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The contribution of familiarity to associative memory in amnesia

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Abstract

In Experiment 1, using the remember/know paradigm with control participants, we compared the contribution of recollection and familiarity to associative recognition for compound stimuli and for unrelated word pairs. It was demonstrated that familiarity makes a greater contribution to associative recognition of compound stimuli than to associative recognition of unrelated word pairs. In Experiment 2, we examined associative recognition memory in medial temporal lobe amnesics, diencephalic amnesics, and control participants for the stimuli employed in Experiment 1. Whereas associative recognition for compounds and unrelated words was nearly identical in control participants, associative recognition was higher for compounds than for unrelated word pairs in amnesic patients. This pattern was observed in the medial temporal amnesic group as well as in the diencephalic amnesic group. These results suggest that associative recognition in amnesia is enhanced to the extent that performance can be supported by study-induced familiarity for the studied pair.

Keywords: Associative memory; Recognition; Amnesia; Recollection; Familiarity; Hippocampus; Medial temporal lobe; Diencephalon

1. Introduction

Patients with global amnesia evidence a dense impairment in the conscious retrieval of recently experienced events. This deficit is revealed on explicit tasks of memory, which ask patients to intentionally retrieve recent experiences in the form of recall or recognition. To date, the majority of studies investigating explicit memory in amnesia have focused largely on patients' item memory (i.e., the form of memory that provides the basis for remembering that a stimulus or event has been encountered). Only recently have investigators extended the study of explicit memory in amnesia from item memory to associative memory (i.e., the form of memory that represents relationships among items or informational elements). This extension has been motivated by the view that the hippocampus – a structure typically damaged in patients with medial-temporal lobe (MTL) amnesia – plays a special role in relating or binding together different components of a learning event (Eichenbaum, Alvarez, & Ramus, 2000; Fried, MacDonald, & Wilson, 1997; Giovanello, Schnyer, & Verfaellie, 2004; Henke, Buck, Weber, & Wieser, 1997; Mitchell, Johnson, Raye, & D'Esposito, 2000; Yonelinas, Hopfinger, Buonocore, Kroll, & Baynes, 2001b). By this view, patients with hippocampal lesions should be more impaired in associative memory than in item memory.

To test this prediction, Stark, Bayley, and Squire (2002) equated item recognition between hippocampal patients and control participants and then examined whether associative recognition was matched as well. When item recognition was equated between groups by providing hippocampal patients with eight study exposures, no impairment in associative recognition was observed for the patient group. However, patients' item recognition appeared to be limited by ceiling effects, possibly masking a disproportionate impairment in associative recognition in the patients. When ceiling effects are avoided, a disproportionate deficit in associative memory does seem to be apparent: Turriziani, Fadda, Caltagirone, and Carlesimo (2004) demonstrated that associative recognition was impaired in a group of MTL patients, some of whom had damage limited to the hippocampus, even when item recognition was matched.

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We obtained similar results in a mixed group of MTL patients (Giovanello, Verfaellie, & Keane, 2003).

Although a disproportionate deficit in associative, relative to item, recognition in hippocampal patients is consistent with the view that the hippocampus plays a critical role in binding, such findings may alternatively be understood with reference to the notion that item and associative memory differentially draw on distinct cognitive processes. Studies in normal participants demonstrate that recognition memory for item and associative information have different rates of forgetting (Hockley, 1992), have different time courses of retrieval (Gronlund & Ratcliff, 1989), are differentially affected by word frequency (Clark, 1992), and have different receiver operating characteristics (Yonelinas, 1997). Many of these differences have been interpreted to reflect the differential contribution of recollection (i.e., intentional retrieval) and familiarity (i.e., the feeling that an item was previously encountered because of its ease of processing) to associative compared to item recognition. Direct support for this interpretation comes from a study by Hockley and Consoli (1999) who, using the remember/know paradigm (Tulving, 1985), demonstrated that associative recognition is based on conscious recollection to a greater extent than is item recognition, and conversely, that item recognition is based on familiarity to a greater extent than is associative recognition. Thus, a deficit in associative recognition in hippocampal amnesia may be a manifestation of a deficit in recollection-based memory.

The notion that hippocampal lesions may interfere with associative recognition because of the demands of such tasks on recollection, accords well with the proposal by Aggleton and Brown (1999) that recollection is mediated by the hippocampus, while familiarity is supported by perirhinal cortex. However, we found associative memory was also disproportionately impaired in patients with large MTL lesions—lesions encompassing both the hippocampus and surrounding cortical areas (Giovanello et al., 2003). Aggleton and Brown's model predicts that such patients should have impairments in both recollection and familiarity, as indeed has been shown (Verfaellie & Treadwell, 1993; Yonelinas, Kroll, Dobbins, Lazzara, & Knight, 1998). However, these studies have also found that recollection is more severely affected than familiarity in such patients. Such a pattern may arise because the perirhinal cortex provides two-thirds of the input to the hippocampus. Extensive lesions including perirhinal cortex will disrupt familiarity-based processing, but recollection-based processing may be more severely impaired because it will be affected directly by hippocampal damage, as well as indirectly by virtue of the fact that the hippocampus will be receiving degraded information from the damaged perirhinal cortex (see Norman & O'Reilly, 2003 for a similar argument). Thus, a disproportionate impairment in recollection compared to familiarity in patients with large MTL lesions is consistent with Aggleton and Brown's model (1999), and may form the basis of the disproportionate impairment in associative relative to item memory in these patients, as well as in patients with restricted hippocampal lesions.

If amnesic patients' impairment in associative memory is due to the higher demands placed on recollection than on familiarity, then it follows that amnesic patients should be less impaired when associative memory can be supported by familiarity. Familiarity-based associative memory may be promoted by requiring participants to process stimulus configurations integratively, as integrative processing enhances the internal organization of a stimulus, which in turn mediates familiarity (Mandler, Graf, & Kraft, 1986). Empirical evidence that integrative processing can lead to familiarity-based associative recognition comes from a study by Yonelinas and colleagues (Yonelinas, Kroll, Dobbins, & Soltani, 1999) who examined memory for facial stimuli—stimuli that consist of configurations of stimulus elements. They examined participants' ability to discriminate between previously studied faces and recombined faces (which were created by rearranging features of studied faces) presented either in upright or in upside down positions. For face presented upright, which are typically encoded as an integrated unit, familiarity made a significant contribution to performance. In contrast, for faces presented upside down, which are not typically encoded as a coherent whole, the contribution of familiarity was greatly reduced. Thus, familiarity can contribute to recognition of associations that are meaningfully integrated.

The goal of the current study was to create conditions in which familiarity contributes to recognition of verbal associations and to examine whether amnesic patients' associative memory impairment is attenuated under these conditions. To promote familiarity-based associative memory, the current study employed compound stimuli (e.g., "pinpoint"). Compounds are unique, having both integrative features (e.g., idiosyncratic meanings not completely predicted by the meanings of the constituent words), as well as some preservation of the distinct constituent components (e.g., as evidenced by increased false alarm rates to novel compounds consisting of studied components not previously seen together). Thus, compound words are uniquely suited to create conditions in which familiarity contributes to associative recognition.

To date, several studies investigating associative memory in amnesic patients have employed compound stimuli such as compound words (Reinitz, Verfaellie, & Milberg, 1996), bisyllabic words (Kroll, Knight, Metcalfe, Wolf, & Tulving, 1996; Stark & Squire, 2003), and nonword compounds (Stark & Squire, 2003). However, the goal of these studies was to address the relative impairment in associative as compared to item recognition in patients with amnesia, rather than to compare performance across different types of verbal associations. In the one study that used a variety of verbal associative stimuli (Stark & Squire, 2003) such a comparison is made difficult by floor effects in several conditions. Therefore, it remains unclear whether amnesic patients' associative recognition performance is less impaired for meaningfully integrated material (i.e., material for which familiarity may contribute to performance), as compared to non-integrated material (i.e., material for which familiarity contributes minimally to performance). Such a finding would provide evidence that when associative recognition is supported by familiarity, amnesic patients' performance can be enhanced.

To evaluate this possibility, we compared the contribution of recollection and familiarity to associative recognition of compound stimuli and unrelated word pairs in individuals with intact memory (Experiment 1) and then examined amnesic patients' associative recognition performance under the two stimulus conditions (Experiment 2). In addition to patients with MTL lesions, we also evaluated the performance of amnesic patients with diencephalic damage. Because there is evidence for structural (Jernigan, Shafer, Butters, & Cermak, 1991; Visser et al., 1999) and/or functional (Caulo et al., 2005; Fazio et al., 1992; Heiss, Pawlik, Holthoff, Kessler, & Szelies, 1992; Reed et al., 2003) disruption of MTL in diencephalic patients, we predicted that both for MTL and for diencephalic amnesic patients associative recognition would be higher for compound stimuli than for unrelated word pairs due to the greater contribution of familiarity to the former than to the latter.

2. Experiment 1

The aim of Experiment 1 was to examine the contribution of recollection and familiarity to associative recognition for stimuli that were meaningfully integrated pre-experimentally (compound words) and for stimuli that were not (unrelated word pairs). We hypothesized that familiarity may contribute to a greater extent to associative recognition for compound stimuli than to associative recognition for unrelated word pairs. This hypothesis arose from Yonelinas et al. (1999) finding that, in the nonverbal domain, when stimuli are encoded as a whole, familiarity makes a larger contribution to associative judgments, whereas when stimuli are encoded as a set of features, the contribution of familiarity is greatly reduced.

Participants studied unrelated word pairs (e.g., surgeon-arrow; telephone-trumpet; towel-wrapper) or compound words (e.g., landscape; blackmail; jailbird) and subsequently discriminated between "old" (i.e., surgeon-arrow) and "recombined" (i.e., telephone-wrapper) word pairs or "old" (i.e., landscape) and "recombined" (i.e., blackbird) compound stimuli. To obtain measures of recollection and familiarity, we asked participants to give "remember" (R) and "know" (K) judgments (Gardiner, 1988; Mandler, 1980; Tulving, 1985). R responses provide a relatively accurate measure of recollection because participants are likely to say "remember" if they experience recollection, regardless of whether recollection is also accompanied by a feeling of familiarity. However, because R and K responses are mutually exclusive, K responses alone underestimate familiarity because they do not capture the familiarity that is experienced on "remember" trials. As a consequence, K responses provide an estimate of familiarity in the absence of recollection. To obtain a more accurate measure of familiarity, we used the independent remember/know (IRK) procedure (Jacoby, Yonelinas, & Jennings, 1997; Yonelinas et al., 1998) in which the proportion of K responses is divided by the proportion of items that were not assigned R.

2.1. Method

2.1.1. Subjects

Ten individuals (two men and eight women) without a history of alcoholism and eight individuals (five men and three women) with a history of alcoholism participated in the experiment. Individuals without a history of alcoholism were similar in age ($M = 58.0$), education ($M = 15.2$), and Wechsler Adult Intelligence Scale (WAIS-III) verbal IQ ($M = 109.5$) to the amnesic patients with nonalcoholic etiologies tested in Experiment 2. Individuals with a history of alcoholism were similar in age ($M = 64.8$), education ($M = 13.8$), and WAIS-III verbal IQ ($M = 104.0$) to the Korsakoff patients tested in Experiment 2. Participants with a history of alcoholism had abstained from drinking for at least 3 months prior to participation in the experiment. Informed consent was obtained in a manner approved by the institutional review boards at Boston University and the Boston VA Healthcare System.

2.1.2. Materials

The stimuli were compound words and unrelated word pairs. Compound stimuli and unrelated stimuli consisted of 24 triplets that were divided into two sets for purposes of counterbalancing across "old" and "recombined" conditions. Each triplet consisted of two compounds words (e.g., pinwheel, needlepoint) or two unrelated word pairs (e.g., wheat-war, salad-business) and a third compound word or pair that was a recombination of the other two stimuli (e.g., pinpoint or wheat-business). This third stimulus was designated the stimulus to appear in the test phase. A study list consisted of 36 stimuli, 12 "old" stimuli and 24 stimuli whose components contributed to 12 "recombined" stimuli in the test phase. A test list consisted of 24 stimuli, 12 "old" stimuli and 12 "recombined" stimuli. The mean frequency for the compound segments and unrelated words was 179.4 and 178.7, respectively (Francis & Kucera, 1982). Assignment of sets to the "old" and "recombined" conditions was counterbalanced across subjects both for compound and for unrelated stimuli.

2.1.3. Procedure

The participants were tested in two sessions separated by 1 week. Half of the participants received the compound stimuli and the other half received the unrelated stimuli during the first session.

During the study phase, participants viewed either compound words or unrelated word pairs on a computer screen. A blank space appeared on the screen between members of unrelated word pairs or between segments of compound words. As the stimuli were presented, the experimenter read a sentence aloud that incorporated either the two words of the pair or the compound word. For each sentence participants were instructed to rate on a scale from 1 to 5 the likelihood of occurrence of the information conveyed in the sentence. A card containing the likelihood values was placed in front of the participants throughout the study phase. Stimuli remained on the computer screen until a likelihood judgment was provided. There was a 10 min delay between the study phase and the test phase.

During the test phase, participants made yes/no recognition judgments on each of 24 trials for compound or unrelated stimuli. A blank space appeared on the screen between members of unrelated word pairs or between segments of compound words. Participants were instructed to say "old pair" if the two words had appeared together on the study list or to say "new pair" if the two words had not appeared together on the study list. Remember and know responses were collected for each endorsed pair to assess the contribution of recollection and familiarity, respectively (Gardiner & Parkin, 1990). The participants were instructed to respond "remember" if they specifically recollected seeing the words as a pair. For instance, because the words evoked a particular thought or impression or because they remembered how the words appeared on the screen. Participants were instructed to respond "know" if they had a clear sense that the words appeared as a pair, knew somehow that the pair felt familiar, but they did not remember any specifics. The instructions remained visible throughout the test phase.

2.2. Results and discussion

Because there were no differences between subgroups as a function of alcohol history, the data were combined into a single group.

Table 1 presents the proportion of studied and unstudied stimuli endorsed as "old" as a function of stimulus type (i.e., unrelated or compound). The results show that overall recognition was similar for unrelated pairs and compound stimuli. There

Table 1
Overall endorsement rates for unrelated word pairs and compound stimuli are broken down into R and K response

	Overall/R	IRK
Unrelated		
Studied	.82 (.12)/.75 (.19)	.22 (.25)
Unstudied	.15 (.20)/.06 (.11)	.11 (.19)
d′	1.99 (.90)	.27 (1.18)
Compound		
Studied	.83 (.13)/.69 (.19)	.47 (.31)
Unstudied	.24 (.22)/.11 (.12)	.16 (.17)
d′	1.78 (.67)	1.10 (.86)

R responses provide a measure of recollection. Familiarity estimates are based on IRK scores (K/1−R) and provide a measure of familiarity-based recognition. Standard deviations are indicated between parentheses.

was no difference in hit rates, in false alarm rates, or in corrected accuracy (hits-false alarms) between unrelated word pairs and compound words, all t's < 1.60. The same pattern of results was evident in R-responses for hits, for false alarms, and for corrected accuracy (hits-false alarms), all t's < 1.63. As an estimate of the contribution of familiarity to associative recognition, IRK values were calculated for compound stimuli and unrelated word pairs (Jacoby et al., 1997; Yonelinas et al., 1998). As can be seen in Table 1, familiarity made a greater contribution to associative recognition of compound stimuli than to associative recognition of unrelated word pairs. Although there was no difference in IRK false alarm rates for the two stimulus types [$t(17) < 1$], there was a significant difference in IRK hits [$t(17) = 3.22$, $p < .01$] and in IRK accuracy (hits-false alarms) [$t(17) = 2.69$, $p < .05$], with familiarity making a greater contribution to associative recognition of compound stimuli than to associative recognition of unrelated stimuli.

Analysis of discriminability scores for overall recognition measured by d' indicated no difference between unrelated ($M = 1.99$) and compound ($M = 1.78$) [$t(17) < 1$] stimuli. Discriminability scores were not computed for R-responses, assumed to reflect recollection, because recollection is thought to be an all-or-none process that is not influenced by variations in response bias (Gardiner & Gregg, 1997; Yonelinas, 2001a). Analysis of d’ scores derived from IRK data revealed a significant difference between unrelated ($M = .27$) and compound stimuli ($M = 1.10$) [$t(17) = 3.10$, $p < .01$], indicating that familiarity-based discriminability was greater for compounds than for unrelated word pairs. Taken together, these findings suggest that familiarity (as measured by IRK), can support associative recognition more so for stimuli that are meaningfully integrated pre-experimentally than for stimuli that are encoded as a set of features.

3. Experiment 2

The aim of Experiment 2 was to examine whether associative recognition performance would be significantly better for compound stimuli than for unrelated stimuli in amnesic patients with MTL or diencephalic lesions. If the deficit in associative memory in amnesia is due in part to the fact that associative memory typically depends on recollection, then patients’ performance should be less impaired under conditions in which associative memory can be supported by familiarity for the association, as is the case for compounds. Alternatively, if the associative memory deficit occurs regardless of the mechanism that supports recognition, than patients’ associative recognition performance should be equally impaired for compound stimuli and for unrelated stimuli.

3.1. Method

3.1.1. Subjects

Sixteen amnesic patients (12 men and four women) participated in the experiment, of whom nine had MTL lesions and seven had diencephalic lesions. In the MTL group, six patients had an etiology of anoxia and three of encephalitis. In the diencephalic group, six patients had an etiology of alcoholic Korsakoff’s syndrome and one had suffered a bithalamic stroke. Visual inspection of MRI scans for patients in the MTL group suggested that damage was restricted to the hippocampal formation in four anoxic patients.[1] The remaining MTL patients had lesions that extended beyond the hippocampus to include the surrounding cortices (i.e., entorhinal, perirhinal, and parahippocampal cortex).

Nine individuals (four men and five women) without a history of alcoholism served as control participants for the MTL amnesics. Seven men with a history of alcoholism and one woman without a history of alcoholism served as the control participants for the diencephalic patients. There were no differences between the MTL and diencephalic amnesic groups and their respective control groups in terms of age t's ≤ 1.7, education t's ≤ 1, or WAIS-III verbal IQ t's ≤ 1.3, p's > .05. None of the control participants in Experiment 2 had participated in Experiment 1.

3.1.2. Materials

The stimuli were identical to those used in Experiment 1.

3.1.3. Procedure

The procedure was identical to that of Experiment 1, except that “remember” and “know” judgments were not collected. In brief, participants were tested in two sessions separated by 1 week. Half of the participants received the compound stimuli and the other half received the unrelated stimuli during the first session. During the study phase, participants viewed either compound words or unrelated word pairs on a computer screen. As the stimuli were presented, the experimenter read a sentence aloud that incorporated either the two words of the pair or the compound word. For each sentence participants were instructed to rate on a scale from 1 to 5 the likelihood of occurrence of the information conveyed in the sentence. There was a 10 min delay between the study phase and the test phase, during which the experimenter conversed with the participant. During the test phase, participants made yes/no recognition

[1] For one patient, only a CT scan was available.

Table 2
Summary of neuropsychological characteristics of medial temporal (MTL) and diencephalic (DNC) patients and control subjects in Experiment 2

	Patient etiology	WAIS-III			WMS-III			
		Age	Ed	VIQ	GM	AD	VD	WM
MTL01	Anoxia	65	20	111	52	64	56	83
MTL02	Anoxia	73	18	122	75	80	72	102
MTL03	Anoxia	52	12	82	52	55	56	91
MTL04	Anoxia	24	10	92	45	58	50	81
MTL05	Anoxia	44	14	90	45	52	53	93
MTL06	Anoxia	46	14	111	59	52	72	96
MTL07	Encephalitis	59	12	106	69	77	68	111
MTL08	Encephalitis	47	14	93	45	55	56	85
MTL09	Encephalitis	74	18	135	45	58	53	141
DNC01	Korsakoff	76	14	99	59	58	65	115
DNC02	Korsakoff	82	14	105	66	64	62	121
DNC03	Korsakoff	57	12	97	66	74	62	108
DNC04	Korsakoff	84	9	100	72	74	75	91
DNC05	Korsakoff	52	18	111	69	64	72	81
DNC06	Korsakoff	78	14	103	72	71	68	115
DNC07	Bithalamic stroke	61	12	84	73	67	84	99
Controls mean	($N = 17$)	59.0	14.9	109.0				

Note. AM: amnesic patient; ED: education; WAIS-III: wechsler adult intelligence scale—third edition; VIQ: verbal IQ; WMS—III: wechsler memory scale—third edition; GM: general memory; AD: auditory delay; VD: visual delay; WM: working memory.

judgments on each of 24 trials for compound or unrelated stimuli (Table 2).

3.2. Results and discussion

The proportion of old responses given by the two amnesic groups and their corresponding control groups to compound stimuli and unrelated word pairs is shown in Table 3. Hits and false alarms, as well as corrected recognition scores, were analyzed separately in 2 (group: control, amnesic) × 2 (etiology: MTL/diencephalic) × 2 (stimulus type: unrelated pairs/compounds) ANOVAs. An analysis of hit rates revealed a significant main effect of group [$F(1,29) = 15.41$, $p < .01$], indicating a higher hit rate in control subjects than in amnesic participants. There was also a main effect of stimulus type [$F(1,29) = 15.68$, $p < .01$], indicating that compound words were endorsed at a higher level than unrelated word pairs. No other main effects or interactions were significant.

Table 3
Proportion of studied (hit) and unstudied (false alarm) unrelated word pairs and compound stimuli endorsed as old, and d' scores, in Experiment 2

	Overall recognition			
	Amnesics		Controls	
	MTL	Diencephalic	MTL	Diencephalic
Unrelated				
Studied	.45 (.29)	.45 (.33)	.76 (.16)	.72 (.14)
Unstudied	.32 (.14)	.27 (.18)	.11 (.16)	.17 (.18)
d'	.26 (1.03)	.46 (.49)	1.95 (.76)	1.64 (1.06)
Compound				
Studied	.66 (.19)	.74 (.11)	.85 (.12)	.84 (.07)
Unstudied	.36 (.19)	.43 (.21)	.23 (.22)	.29 (.24)
d'	.80 (.75)	.86 (.73)	1.85 (1.00)	1.62 (.55)

Standard deviations are indicated between parentheses.

An analysis of false alarm rates revealed a significant main effect of group [$F(1,29) = 6.64$, $p < .05$], indicating higher false alarms in the amnesic than in the control group. There was also a main effect of stimulus type [$F(1,29) = 9.90$, $p < .01$], indicating higher false alarms to compounds than to unrelated word pairs. No other effects were significant.

An analysis of corrected recognition scores (hits-false alarms) revealed a significant main effect of group [$F(1,29) = 20.59$, $p < .01$], reflecting lower accuracy in the amnesic than in the control group. There was also a marginal group × stimulus type interaction [$F(1,31) = 4.05$, $p = .066$]. Follow up *t*-tests indicated that amnesic participants [$t(15) = 2.48$, $p < .05$], but not controls [$t(16) < 1$], showed higher accuracy for compound stimuli than for unrelated word pairs. No other effects were significant. Notably, the group × etiology × stimulus type interaction was not significant ($F < 1$), indicating that the pattern of results was similar in the two amnesic groups.

The same pattern of results was obtained using discriminability scores. An ANOVA on d' scores revealed a significant main effect of group [$F(1,29) = 21.31$, $p < .01$] and a marginal group × stimulus type interaction [$F(1,29) = 3.53$, $p = .070$]. Again, amnesic participants [$t(15) = 2.63$, $p < .05$], but not controls [$t(16) < 1$], showed higher accuracy for compounds than for unrelated word pairs.

Within the MTL group, we further compared the magnitude of the associative recognition advantage for compound stimuli in patients with lesions restricted to the hippocampal formation and patients with larger MTL lesions. To do so, we calculated for each patient the difference in performance in the unrelated condition and the compound condition. This measure represented the percent improvement in the compound condition. Patients with restricted hippocampal lesions showed a numerically greater improvement (mean = 27%) than did patients with extensive MTL lesions (mean = 9%), but this difference was not statistically significant ($t < 1$). This may well represent a lack of power associated with the small number of patients in each subgroup.

4. General discussion

In two experiments, we examined whether familiarity makes a greater contribution to recognition of verbal stimuli that are meaningfully integrated pre-experimentally than to verbal stimuli that are not integrated pre-experimentally, and if so, whether patients' associative memory is enhanced in the former condition. In Experiment 1, we compared the contribution of recollection and familiarity to associative recognition for compound stimuli and for unrelated word pairs. The results showed that familiarity makes a greater contribution to associative recognition of compound stimuli than to associative recognition of unrelated word pairs. In Experiment 2, we examined associative recognition memory for the stimuli employed in Experiment 1 in amnesic participants with MTL or diencephalic lesions. Associative recognition in the amnesic group was higher for compound stimuli than for unrelated word pairs, whereas there was no difference in the performance of the control group. These results suggest that familiarity of stimulus compounds boosted associative recognition in amnesic participants beyond the level observed for unrelated word pairs. This finding was evident both in the performance of the MTL group and the diencephalic group, and adds to a growing body of findings suggesting qualitatively similar deficits in the two groups (O'Connor & Verfaellie, 2002).

For compound stimuli, as for unrelated word pairs, accurate performance required discrimination between an association that was formed (or reinforced) during the study phase and one that was not. The enhanced familiarity induced by studying compounds led amnesic participants to discriminate more effectively between studied and recombined compounds than between studied and recombined word pairs. This may have been due to the fact that those stimuli were already integrated pre-experimentally. Such integration, like that for upright faces (Yonelinas et al., 1999), may provide ideal conditions for study-induced familiarity to operate in an associative memory task.

In principle, the study-induced familiarity unique to compounds could be either perceptually or conceptually based. Perceptually based familiarity arises from the repetition at study and test of the same orthographic pattern, allowing for more fluent processing upon repetition. Such familiarity may be enhanced for compound words in comparison to unrelated stimuli because compounds have a pre-existing orthographic representation that supports study-induced familiarity. This possibility is somewhat weakened by the fact that compound words were presented in a non-canonical form (i.e. with a space between the two components). Such disruption, however, may only minimally affect access to the orthographic representation, and may not preclude a perceptually based familiarity effect. The nature of such perceptually based familiarity is not well understood, and whether it shares a common basis with perceptual priming is a matter of continuing debate (Keane, Orlando, & Verfaellie, 2006; Stark & Squire, 2000; Conroy, Hopkins, & Squire, 2005). Nonetheless, the fact that perceptual priming of novel associations is spared in amnesia (Gabrieli, Keane, Zarella, & Poldrack, 1997; Goshen-Gottstein, Moscovitch, & Melo, 2000) leaves open the possibility that perceptual associative priming contributes to familiarity-based associative recognition in amnesia.

Another possibility is that the study-induced familiarity associated with compound stimuli is conceptually based, and reflects the enhanced fluency with which the meaning of study pairs is processed upon repetition. Such familiarity may be enhanced for compound words compared to unrelated word pairs because of the pre-existing conceptual integration of the components of compounds. Although the nature of conceptual familiarity and its relationship to conceptual priming remains unclear (Verfaellie and Keane, 2003), it is possible that the study-induced familiarity that supports recognition of compounds is based in conceptual priming. A similar suggestion has been made to account for amnesic patients' surprisingly good paired associate learning of related word pairs (Cutting, 1978; Shimamura & Squire, 1984; Winocur & Weiskrantz, 1976), but other evidence is inconsistent with this view (Levy, Stark, & Squire, 2004).

Finally, our findings also give rise to several neuroanatomical considerations. First, the recognition advantage for compound stimuli was numerically greater in MTL patients with lesions limited to the hippocampus than in those with larger lesions. This finding suggests that patients with restricted hippocampal lesions were better able to take advantage of the study-induced familiarity associated with compound stimuli than were patients whose lesions encroach on perirhinal cortex. Such a finding can be understood with reference to the notion that familiarity is mediated by perirhinal cortex (Aggleton & Brown, 1999), as this structure is intact in patients with limited hippocampal lesions. Second, our results suggest that the hippocampus is not equally involved in all forms of relational memory. In particular, we have demonstrated that when stimuli are meaningfully integrated, such that familiarity-based processes can support recognition, the associative memory deficit associated with hippocampal lesions is attenuated. It remains to be seen whether there are manipulations other than those involving the nature of task stimuli that may influence the dependence of associative memory on the hippocampus.

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