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Effect of Unitization on Associative Recognition in Amnesia

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ABSTRACT: We examined how associative recognition performance in amnesic patients is mediated by use of a unitized (i.e., holistic) encoding strategy, and the degree to which the unitization effect is related to sparing of familiarity-based recognition. Participants studied word pairs as either separate lexical units in sentences (i.e., nonunitized) or as compounds (unitized). Under standard recognition instructions, normal controls and patients with left-temporal lobe damage (previously determined to have impairments in both recollection and familiarity) showed no difference for unitized and nonunitized pairs, whereas hypoxics (previously determined to have impaired recollection but relatively preserved familiarity) showed an advantage of unitized over nonunitized pairs. This effect was reproduced in normal healthy participants under instructions to restrict responses to judgments of familiarity. The results indicate that unitization may mediate the degree of associative recognition impairment exhibited by some amnesic patients, and that the effect is related to preserved familiarity capacity. The relevance of the results to the debate over the importance of the hippocampus in memory for associations is discussed. © 2007 Wiley-Liss, Inc.

KEY WORDS: associative memory; medial temporal lobes; hypoxia; familiarity; recollection

INTRODUCTION

An influential view of medial-temporal lobe amnesia is that damage to the hippocampus results in a deficit that is fundamentally *relational* in nature (Eichenbaum et al., 1994; Cohen et al., 1997; Eichenbaum and Cohen, 2001). According to this view, the hippocampus is critical for forming representations of the episodic relations *between* separable items and features of a study event, whereas the surrounding cortical regions are important for forming representations that "fuse" conjunctions of features *within* an item into a unified whole. As such, amnesics with hippocampal damage should be impaired on a test of memory to the extent that it relies on recovering relational representations that link the items and contextual features of a study event, but they should be unimpaired (or at least less-impaired) to the extent that performance can be supported by the strength of holistic representations of the items themselves.

The distinction between item and relational forms of memory is especially relevant to tests of item and associative recognition. In tests of item recognition, individuals are asked to distinguish single items (e.g., words, faces, pictures) that were previously encountered from single items that were not encountered (i.e., did this item occur before). In tests of associative recognition, participants are presented with two or more items at a time and are asked to distinguish pairings of items that occurred *together* previously (e.g., intact pairs) from pairings of items that did not occur together previously (e.g., recombined pairs). The critical distinction between item and associative recognition is that the prior occurrence of an individual item is diagnostic for item recognition but not for associative recognition. In associative recognition, all individual items that make up intact and recombined pairs occurred previously. Thus, memory for individual items does not distinguish intact pairs from recombined pairs; one must retrieve information about the co-occurrence of items to perform the task.

A basic prediction of the relational view is that amnesic patients with relatively limited hippocampal damage should be more impaired on tests of associative recognition than on tests of item recognition. This prediction has been supported by some studies (e.g., Giovanello et al., 2003; Turriziani et al., 2004), whereas others have revealed comparable deficits on associative and item tests (Stark et al., 2002; Stark and Squire, 2003). Additionally, patients with damage limited to the hippocampus sometimes show spared associative recognition for pairings of the same type of item (e.g., word-word, face-face), but impaired associative recognition for pairing of different types of items (e.g., word-face, face-voice; Vargha-Khadem et al., 1997; Mayes et al., 2004). To some extent, the inconsistency of results across studies can be explained by the use of different patient groups and different experimental materials. However, the range of associative recognition deficits in amnesia appears to be more variable than is expected by a simple relational account alone. A more nuanced consideration of cognitive and strategic factors mediating amnesics' performance on associative recognition tasks may be warranted.

At a more detailed level, associative and item recognition can be understood as relying differentially on recollection of episodic details and feelings of familiarity (e.g., Yonelinas, 2002). Recollection involves retrieval of qualitative details about a study event whereas familiarity judgments involve assessments of undifferentiated memory strength of a presented stimulus. In studies where recollection and familiarity have been measured directly, both familiarity and recollection contribute to item recognition (e.g., Gardiner and Java, 1990; Jacoby,

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1991; Yonelinas, 1994) whereas associative recognition relies primarily on recollection (Yonelinas, 1997; Hockley and Consoli, 1999). Most behavioral studies comparing item and associative recognition have compared words to word pairs. A generally accepted interpretation of this effect is that familiarity is relatively item-specific, tending to operate only on well-integrated units of information such as single words, which are processed with a high degree of coherence and internal integration due to their extensive pre-experimental exposure. Associative recognition is often assessed for novel pairings of items (e.g., arbitrarily paired words) that lack a comparably coherent level of integration; thus, the familiarity of a pairing is driven largely by the individual familiarities of its component words. Because intact and recombined pairings both contain items that were studied, they should (on average) be equally familiar.

However, there are indications that familiarity may be involved in associative recognition when elements of the association are processed as a single integrated unit or *unitized* (e.g., Graf and Schacter, 1989) as opposed to being processed as a relation among separable elements. Yonelinas et al. (1999) had individuals distinguish between studied and nonstudied associations between internal and external features of faces, that were either presented right-side-up (processed holistically) or upside-down (processed as a collection of separable features). When faces were presented right-side-up, both recollection and familiarity contributed to performance. When faces were presented upside-down, performance was based mostly on recollection. Thus, associations between elements of well-integrated units may increase the extent to which associative recognition loads on familiarity. This observation is potentially important for understanding amnesic patients' associative recognition performance: Several studies have obtained results suggesting that familiarity-based recognition is relatively spared in some amnesic patients, particularly in cases in which limited damage to the hippocampus was confirmed or suspected (Holdstock et al., 2002; Yonelinas et al., 2002; Aggleton et al., 2005). To the extent that familiarity-based recognition is spared in a particular patient, increasing the contribution of familiarity to associative recognition (via unitized encoding) may lead to improved associative memory performance.

In keeping with this view, two recent studies have found that memory for unitized associations can be relatively preserved following hippocampal damage. In a recent study of object discrimination learning, Barense et al. (2005) found that amnesics with selective hippocampal damage performed normally in an "ambiguous feature" discrimination learning task that could only be solved by responding to particular feature *conjunctions* within an object (individual features occurred in both rewarded and unrewarded objects), whereas patients with damage extending beyond the hippocampus were impaired. Thus, the hippocampus seemed to be less important when the to-be-associated entities are parts of a coherent item. Giovanello et al. (2006) provided direct evidence that associative recognition is less impaired in amnesia for more-unitized pairs of items than for less-unitized pairings. They examined associative recognition of compound words in a conjunction paradigm (e.g., Reinitz et al., 1996) where participants studied pre-experimentally unitized compound words (e.g., landscape, blackmail, jailbird), and were asked to discriminate target pairs (e.g., landscape) from recombined conjunction lures (e.g., blackbird). Amnesics exhibited better performance on the compounds than on arbitrary word pairs (e.g., surgeon-arrow), whereas controls performed about the same on the two types of association. Giovanello et al. (2006) also found that normal participants were more likely to make judgments about compounds on the basis of familiarity than arbitrary pairs, as measured by the remember-know procedure. These results are consistent with the hypothesis, discussed above, that amnesic patients' improved performance for unitized compounds (vs. nonunitized, arbitrary word pairs) is due to familiarity contributing more to recognition of unitized (vs. nonunitized) stimuli.

In present study, we set out to directly address whether associative recognition in amnesia is mediated by encoding associations in a unitized fashion (i.e., as single items) vs. as relations between separable items. Previous studies have examined the effects of unitization resulting from strongly pre-experimentally integrated items. In the present study, all associations were arbitrarily paired words; we manipulated unitization by using study procedures that either encouraged or did not encourage encoding the pairs holistically. Thus, the level of pre-experimental integration was expected to be equally low, on average, for both unitized and nonunitized pairings. Using this approach, we tested the following predictions: If spared associative recognition in amnesia is a function of unitization and spared familiarity capacity, then amnesic patients with relatively spared familiarity (but impaired recollection) should also show better memory for unitized associations than nonunitized associations; patients with both impaired familiarity and impaired recollection should show more similar impairments in performance on unitized and nonunitized associations. Additionally, if unitized encoding functions to increase the involvement of familiarity at test, then normal healthy participants should also show an advantage for unitized associations over nonunitized associations when instructed to respond in a way that facilitates the involvement of familiarity in recognition. Experiment 1 was conducted to address the first prediction and Experiment 2 was conducted to address the second prediction.

EXPERIMENT 1

In Experiment 1, we examined the effects of unitized encoding on associative recognition in healthy controls and in patients with medial temporal lobe amnesia. Unitization was manipulated for arbitrary word pairs by encoding the pairs as compound words (the *compound encoding* condition), or by judging them separately as segregated words in a sentence (the *separate encoding* condition). To explore how unitization interacts with familiarity sparing, we looked at two patients with left medial-temporal lobe damage (left temporal lobectomy) and three patients with mild hypoxia. The two lobectomy patients and two of the three hypoxic patients participated in a previous study (Yonelinas et al., 2002) where we measured the contribution of recollection and familiarity to item recognition using a variety of methods including the Remember-Know procedure, Receiver-Operating Characteris-

tic (ROC)-modeling, and structural equation modeling. The measurement techniques indicated that the lobectomy patients showed moderate deficits in both recollection and familiarity, whereas the hypoxic patients had severe recollection deficits and near-normal levels of familiarity (Yonelinas et al., 2002). This finding of relatively spared familiarity but impaired recollection in the hypoxic patients is consistent with findings from other hypoxic patients showing severely impaired recall, but some degree of preserved item recognition (presumably based on familiarity; Vargha-Khadem et al., 1997; but see Manns et al., 2003). If unitization increases the usefulness of familiarity for associative recognition, then hypoxics, who show relatively spared familiarity and impaired recollection, should be less impaired on unitized pairs than nonunitized pairs; the lobectomy patients, who show impairments in both familiarity and recollection, should be similarly impaired on unitized and nonunitized pairs.

Participants

Amnesic patients

Five individuals with anterograde memory impairments were recruited for participation from the University of California, Davis Medical Center (UCDMC) and the Veteran's Administration Northern California Health Care System (VANCHCS). Demographic information from these patients and standardized test scores are presented in Table 1. Four of the patients participated in a previous study of recollection and familiarity in amnesia (Yonelinas et al., 2002). Two of the patients (D.S. and M.G.) had undergone left unilateral temporal lobectomy for intractable epilepsy, and magnetic resonance imaging (MRI) confirmed damage to the anterior portion of the left hippocampus as well as left perirhinal and entorhinal cortex (EC), and left parahippocampal cortex (described in Yonelinas et al., 2002). The other three patients (R.M., G.H., and E.R.) were survivors of sudden cardiac arrest. These patients could not be scanned because they had defibrillators, but were expected to have sustained bilateral damage relatively limited to the hippocampus as a result of cerebral hypoxia (Rempel-Clower et al., 1996). Although cardiac arrest can lead to a variety of different types of neuropathology (Markowitsch et al., 1997; Grubb et al., 2000) and a variety of impairments (Lim et al., 2004), none of the hypoxics in the present study exhibited impairments suggestive of extrahippocampal pathology.

All of the patients exhibit mild or moderate memory impairments, most consistently in delayed verbal recall. None showed evidence of gross executive dysfunction. All scored below the fifth percentile on either the forgetting score or overall scaled score of the Doors and People test (Baddeley et al., 1994; note R.M and G.H. appear to have normal forgetting chiefly because their immediate scores were low). The hypoxics who participated in Yonelinas et al. (2002) were shown in that study to have relatively specific recollection deficits in single-item recognition across several different measurement methods, whereas the lobectomy patients had deficits in both recollection and familiarity. E.R. was the only one who did not participate in any of our previous studies; his recollection and familiarity performance is unknown, but his neurobehavioral profile shows no evidence of being different from the other hypoxics. E.R.'s cardiac arrest occurred more recently prior to testing (14 months) compared with R.M (11 yr) and G. H. (10 yr).

Healthy controls

Two groups of healthy control participants were recruited for participation. Thirty-six undergraduates from the University of California, Davis received extra course credit for their participation, and were included as a young control group. An additional seven older controls were recruited from the greater Sacramento Metropolitan community to serve as an age- and education-matched control group for the amnesic patients. The average age ($M = 51.3$) and years of education ($M = 15.1$) were highly similar to those of the amnesic group ($M = 50.2$ and $M = 15.8$, respectively). None of the controls had a history of neurological or psychiatric disease and all scored above the 25th percentile on the on the Doors and People test.

Materials

Five hundred seventy-six four- to six-letter English nouns with medium-to high-word frequency (10–1,000 occurrences per million; Kucera and Francis, 1967) were used to construct 12 lists of 24 novel pairings each. Items in each list were paired

TABLE 1.

Demographic Information and Standardized Test Results for Amnesic Patients

						WMS-R					Doors and People	
	Sex	Age	Ed	Etiology	IQ	ATT	GEN	Log	Rep	PA	Ovr	For
R.M.	F	46	13	Hypoxia	100	96	87	−0.75	−2.04	−0.86	1	50
G.H.	M	49	16	Hypoxia	110	100	77	−2.27	−0.77	−2.43	<1	63
E.R.	M	78	18	Hypoxia	119	115	77	−1.59	−0.90	−1.21	9	<1
D.S.	M	49	16	L. Lob.	121	125	88	−0.86	0.35	−0.37	16	1
M.G.	M	29	16	L.Lob.	95	90	82	1.07	1.20	−2.29	9	2

Age, age at testing; Ed, years of education; IQ, estimate of Wechsler Intelligence scale; WMS-R, Wechsler memory scale, revised; Log, delayed logical memory; Rep, delayed visual reproduction; PA, verbal paired associate recall; Ovr, Doors and People overall percentile; For, Doors and People forgetting percentile.

randomly. Two versions of each list were made to counterbalance which pairings appeared as intact trials and which pairings appeared as recombined trials. For example, if one version contained the parings A–B, C–D, E–F, and G–H, the other version would contain A–D, C–B, E–H, and G–F. Each item appeared in only one pairing across all lists. For each participant, four lists were selected for use in two associative recognition tests (i.e., two lists were used for each test). The remaining lists were used for other unrelated tests not presented here, but all participants studied all the pairings used for these tests in a single study phase. The lists did not differ in word frequency, concreteness, imageability, number of syllables and number of letters (all $F < 1$). The two associative recognition tests were each composed of 48 items from two lists. One list was used for intact pairings (study A–B, C–D; test A–B, C–D), and the other list was used for recombined pairings (study A–B, C–D; test A–D, C–B). The two lists were then assigned to sentence and compound conditions.

For each studied pairing, a compound definition was derived for the compound encoding condition, and a simple sentence frame in which the two words fit plausibly was derived for the separated encoding condition. In all compound definitions, the pair was interpreted such that the second word was the head noun, and the first word served as a modifier. The definitions contained only synonyms or associates of the study items. For example, the compound *CLOUD-LAWN* was interpreted as a lawn used for viewing clouds, and given the definition, "A yard used for sky-gazing." The sentence frames used in the separate encoding condition were constructed with two blank spaces where the first item was intended to fit in the first space, and the second item fit into the blank space. The sentences were constructed to give noun interpretations to the list items. For example, the pair *CLOUD-LAWN* was given the sentence, "The __ could be seen from the __." All sentence frames and compound definitions were presented below the pair on the screen.

Procedure

The encoding condition (compound vs. sentence) was manipulated within-subjects with the two conditions presented in different sessions on separate days. Each study phase contained 112 word pairs presented with corresponding sentence frames or compound definitions. Four pairs were primacy and recency buffers and were not tested later. Forty-eight pairs were later used for the associative recognition test, and the remaining 60 pairs were later used in other unrelated tasks not reported here. No items appeared on more than one test. In the sentence session, participants were instructed to rate *each item in the pair separately* according to how well it fit into a corresponding blank in the sentence frame on a scale of 1 (not well at all) to 4 (very well). The first blank was always for the first word, and the second blank was always for the second word. Participants were told to pay close attention to the interpretation given to each word by the sentence context, and how this might be affected by the other word in the pair. In the compound session, participants were instructed to rate *the pair as a whole* on a 1–4 scale according to how well the definition combined the meanings of the two words into a sensible compound. They were told that the compounds did not have to refer to something familiar, but it had to be conceivable that the compound could be used in everyday communication.

After the study phase, patients and age-matched controls were given two subtests of the Doors and People test. People and Door tests were given on the first session, and Shape and Name tests were given on the second session. Each of the Doors and People sessions took 15–20 min to administer. Following the Doors and People test, there was an unrelated speeded word-identification task containing 24 intact pairs, 24 recombined pairs, and 24 new pairs. Immediately following the identification test, the associative recognition test was given containing 24 intact pairs and 24 recombined pairs from the study phase. Participants responded by rating confidence on a 1 (confident new recombined pair) to 6 (confident old intact pair) scale. The delay between end of the study phase and the beginning of the recognition test was ~30 min for each session.

Results and Discussion

Confidence ratings were used to obtain multiple pairs of hits and false alarms at different levels of response bias, and these response rates were used to construct ROC curves for performance in each condition. The most conservative level was the proportion of items given a rating of "6." The next most conservative level was the proportion of items given either a "5" or a "6." By cumulating across successive confidence points in this manner, five increasing pairs of hit and false alarm frequencies were obtained from six levels of confidence that corresponded to increasingly liberal levels of response bias. The resulting hits and false alarms were converted to response rates by adding 0.5 response to each frequency bin and dividing by the total number of items plus one, as recommended by Snodgrass and Corwin (1988) to avoid hit and false alarm rates of 0.0 and 1.0. These pairs of hit and false alarm rates were then plotted as ROC points and used to obtain estimates of the area under the ROC, A_z a bias-free measure of recognition sensitivity (Macmillan and Creelman, 1991). A_z is obtained from the slope and intercept of the best-fitting straight line when ROC points are z-transformed. It assumes a signal-detection model with unequal variances of old and new items (although note the model does not inherently assume a single process; Wixted and Stretch, 2004), and is appropriate when this model provides a reasonable approximation to the data. Since d' assumes a symmetric ROC, A_z is preferred when ROC curves are asymmetric, as they are in the present study. All analyses were performed on A_z scores obtained from individual participants' ROCs.

Figure 1A shows the average ROCs for young controls, age-matched controls, hypoxic patients, and left lobectomy patients for pairs in the compound condition and Figure 1B shows the ROCs for the same groups in the sentence condition. A visual comparison of Figures 1A and B reveals that performance is at about the same level for compounds and sentences for every group except the hypoxics, who performed better on pairs from

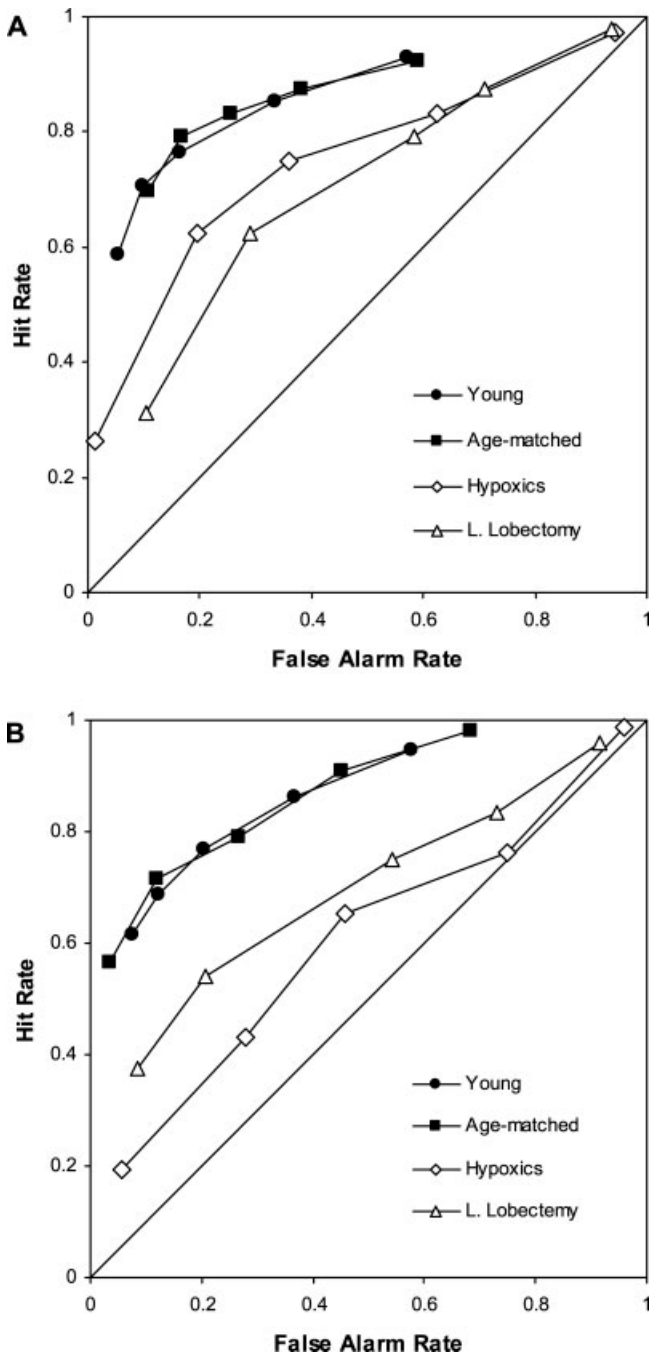

FIGURE 1. Mean ROC curves for associative recognition of compound pairings (A) and sentence pairings (B) for young controls (N = 36), age-matched controls (N = 7), mild hypoxic patients (N = 3), and left temporal lobectomy patients (N = 2).

compounds than from sentences. However, both groups of patients are lower than the controls' average for both types of association. The average A_z values for all groups in Experiment 1 are presented in Figure 2. The A_z values confirm that performance on compound and sentence conditions were matched for young and age-matched controls with highly similar means and standard deviations (SDs). There was no reliable difference between the two conditions for either the young controls, $t(34) = 0.32$, $P = 0.589$, or for the age-matched controls, $t(6) = 0.56$, $P = 0.646$. Of the age-matched group, two participants performed slightly better on the compound condition, and five were slightly better on the sentence condition. The hypoxic patients, by contrast, showed greater performance for the compound condition than for the separate condition, $t(2) = 4.79$, $P = 0.02$. All three hypoxics performed much worse for recognition of pairs from sentences than from compounds compared to age-matched controls (differences of 0.11, 0.22, and 0.22 for E.R., R.M., and G.H., respectively). When A_z values for hypoxics and controls were entered into a 2 (hypoxic vs. control) by 2 (separate vs. compound judgment) mixed analysis of variance (ANOVA), there was an interaction effect, $F(1,8) = 18.48$, $P = 0.003$. The A_z scores for controls were the same in the two conditions, but for hypoxics A_z scores were greater in the compound condition than the separate condition. The lobectomy patients were more similarly impaired on average for the two conditions, although their impairments were in different directions. M.G. was better for compound pairs and D.S. was better for sentence pairs; both differences were numerically smaller than those of the hypoxic patients; however, D.S. was also much better than M.G in the sentence condition (nearly at the level of normals), but at a similar level in the compound condition. This could reflect simply that M.G. has a greater recollection impairment than D.S. (note M.G. is much worse on verbal paired associate recall scale of the WMS-R; Table 1), whereas their familiarity impairments may be more similar.

In summary, there was a consistent effect of unitization on associative recognition for hypoxics but not for the patients with left temporal lobe damage. This is exactly the result expected if performance in the sentence encoding condition loads relatively heavily on recollection, whereas performance in the compound encoding condition loads more than usual on familiarity. According to this view, the hypoxics were consistently more impaired in the sentence encoding condition because their deficits are relatively specific to recollection; the lobectomy patients'

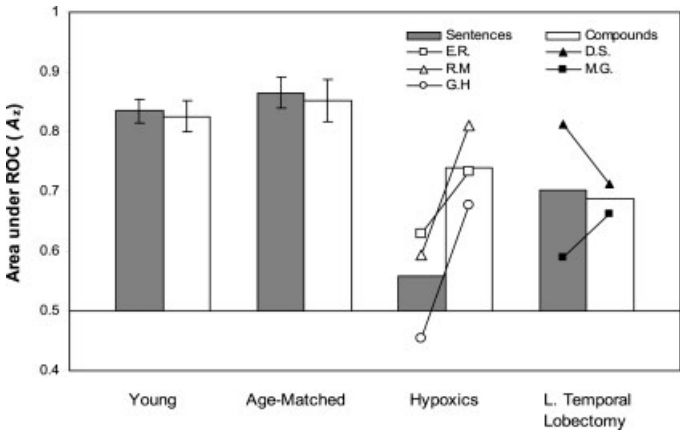

FIGURE 2. Mean associative recognition sensitivity for compound and sentence pairings for young and age-matched controls, and for hypoxic and left-temporal lobectomy patients.

impairments were more similar on average in the two conditions because both recollection and familiarity are impaired.

EXPERIMENT 2

The results from Experiment 1 indicate that amnesics' associative recognition deficit is mediated by the degree to which the association is unitized. The results also suggest that the size of the unitization effect depends on the extent to which participants rely on familiarity to make recognition decisions. If this is the case, it should be possible to obtain a unitization effect in normal individuals by asking them to base their associative recognition decisions on familiarity. In Experiment 2, we tested this possibility by instructing some participants to quickly judge the familiarity of a pairing, irrespective of whether they specifically recollected seeing it before; other participants were given standard recognition instructions. The familiarity-only instruction was not expected to eliminate recollection completely; rather, the goal was to reduce somewhat the number of recollection-based responses, and facilitate participants' use of familiarity if that information is available (Montaldi et al., 2006). We hypothesized that, like the controls in Experiment 1, participants given standard recognition instructions would perform equally well in the compound and separate encoding conditions. However, participants given instructions emphasizing familiarity-based responding should perform better in the compound condition than in the separate condition (like hypoxics in Experiment 1).

Participants

One hundred twenty-eight Princeton University students participated. Thirty were paid $10 for participation. The rest of the participants received course credit for participation.

Materials

The same materials from Experiment 1 were used; six of the 12 pair lists were used for critical study pairs in Experiment 2. Two more lists were used for practice. For each participant, pairs from three lists were presented in intact form on test, and pairs from three lists appeared as recombined lures. The lists were counterbalanced such that A–B/C–D and A–D/C–B versions of each list were equally likely to appear as intact and rearranged pairs (i.e., different participants might study list one as A–B/C–D or as A–D/C–B, but either version could appear later as intact or recombined).

Design and Procedure

The design and procedure for Experiment 2 was similar to the study and test portions of Experiment 1, with a few exceptions. First, participants received either compound or sentence encoding instructions, and either standard-recognition or familiarity-only test instructions. A between-subjects design was used to prevent instructions from one condition from affecting performance on another condition. Second, participants in the familiarity-only condition were instructed to rate, on a scale of 1–6, how familiar the pairing was. They were told that it was important they focus only on how familiar the pair was, and not to worry about whether they remembered seeing it earlier in the experiment. They were told to respond as quickly as possible once they had a feeling for how familiar the pairing was, and that if they happened to recollect something about the pairing, they should try to ignore that information. They were instructed that if they found themselves recollecting often, they should try to respond faster. Participants studied and were tested on 144 pairs, half appearing as intact pairings on the test, and half appearing as recombined pairings. A practice encoding phase was given with 24 pairs from an unused list in which participants had to justify their responses. A practice test phase was also given which included intact and recombined items from the encoding practice.

Results and Discussion

ROCs and A_z scores were obtained from confidence ratings in Experiment 2 using the same procedure from Experiment 1. A_z scores of four participants qualified as outliers relative to their conditions according to Tukey's (1977) criteria (the compound-recognition and sentence-recognition conditions each had one outlier, and there were two outliers in the compound-familiarity condition). All four scores were also more than 2.5 SD below the mean of their respective conditions. They were replaced with four new participants.

The ROCs of all conditions are shown in Figure 3. Overall performance of all conditions as measured by A_z is shown in Figure 4. When the four groups were entered into a 2 × 2

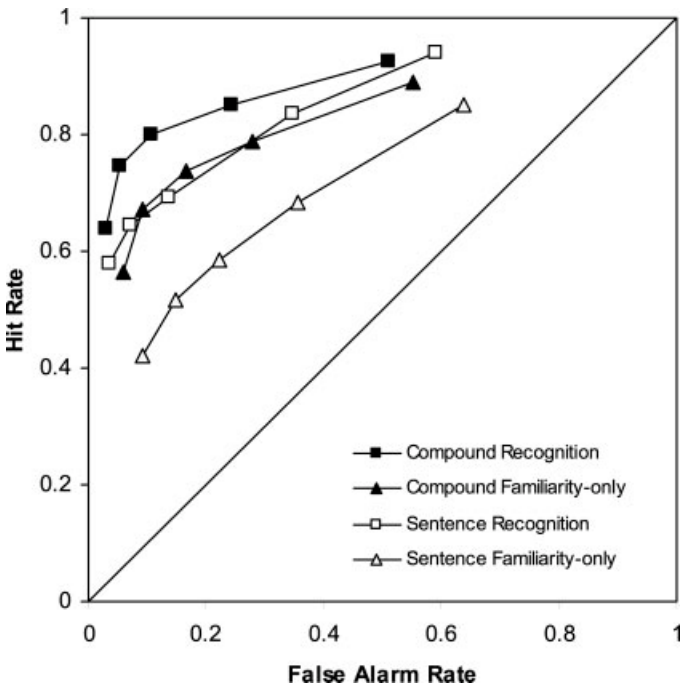

FIGURE 3. Mean ROC curves for associative recognition of compound and sentence pairings for young healthy participants under standard recognition test instructions and familiarity-only test instructions in Experiment 2.

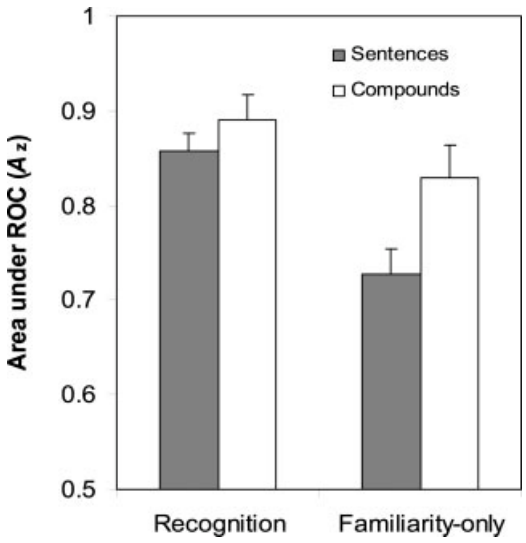

FIGURE 4. Mean associative recognition sensitivity for compound and sentence pairings for young healthy participants under standard recognition test instructions and familiarity-only test instructions in Experiment 2.

between-participants ANOVA, there were reliable main effects of encoding type $F(1,112) = 19.50$, $P < 0.001$ and test type $F(1,112) = 34.04$, $P < 0.001$. As predicted, there was also an interaction between encoding type and test type, such that unitization (compound vs. sentence encoding) had a larger effect on recognition sensitivity in the familiarity condition than in the recognition condition $F(1,112) = 4.35$, $P = 0.039$. Performance in the compound condition was significantly better than the sentence condition under familiarity-only instructions, $t(62) = 3.99$, $P < 0.001$, but the difference did not reach significance under standard recognition instructions, $t(62) = 1.84$, $P = 0.07$.

In summary, the pattern of results that was observed in hypoxic patients in Experiment 1 (whereby hypoxia affected associative recognition for nonunitized pairs more than unitized pairs) was replicated in Experiment 2 using normal healthy subjects who were instructed to rely on familiarity when making their recognition decisions. The results are consistent with the hypothesis that the unitization effect observed for hypoxic patients in Experiment 1 is attributable to their reliance on familiarity.

GENERAL DISCUSSION

The current experiments indicate that the performance of amnesics on associative recognition tasks can depend on whether the item pairings are encoded in a unitized or nonunitized manner, and the extent to which the patients exhibit deficits in recollection and/or familiarity. Patients with relatively selective recollection deficits, presumably related to selective hippocampal damage, were much less impaired when items were encoded in a unitized manner. Patients with extensive medial temporal lobe damage that disrupts both recollection and familiarity did not benefit as consistently or as substantially from unitization. Also, the experiments provide support for the hypothesis that, in general, unitization boosts the extent to which familiarity supports associative recognition. The only groups showing reliable and substantive effects of the unitization manipulation were the hypoxic patients from Experiment 1, who have relatively specific recollection deficits, and college students in Experiment 2 who received instructions to focus on familiarity. These were the conditions in which we expected the contribution of familiarity to be the largest (relative to the contribution of recollection); as such, these were the conditions under which the beneficial effect of unitization on familiarity should have the largest effect on overall recognition performance. In all other conditions, the performance was about equal for sentence and compound pairs.

In comparing the performance of the two patient groups, the lobectomy patients both performed near the hypoxic level on compound pairs, but they performed better on average than hypoxics on the sentence pairs. This may seem odd at first: If (as argued above) compound recognition receives an increased contribution from familiarity, and the hypoxic patients show spared familiarity relative to the lobectomy patients, why is there not a larger advantage favoring hypoxics in the compound recognition condition? Also, if sentence recognition is primarily driven by recollection, and both groups show impaired recollection, why do the lobectomy patients perform better than the hypoxics in the sentence recognition condition? In both cases, this is probably because lobectomy patients have only unilateral damage, whereas the hypoxics are likely to have bilateral damage. Recollection for the left temporal lobe group in Yonelinas et al. (2002) was actually *better* than that of hypoxics. Because performance in both conditions should benefit from recollection, lobectomy patients' greater recollection should give them an advantage for sentences, and it should also offset their familiarity impairment somewhat for compounds relative to hypoxics.

The present results demonstrate that unitization effects on amnesic performance and on familiarity-based recognition are a function of the type of processing engaged at encoding. Other studies of holistic processing in associative recognition have manipulated the level of pre-experimental integration between elements of the association, such as components of familiar compound words or the features of faces. The present study demonstrates these findings are not limited to pre-experimental associations—for at least some types of patients, these findings are generalizable to relatively novel associations between separable items. Specifically, the present study shows that unitized encoding operations, applied to previously unrelated stimuli, are sufficient to generate familiarity-based associative recognition in some amnesic patients.

Our interpretation of the results is that unitized encoding brings cortical learning mechanisms to bear on pairings of stimuli, more so than what occurs normally. These cortical learning mechanisms generate representations of the stimulus pairs that are more tightly integrated into a unified whole; these representations selectively boost the familiarity strength of intact pairs (compared to recombined pairs), thereby making the familiarity of unitized pairs diagnostic of whether the pair is intact or recombined. In this respect, associative recognition of unitized

pairs is similar to recognition of single items. However, while unitized encoding may lead people to perform associative recognition tasks in the same way they perform item recognition tasks, we do not wish to argue that pre-experimentally familiar single words and experimentally-unitized associations between words are necessarily the same in all respects. We did not directly compare associative recognition to item recognition in this study, and so we do not know the full extent to which recognition of unitized pairs behaves similarly to recognition of single words. Also, it is doubtful that a single unitized encoding trial (applied to an arbitrary word pair) will have effects that are equivalent to the long-term cortical sharpening processes that result in unitization of pre-experimentally familiar single words.

Can unitization help to explain the results of previous studies on associative recognition in patients with hippocampal damage? Stark and Squire (2003) reported general impairments across both within-item associations (presumably unitized) and between-item associations (presumably not unitized) that would appear to contradict our interpretation. However, three of their five patients were part of a group reported by Manns et al. (2003) to have similarly-impaired levels of recollection and familiarity. Unless recollection is relatively more impaired than familiarity, our account gives no reason to expect a benefit from unitization.

Other studies have found that patients with limited hippocampal damage show similar sparing of item recognition, within-item associations, and between-item associations of the same type (e.g., word-word, face-face), despite severe deficits in between-item associations of different types, and no attempt to induce unitized encoding of the pairings (e.g., word-face, object-location; Vargha-Khadem et al., 1997; Mayes et al., 2004). These authors have interpreted this result as a demonstration that spared familiarity in these patients supports both recognition of single items and associative recognition of items of the same type. Sparing of same-type between-item associations in the absence of unitization would appear to indicate that unitization is not a necessary condition for familiarity. However, while these studies did not attempt to encourage unitized encoding, they also did not attempt to minimize it such as we did with the sentence task in the present study; thus, it is possible that some hippocampal patients such as Y.R. (Mayes et al., 2004) normally utilize some degree of unitization for items of the same type as a compensatory strategy. If so, it would appear that the effectiveness of unitized encoding operations are at least limited to associations of the same type, since these patients did show severe deficits for pairs of different types.

It is important to note that the present study does not address whether unitized encoding is a *necessary* condition for familiarity-based associative recognition or associative sparing in patients with hippocampal damage. What the results do suggest, however, is that unitization per se is a *sufficient* condition for generating familiarity-based associative recognition in some patients who have preserved capacity for familiarity discriminations. The present study addresses two criteria put forth by Mayes et al. (2004) as important for establishing the role of unitization in familiarity-based associative recognition. First, in using standard English compounding rules, the study provides an operational definition of unitization independently of actual recognition performance. Second, the unitization effect in the hypoxic patients is unlikely to be attributable to recollection since the hypoxic patients have consistently shown limited and severe recollection deficits in our previous work (Yonelinas et al., 2002; Quamme et al., 2004), and the unitization advantage appears under conditions of reduced attention to recollective information. Additionally, pairs were counterbalanced across unitized and nonunitized conditions, and so materials differences cannot explain the effect. More work is required to determine the necessity of unitization for familiarity-based responding; it is possible that unitization is just one of several routes to the same learning mechanisms that generate representations sufficient for supporting familiarity discriminations. To address this, future studies will need to examine more systematically the effect of different encoding procedures and strategies on performance; at the very least, the differences between the present encoding conditions and those employed in previous studies will need to be compared in the same patients, using the same materials.

In summary, the present results join a growing literature linking limited medial-temporal lobe amnesia, spared capacity for making familiarity discriminations, and a relative sparing of memory for associations that are unitized. The present study also may provide a way of reconciling the relational-deficit view of hippocampal damage (e.g., Eichenbaum and Cohen, 2001) with findings of spared between-item associative recognition in amnesia: If hippocampal amnesic patients can encode a studied association in a unitized fashion, they may be able to perform associative recognition tasks based on the familiarity of this unitary representation (i.e., in a manner similar to how item recognition tasks are performed) without needing to rely on recollection via relational representations.

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