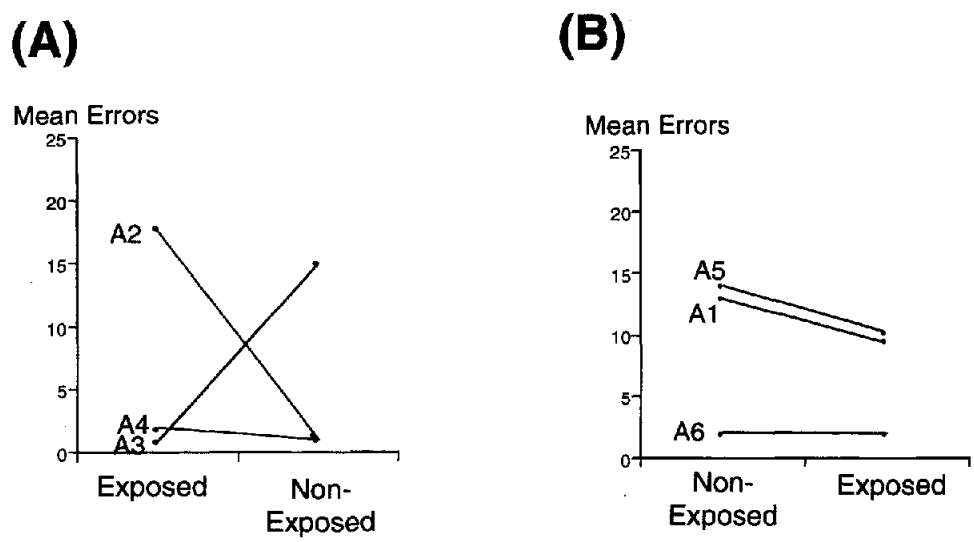

Figure 3. Individual Phase 2 performances from Experiment 1, showing amnesic participants given the nonexposed session first (A) and amnesic participants given the exposed session first (B).

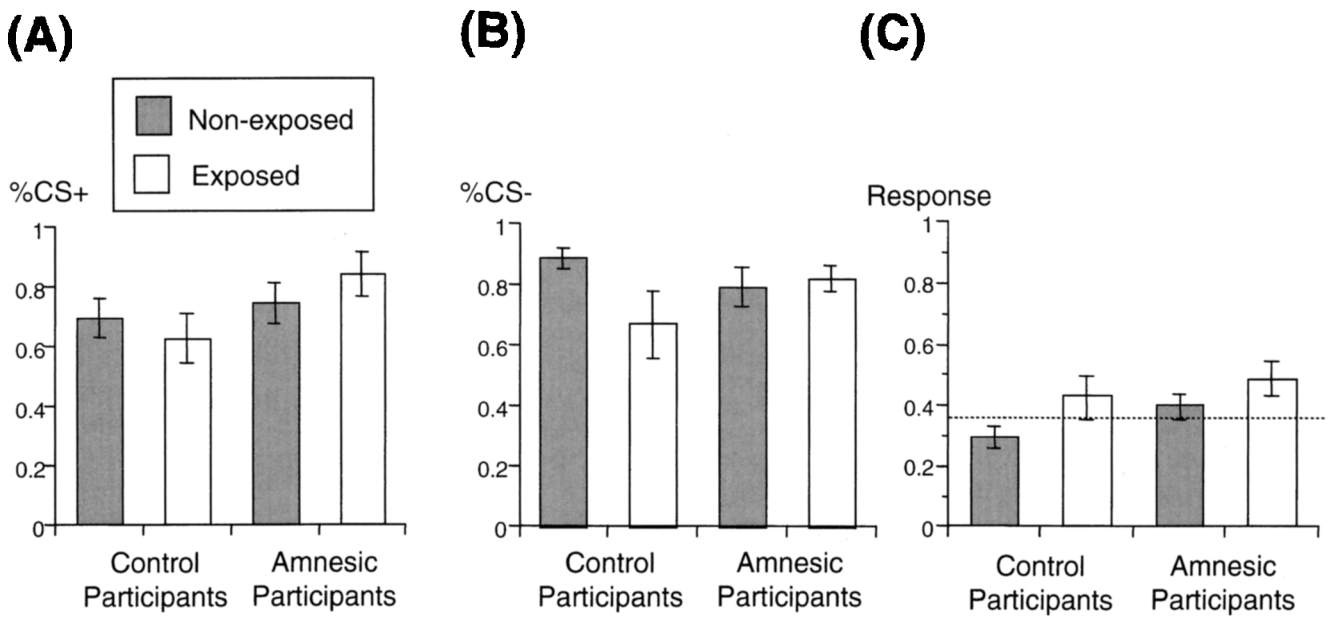

Figure 4. A: Total percentage correct responses on trials with conditioned stimulus present (%CS+). B: Total percentage correct responses on trials with CS absent (%CS–). C: Response rate, defined as proportion of trials generating a *yes* response. Optimum responding would be a response rate of 0.33 (dashed line).

errors than participants in the other conditions (see Figure 4B), consistent with their relatively poorer performance overall; this difference, however, failed to reach statistical significance (ANOVA, all *ps* > .05). We also investigated the baseline response rates in terms of proportion of *yes* responses as a function of total trials; the CS+ was present on 33% of trials, and the groups tended to generate close to this rate of *yes* responses (see Figure 4C). The nonexposed control condition appeared to generate slightly fewer *yes* responses than the exposed control condition or the amnesic groups, but this difference did not reach statistical significance (ANOVA, all *ps* > .05).

In sum, then, control participants appeared to show learned irrelevance, reflected in more total Phase 2 errors following uncorrelated exposure in Phase 1. The amnesic participants did not show such an effect. Both the exposed and nonexposed conditions showed Phase 2 performance similar to nonexposed control participants.

Discussion

The results of Experiment 1 show a learned irrelevance effect in control participants but not in amnesic participants. Among the amnesic participants, there were no differences between exposed and nonexposed conditions in terms of total errors, overall response rate, percentage correct responding on CS+ (rabbit-present) trials, or percentage correct responding on CS– (rabbit-absent) trials.

Studies with normal animals have established that the critical basis of learned irrelevance is the absence of a correlation between the CS and the US in the exposure phase (Baker & Mackintosh, 1979; Overmier & Wielkiewicz, 1983; Matzel et al., 1988), and that this is largely independent of motivational factors (Matzel et al., 1988). The disruption of learned irrelevance in amnesic participants is therefore consistent with models of hippocampal function that suggest that the hippocampal region is critically involved in monitoring predictive relationships between stimuli in the environment, particularly determining which stimuli are predictive of future reinforcement and which are simply occasionally occurring cues that ought to be configured together with other contextual stimuli (e.g., Myers & Gluck, 1994).

One concern in Experiment 1 is that the lack of an exposure effect in the amnesic participants simply reflects their faster forgetting of information from Phase 1. One purpose of Experiment 2 was to address this issue and determine whether amnesic participants could maintain associative information across this time period. A second issue is whether the failure of amnesic participants to show learned irrelevance reflects a specifically representational deficit or whether amnesic participants are globally impaired at any complex learning that involves contingencies beyond a simple CS–US association. To explore this issue, Experiment 2 considered a latent learning paradigm that has previously been shown to be disrupted in humans with attentional impairments.

Experiment 2

Latent inhibition refers to the retarded CS–US learning that follows unreinforced exposure to the CS (Lubow, 1973). This is a robust effect that has been demonstrated in many species using both operant and classical paradigms (see

Lubow, 1989). As described above, latent inhibition may reflect both attentional processes (Lubow, 1989; Mackintosh, 1975; Pearce & Hall, 1980) and representational processes (Eichenbaum, 1992; Hirsh, 1974; Levy, 1989; Mackintosh, 1973; Myers & Gluck, 1994). The extent to which a particular latent inhibition paradigm is disrupted following hippocampal-region damage may depend on the extent to which that paradigm reflects representational processing.

Lubow and colleagues (Ginton, Urca, & Lubow, 1975; Lubow et al., 1992) demonstrated latent inhibition in humans using a computer-based task. In the first exposure phase, some participants (exposed condition) heard an auditory stimulus (conceptually, the CS) embedded in an auditory masking task; other participants (nonexposed condition) received the masking task alone. In the second phase, all participants were required to learn to associate the auditory stimulus with a visual screen event (conceptually, the US). Among normal participants, those in the exposed condition learned the association slower than participants in the nonexposed condition (Ginton et al., 1975; Lubow et al., 1992). This latent inhibition effect was disrupted in participants with acute schizophrenia (Baruch et al., 1988).

One important characteristic of the latent learning paradigms studied by Lubow and colleagues in humans is the presence of a masking or distractor task in Phase 1. In the case of the Lubow et al. (1992) paradigm, the auditory masking task actively interferes with presentation of the auditory CS. In this case, one might expect that the participant is forced to tune out the CS in order to complete the masking task. This attentional process is presumably altered or destroyed in schizophrenia, which may be why schizophrenic participants fail to show any effects of CS exposure—learning about exposed CSs at the same speed as nonexposed CSs.

A second important aspect of the Lubow et al. (1992) latent inhibition task is that there is a dramatic change in task between the exposure and association phases: a masking task in Phase 1 and a CS–US association in Phase 2. This dramatic change may represent a kind of context shift. One should recall that the representational account of latent inhibition assumes that compression of the representations of CS and context during Phase 1 inhibits learning to respond to the CS but not context in Phase 2. If the context is changed between phases, then any compression with the earlier context is largely irrelevant when it comes to learning to respond to the CS but not the current context. Thus, a context shift may largely eliminate the effects of representational compression in latent inhibition. In fact, in animal studies, a context shift between Phases 1 and 2 does greatly reduce latent inhibition (Hall & Honey, 1989); a similar effect may possibly occur in humans (Lubow, Rifkin, & Alek, 1976; Zalstein-Orda & Lubow, 1994). By this argument, then, it may well be the case that the Lubow et al. (1992) latent inhibition paradigm does not depend particularly on representational mechanisms and, as such, may be preserved in individuals with MT amnesia.

In summary, then, although latent learning may in general reflect both attentional and representational processes, it seems likely that the Lubow et al. (1992) latent inhibition paradigm reflects primarily attentional processes. For this reason, we expected that latent learning in this paradigm—although greatly disrupted by schizophrenia—might be largely spared in individuals with MT amnesia.

Method

Participants. Six individuals with severe anterograde amnesia served as the amnesic group (A1–A4, A7, A8); 4 of these individuals also participated in Experiment 1. As shown in Table 1, all participants but A4 had confirmed damage that included the temporal (particularly medial temporal) lobes. Again, the amnesic participants showed normal scores on the WAIS–R and the WMS–R attention–concentration index, with the exception of participant A4 (refer to Table 1). All amnesic participants showed strong memory impairments, as assessed by WMS–R Delay subscore.

We again also tested twelve control participants and equally assigned them to two conditions (exposed and nonexposed). Within each condition, control participants were matched to the amnesic participants for age, gender, and WAIS–R Verbal IQ. Among participants in the exposed control group, the average age was 44.8 (SD = 11.5) and the average WAIS–R Verbal IQ was 110.7 (SD = 13.9). Among participants in the nonexposed control group, the average age was 47.7 years (SD = 12.4) and the average WAIS–R Verbal IQ was 107.6 (SD = 5.1). Neither age nor Verbal IQ for either condition differed significantly from the amnesic group (ANOVA, all $ps > .05$). Amnesic participants were tested at the Boston University MDRC and at Rush-Presbyterian-St. Luke's Medical Center. Control participants were tested at the MDRC and at Rutgers University. All participants were offered compensation for their participation at a rate of $10 per hour plus $5 for travel expenses.

Apparatus. The experiment was automated on a Macintosh LC, PowerBook, or equivalent computer programmed in the SuperCard language. Stimulus sounds were recorded directly into the computer, using SoundEdit Pro (MacroMind Paracomp, San Francisco), and played back through headphones attached to the computer output. Participants entered responses by clicking the computer mouse button.

Stimuli. A male native speaker of English recorded 30 monosyllabic pronounceable English nonwords (not the same as those used in Experiment 1). Each recording lasted approximately 1.5 s. Each syllable was then rerecorded with a coincident burst of static about half the volume of the syllable. Two syllable lists were then generated. List Lclean consisted of five blocks, each containing one presentation of each of the 30 syllables in random order. A second list, Lstatic, was generated from List Lclean by replacing a random six syllables from each block with recordings of the same syllable overlaid by static. No syllable co-occurred with static more than twice in List Lstatic. Thus, there were 30 static presentations in List Lstatic. In both lists, the intertrial interval (the time between the onset of one syllable and the onset of the next syllable) was fixed at 2.5 s.

Procedure. Each amnesic participant was tested twice, once in the exposed condition and once in the nonexposed condition, with at least 1 month elapsing between sessions. Session order was counterbalanced between participants. The experimenter sat the participant in front of the computer and read aloud the following instructions when they appeared on the screen: "In a moment, you will hear a series of nonsense words. Listen carefully and count how many times you hear the word 'ratch'." At this point, the experimenter placed headphones on the participant's head and

played the recording of the syllable *ratch* until the participant was ready to begin the experiment. The experimenter then asked the participant to repeat the instructions back, to ensure that the participant understood the task.

For control and amnesic participants in the exposed condition, List Lstatic was played; for control and amnesic participants in the nonexposed condition, List Lclean was played. The instructions remained on the screen throughout Phase 1. In both lists, there were five repetitions of the 30 syllables and hence five occurrences of the word *ratch*. Participants in the exposed condition also heard the occasional static bursts (conceptually, the CS). At the end of Phase 1, a tone sounded and the participant was asked how many times *ratch* had occurred. The experimenter helped the participants enter this number into the computer, using the mouse button to increment a counter.

Phase 2 was the same for all participants. A large counter, initialized to zero, appeared on the screen, together with the following instructions: "Now, during the recording, you will see the number below. It sometimes changes—depending on the recording. Press the button just before you think the number will change." Again, the experimenter read these instructions aloud and explained that the counter would increase numerically from zero to one to two and so on. The participant was then asked to repeat the instructions, to make sure they had been understood.

In this phase, the counter increment (conceptually, the US) occurred immediately following each burst of static (conceptually, the CS). All participants heard List Lstatic, including 30 bursts of static. The instructions, "Press the button just before you think the number will change," remained on the screen throughout Phase 2, as did the counter, which was highlighted briefly each time the subject pressed the mouse button.

Data collection. In Phase 1, the computer recorded the total occurrences of *ratch* reported by the participant. Because Phase 1 lasted approximately 10 min, participants occasionally lost count; for this reason, a report of 5+/–1 occurrences of *ratch* was considered acceptable.

In Phase 2, the computer scored a response as correct if the response occurred between the onset and offset of the static, whereas a response at any other time was counted as a false positive. Failure to respond during the static was scored as a false negative. The session ended when the participant made five consecutive correct responses with no intervening false positive responses. The computer then recorded a score for each participant, defined as the number of static presentations remaining after the participant reached criterion performance. Thus, if the participant never reached criterion performance, a score of 0 would be assigned. On the other hand, if the participant correctly responded to the first 5 static bursts with no false positives, a maximal score of 25 (30 – 5) would be assigned.

Results

All participants reported 5+/–1 occurrences of the word *ratch* in Phase 1. Among control participants, the Phase 2 score was greatly influenced by exposure condition (see Figure 5). All control participants in the nonexposed condition reached criterion performance; by contrast, only 2 control participants in the exposed condition reached criterion. Amnesic participants showed the same general pattern of results as the control participants. All amnesic participants in the nonexposed condition reached criterion performance; only 2 amnesic participants in the exposed condition reached criterion performance. Because the distribution of scores was bimodal, nonparametric tests were used. Planned

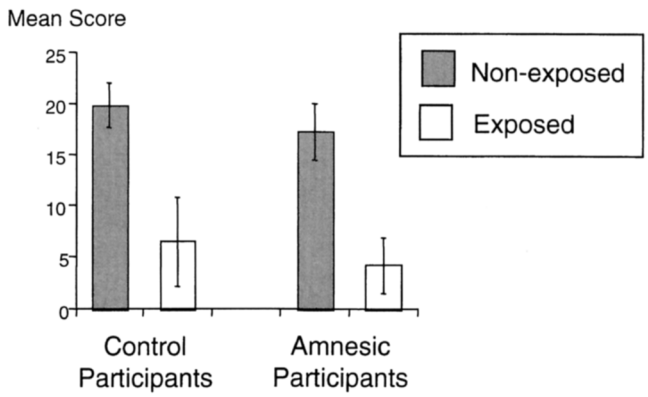

Figure 5. Results from Experiment 2, Phase 2 scores.

pairwise comparisons revealed significant effects of exposure condition among both control participants (Mann–Whitney $U = 5.50$, $p = .04$) and amnesic participants (Mann–Whitney $U = 3.50$, $p < .02$) but no significant effects of group (control vs. amnesic), participant age or Verbal IQ (all $ps > .05$). In summary, both the amnesic and control participants showed a latent inhibition effect, with Phase 1 exposure to the static impairing Phase 2 learning of a static-increment contingency.

Because we ran the amnesic participants twice, once each in the exposed and nonexposed conditions, it is also possible to consider within-subject effects. Figure 6 shows the performance for each amnesic participant in both conditions; every amnesic participant scored better on the nonexposed

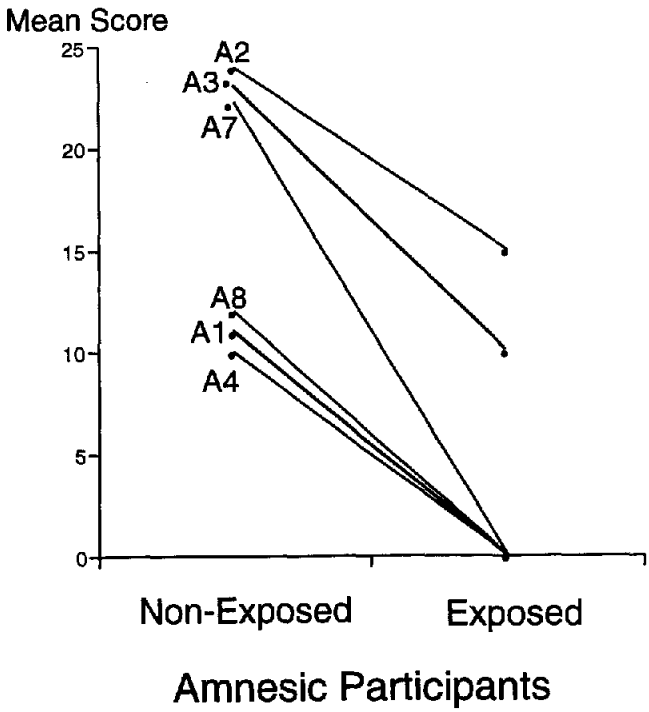

Figure 6. Individual performances from Phase 2 for the amnesic participants.

than the exposed session, regardless of session order. This effect reached statistical significance (planned t test with dependent means), $t(6) = 4.36$, $p = .005$. In summary, both control and amnesic participants showed latent learning using the Lubow et al. (1992) paradigm.

Discussion

This experiment replicated Lubow et al.'s (1992) finding that a computer-based instrumental learning paradigm could be used to demonstrate latent inhibition in normal humans. A group of amnesic individuals, tested with the same paradigm, also showed a strong latent inhibition effect. One important implication of this result is that although the amnesic participants exhibited severe memory deficits (e.g., WMS–R Delay subscore), at least some of the information presented during phase 1 of the experiment survived to interfere with learning in Phase 2.

The finding of preserved latent inhibition in the amnesic participants contrasts with an earlier study in which Baruch et al. (1988) found disrupted latent inhibition, using the same paradigm, in individuals with acute schizophrenia. In that study, over 75% of control participants previously exposed to the static cue received scores of 5 or less, whereas about 80% of nonexposed control participants received scores over 20. This is comparable to the performance of control participants in the current study (compare with Figure 5). By contrast, participants with acute schizophrenia did not show latent inhibition, indicated by equivalent scores in exposed and nonexposed groups (averaging around 20 and similar to nonexposed controls). Thus, this latent inhibition task appears to be disrupted in acute schizophrenia but not in amnesia.

The finding of preserved latent inhibition in the amnesic participants also contrasts with results from the animal literature that demonstrate that latent inhibition is attenuated or eliminated after broad hippocampal-region lesions (Ackil, Mellgren, Halgren, & Frommer, 1969; Kaye & Pearce, 1987; Solomon & Moore, 1975). More recent animal studies have suggested that selective lesions of the hippocampus that spare surrounding cortical areas do not impair latent inhibition (see Myers et al., 1995, for review). However, most of the amnesic participants tested here have diffuse damage throughout the medial temporal lobes (refer to Table 1) rather than lesions strictly limited to the hippocampus proper.

It is more likely that the difference in results may reflect the differences in paradigm between the animal and human studies. As discussed above, the latent learning paradigm in Experiment 2 may emphasize attentional mechanisms—presumably functional in the amnesic participants—but not representational mechanisms. This argument would explain the finding of preserved latent inhibition in the amnesic participants in the Lubow et al. (1992) paradigm. However, the argument leaves open the question of whether other latent inhibition paradigms would be disrupted. For example, in a classical conditioning preparation, such as motor-reflex learning, where there might be no context change between phases and no distractor task to force participants to tune out the CS from attention, amnesic participants might indeed show a reduction or abolition of latent inhibition, consistent with animal conditioning studies.

General Discussion

This study compared the performance of amnesic participants on two latent learning tasks: a learned irrelevance task, which we argued would invoke primarily representational processes, and a latent inhibition task, which we argued would invoke primarily attentional processes. The former but not the latter effect was disrupted in amnesic participants. These results were consistent with the predictions of the Gluck–Myers model of hippocampal-region function (Gluck & Myers, 1993; Myers & Gluck, 1994), which argued that the hippocampus and associated MT structures are critical for the formation of new stimulus representations that reflect arbitrary relations between cues. The Gluck–Myers theory is similar to many qualitative theories of hippocampal-region function that focus on the hippocampal region's role in stimulus configuration, stimulus relation, and contextual processing (Eichenbaum, 1992; Hirsh, 1974; Sutherland & Rudy, 1989).

The failure of amnesic participants to show latent learning in Experiment 1 did not appear to be due to a simple associational deficit because amnesic participants in the nonexposed condition learned at a similar speed to control participants in the same condition. Additionally, the lack of learned irrelevance in the amnesic participants was probably not due to forgetting of the Phase 1 information because amnesic participants in Experiment 2 were able to maintain information across a similar interval. Instead, the amnesic participants seemed specifically impaired in their ability to learn a nonpredictive relationship between the CS and the US during the exposure phase. Because all of the amnesic participants (except A4) had damage that included the medial temporal lobes, it seems reasonable to assume that hippocampal-region dysfunction contributed to the observed impairment. We do note, though, that most participants had additional damage to extrahippocampal structures, which could have contributed as well.

By contrast with the results of Experiment 1, the amnesic participants showed robust latent learning in Experiment 2—performing no differently from control participants. Therefore, the first implication of this result is that latent learning is not necessarily universally abolished in amnesia. Latent inhibition in the Lubow et al. (1992) paradigm appears to depend on the ability to inhibit attention to irrelevant stimuli. This is consistent with prior findings that this task is disrupted in individuals with attentional disorders such as acute schizophrenia (e.g., Baruch et al., 1988). Unfortunately, attention is notoriously hard to index or even define. Several kinds of tasks appear to index aspects of attention, although none may capture it fully; these include the Wisconsin Card Sort Task (Berg, 1948; Grant & Berg, 1948), the F-A-S word fluency test, and tests measuring span of apprehension (attention span), such as the attention–concentration components of the WMS–R. These tasks are normally disrupted in schizophrenia (see Randolph, Gold-

berg, & Weinberger, 1993, for review) but normally spared in MT amnesia (e.g., Chao & Knight, 1995; Drachman & Arbit, 1966; Hopkins, Kesner, & Goldstein, 1995; Janowsky, Shimamura, Kritchevsky, & Squire, 1989; Shoqeirat, Mayes, MacDonald, Meudell, & Pickering, 1990). In one particularly telling study, participants with frontal lobe damage (an etiology usually agreed to cause attentional impairments) were impaired at an extradimensional shift, which required shifting attention to a previously irrelevant stimulus dimension, whereas participants with combined lesion to amygdala and hippocampus were unimpaired in their ability to perform the shift (Owen, Roberts, Polkey, Sahakian, & Robbins, 1991).

In the absence of more sensitive tests, there is little neuropsychological evidence to suggest that amnesic participants have specific attentional deficits of the kind seen in schizophrenia. This, in conjunction with a context shift that minimizes representational processing, could account for the preserved latent inhibition shown by the amnesic participants in Experiment 2. Possibly, a different latent inhibition paradigm that emphasizes representational processes but not attentional processes might be more sensitive to hippocampal-region damage. This possibility remains to be more fully explored.

Given the existence of previous studies showing that individuals with various attentional deficits do not show latent inhibition using the paradigm of Experiment 2, it would be interesting to try the converse experiment: testing schizophrenic participants on the learned irrelevance paradigm of Experiment 1. If our argument that this task emphasizes representational but not attentional processes is valid, then schizophrenic participants might show preserved learned irrelevance, in contrast to their disrupted latent inhibition. If so, these two paradigms could provide a double dissociation between the two patient populations. Again, this would not imply that learned irrelevance per se was disrupted or spared in amnesic or schizophrenic participants, but rather that specific latent learning paradigms that tap primarily representational processes are especially vulnerable in MT amnesia, whereas paradigms that tap primarily attentional processes are more vulnerable in schizophrenia. A further complication is the existence of hippocampal pathology in schizophrenia, which might mean that schizophrenic participants were prone to disruptions in both attentional and representational processing.

A related question is whether the kind of attentional–representational dissociation demonstrated here can be shown using other paradigms. One paradigm that may prove fruitful is the negative priming effect. *Negative priming* refers to the phenomenon of slower responding to a stimulus that has been ignored on a previous trial. For example, on each trial the participant might see a green letter and a red letter superimposed and be required to name the red letter; response times will be slower if the current red target letter was the (ignored) green distractor letter on the previous trial (Tipper, 1985). Negative priming shares many features with latent inhibition and learned irrelevance, most notably the ability of a previously ignored stimulus to interfere with current processing. In fact, Graham and McLaren (in press) have argued that many studies that claim to demonstrate latent inhibition in humans are actually demonstrating negative priming. Interestingly, recent evidence indicates that there may be at least two processes underlying the negative priming effect—an attentional (inhibitory) process and a representational (memorial) process (May, Kane, & Hasher, 1995; Fox, 1995)—and that these two processes can be manipulated independently. Some studies have suggested that schizophrenic individuals show representational but not attentional negative priming (May et al., 1995). This seems parallel to our suggestion that schizophrenic individuals show representational but not attentional processing in associative learning. Therefore, we would expect that individuals with MT amnesia would show attentional but not representational negative priming. Although this prediction remains to be tested explicitly, there is some evidence from individuals with Alzheimer's disease (AD), a progressive degenerative disease that in its early stages is associated with dysfunction and atrophy of the hippocampus and nearby MT structures (de Leon et al., 1997; Winblad, Hardy, Backman, & Nilsson, 1985). Participants with AD, given a negative priming task that may encourage representational processing (May et al., 1995), showed no negative priming (Sullivan, Faust, & Balota, 1995). Thus, it seems plausible that the same deficits in episodic memory that lead to impairments in AD and in MT amnesia may be reflected in similarly disrupted performance on representational components of negative priming and learned irrelevance.

One advantage of the learned irrelevance paradigm is that it tends to produce very robust effects, both in magnitude and in insensitivity to parametric changes (Baker & Mackintosh, 1979; Matzel et al., 1988; Overmier & Wielkiewicz, 1983); this is valuable when considering patient studies that typically have small population size and hence high variability. Additionally, disrupted learned irrelevance leads to faster Phase 2 learning; therefore, individuals with MT amnesia may perform better than control participants in the exposed condition (see Figure 2B). In sum, learned irrelevance may be a valuable tool for studying and assessing representational impairments in MT amnesia and other etiologies. Further work is needed to confirm our hypothesis of dissociable representational and attentional processes in latent learning, but the converging evidence from studies of individuals with schizophrenia or amnesia provides hope that such a dissociation is possible.

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Received December 21, 1998
Revision received July 6, 1999
Accepted July 7, 1999 ■