Research Report

PRESERVATION OF IMPLICIT MEMORY FOR NEW ASSOCIATIONS IN GLOBAL AMNESIA

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Abstract—*This study examined whether amnesic patients have preserved implicit memory for new associations between unrelated words, as measured by repetition priming, despite impaired explicit memory for such new associations. Prior studies provide conflicting and ambiguous results. Amnesic and control participants read aloud visually presented, unrelated word pairs and then attempted to identify old, recombined, and new word pairs shown at threshold durations. Amnesic and control groups showed equivalent priming for new associations by identifying old pairs better than recombined pairs. Amnesic patients were impaired on a matched explicit test of memory for new associations. The preserved priming in amnesia indicates that implicit memory for new associations need not be supported by the mnemonic processes and brain structures that mediate explicit memory for new associations.*

Global amnesia is a neurological syndrome characterized by a severe deficit in remembering new episodes and facts that is not secondary to any other behavioral incapacity. The syndrome typically results from bilateral lesions of medial temporal, diencephalic, or basal forebrain structures. Amnesic patients perform poorly on explicit memory tests of recall and recognition, which require conscious and deliberate recollection of recent experience (Graf & Schacter, 1985). Amnesic patients, however, often perform normally on implicit tests of memory, which measure information gained in recent experience as a change in behavior without any reference being made to that experience. Implicit measures have revealed intact memory in amnesic patients on tests of classical conditioning (e.g., Gabrieli, McGlinchey-Berroth, et al., 1995), skill learning (e.g., Cohen & Squire, 1980; Milner, 1962), and repetition priming, which is the difference in test-phase performance between items presented earlier in a study phase and baseline items (e.g., Cermak, Talbot, Chandler, & Wolbarst, 1985; Graf, Squire, & Mandler, 1984).

The formation of new associations between previously unrelated items is a hallmark of explicit memory. In the laboratory, such memory may be measured via paired-associate learning of unrelated words (e.g., seeing *march-shave* at study and recalling what word was presented with *march* at test). Amnesic patients have virtually no explicit memory for new associations between unrelated words (e.g., Shimamura & Squire, 1984). For the past decade, investigators have tried to discover whether implicit memory mechanisms can also mediate new associations between previously unrelated words by asking whether amnesic patients can show normal priming for new associations. A way to measure priming for new associations is to expose participants to unrelated word pairs in a study phase (e.g., *marchshave, above-fleet, amaze-voter*) (Graf & Schacter, 1985; Moscovitch, Winocur, & McLachlan, 1986). In a test phase, participants perform a task with three kinds of word pairs: (a) old pairs seen in the study phase (*march-shave*), (b) recombined study-phase pairs (*above-voter*), and (c) new baseline pairs. Superior performance for recombined relative to new pairs reflects single-word priming. Superior performance for old relative to recombined pairs must reflect new associations made between words by their arbitrary study-phase pairing because all words in old and recombined pairs were seen in the study phase. The test-phase task may require participants to complete word stems (*march-sha___*) or to identify word pairs presented at threshold duration. Such tasks are known to yield intact single-word priming in amnesia (e.g., Cermak et al., 1985; Graf et al., 1984).

Amnesic patients have demonstrated impaired priming of new associations as measured by word-stem completion (Cermak, Bleich, & Blackford, 1988; Schacter, 1985; Shimamura & Squire, 1989) or word identification when each pair of words was presented sequentially at test (Paller & Mayes, 1994). Because amnesic patients showed intact single-word priming in all of these studies and intact priming for known associations in one of them (e.g., *table-chair*, Shimamura & Squire, 1984), the impaired priming for new associations suggested a limit as to what could be learned by implicit memory processes. Using reading speed as a priming measure, Moscovitch et al. (1986) reported unimpaired priming for new associations between word pairs in a mixed group of amnesic and Alzheimer's patients (priming in the amnesic group alone was not examined). Musen and Squire (1993), however, were unable to find priming for new associations by the reading-speed measure in either normal or amnesic groups unless word pairs were combined into single, continuous nonwords (e.g., *marchshave*) and presented for 10 study trials. In that case, amnesic patients showed normal priming for new associations. Combining words into continuous nonwords, however, makes it unclear whether each stimulus was treated as a single nonword or as two distinct words associated by their co-occurrence. Also, explicit memory after intensive 10-trial training was not examined, making it uncertain whether the patients would have shown explicit memory impairments, and precluding finding a dissociation between implicit and explicit memory for new associations.

Musen and Squire (1993) also examined priming for new associations on a word-pair identification test. A combined analysis of amnesic and control groups yielded priming for new associations, but neither group alone showed reliable priming for new associations. Thus, it is unclear whether amnesic patients showed normal priming for new associations, or whether they appeared unimpaired because such priming was minimal even in normal control participants. Musen and Squire noted that given the modest amount of associative priming in healthy individuals, it is important to verify not only that amnesic patients are unimpaired relative to control groups, but that the amnesic patients themselves show priming for new associations. Musen and

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Squire concluded that implicit memory mechanisms are not well suited for fast learning of new associations between separate items.

In sum, amnesic patients have shown either clearly impaired priming or uncertain priming for new associations. A review of this literature concluded that "amnesics show little or no associative priming following study of novel, unrelated word pairs" (Bower, 1996, p. 60). Although some findings suggest that amnesic patients may show intact priming for new associations (Moscovitch et al., 1986; Musen & Squire, 1993), amnesic patients have never shown intact priming for new associations in a study that meets three minimal criteria: (a) word pairs shown as separated words, (b) reliable priming for new associations by amnesic patients, and (c) impaired explicit memory for new associations under the same study conditions that yield intact priming for new associations. By attempting to meet these criteria in the present study, we aimed to settle unambiguously whether amnesic patients can show intact priming for new associations.

METHOD

Participants

There were two amnesic groups, patients with alcoholic Korsakoff syndrome and patients with various etiologies. In the latter group, amnesia was due to anoxia ($n = 2$), encephalitis ($n = 2$), bilateral thalamic infarction ($n = 1$), and status epilepticus following head injury ($n = 1$). The control group for the Korsakoff patients had a history of alcoholism, but had abstained from alcohol for at least 1 month prior to testing and had no history of neurological or psychiatric illness. The control group for the other amnesic patients met the same criteria, but had no history of alcohol abuse. Neither amnesic group differed significantly from its control group in terms of age, education, or verbal IQ (see Table 1).

Design

An exposure duration yielding 30% accuracy for word-pair identification was established for each participant. Then, participants saw word pairs in a study phase and received subsequently a word-pair identification test. After a second study phase with another set of word pairs, participants performed a three-alternative forced-choice recognition test.

Materials

The stimuli were 408 five-letter words randomly paired to form 204 unrelated word pairs. Eighty-four pairs were used to set exposure durations. The remaining 120 pairs were divided into six lists of 20 word pairs for counterbalancing purposes. For each list, the average frequency of the first and second words from each pair was 19 per million (Kucera & Francis, 1967). No two words in a pair began with the same letter. Fifty-four additional word pairs were used as fillers. Six study forms were created by combining two lists (40 pairs). Pairs were shown twice for a total of 80 study trials. Pairs were ordered pseudorandomly such that each pair appeared once in the first half and again in the second half of the study list. Three filler word pairs occurred at the beginning and at the end of each study form.

The test forms for word-pair identification comprised 20 pairs identical to those shown in a preceding study phase (old pairs), 20 pairs that were recombinations of first and second words presented in separate study-phase pairs (recombined pairs), and 20 baseline pairs not seen in the study phase (new pairs). Words in recombined pairs were unrelated, began with different letters, and were in the same left-right position as seen in the study phase. Recognition tests comprised 20 trials. Each trial had the first word of a study-list pair appearing centrally above a row of three other words: (a) the second word of that study-list pair (old choice); (b) a second word from another study-list pair (recombined choice); and (c) a word not shown in the study phase (new choice). Order of choice types was counterbalanced.

Each participant saw different words in the identification and recognition tests. Across participants, stimuli were counterbalanced such that each word pair appeared equally often in the identification and recognition tasks and equally often in the old, recombined, and new conditions.

Procedure

Stimuli were presented on a Macintosh computer monitor. Word pairs were shown in uppercase Courier 28 black font and separated by

Table 1. *Participants' characteristics*

Group	*n*	Mean age (years)	Mean education (years)	WAIS-R Verbal IQ	WMS-R indices: Attention/ Concentration	WMS-R indices: Delayed Memory
Amnesic						
Alcoholic Korsakoff	6 men	63.7	9.8	95.0	100.3	55.5
Other etiology	4 men, 2 women	48.0	16.0	106.3	105.7	60.0
Control						
Alcoholic	6 men	61.5	11.7	103.7		
Normal	4 men, 2 women	50.7	16.5	108.8		

Note. WAIS-R = Wechsler Adult Intelligence Scale-Revised (Wechsler, 1981); WMS-R = Wechsler Memory Scale-Revised (Wechsler, 1987). The WAIS-R and two WMS-R indices yield a mean score of 100 with a standard deviation of 15 in the normal population.

a space, dash, and another space (e.g., "UPPER - LOGIC"). Subjects sat approximately 22 in. from the screen.

Individualized exposure durations yielding approximately 30% identification accuracy were determined by having each participant identify 60 word pairs presented at 10 different exposure times ranging from 50 to 200 ms. A fixation character ("+") preceded each word pair, which was then followed immediately for 500 ms by a mask consisting of superimposed "X" and "H" characters. The same fixation and mask were used in the identification test. Following initial establishment of an exposure duration, four more lists of 6 word pairs each were presented, and exposure duration was adjusted if necessary to maintain 30% accuracy.

In each study phase, the participant read aloud word pairs appearing centrally, one pair at a time; the examiner terminated each trial when the participant had read the word pair. In the identification task, the participant attempted to identify, guessing if uncertain, word pairs presented for the predetermined exposure duration. In the recognition test, the participant selected which of the three words in the bottom row he or she thought had appeared in the study phase together with the top word. The examiner recorded responses.

RESULTS

Scores from the identification and recognition tests (Fig. 1) were analyzed separately.

Identification

For each participant, percentages of correct answers (accurate identification of both words in a pair) for old, recombined, and new pairs were calculated. A 2 (alcoholic vs. nonalcoholic groups) × 2 (amnesic vs. control groups) × 3 (old vs. recombined vs. new word pairs) mixed analysis of variance (ANOVA) was performed with groups as between-subjects factors and pair type as a within-subjects factor. No group effect was significant. Priming was indicated by significant differences in identification of word-pair types, $F(2, 40) = 52.75$, $MSE = 118.71$, $p < .001$. Participants identified old pairs more accurately than recombined pairs, $t(23) = 3.04$, $p < .01$, and recombined pairs more accurately than new pairs, $t(23) = 6.98$, $p < .001$. Normal priming in the amnesic group was indicated by the absence of any interaction between pair type and amnesic-versus-control groups ($p > .95$). No other effect was significant. The absence of a three-way interaction indicates that priming was intact in the amnesic patients regardless of etiology. Separate analyses of the amnesic group alone indicated reliably superior identification of old versus recombined pairs, $t(11) = 2.35$, $p < .05$, and recombined versus new pairs, $t(11) = 4.96$, $p < .001$.

Exposure durations used in the identification task were examined in a 2 (alcoholic vs. nonalcoholic groups) × 2 (amnesic vs. control groups) ANOVA. The alcoholic group ($M = 227$ ms) required longer durations than the nonalcoholic group ($M = 119$ ms), $F(1, 20) = 4.84$, $MSE = 14,488$, $p < .01$, and the amnesic group ($M = 240$ ms) required longer durations than the control group ($M = 107$ ms), $F(1, 20) = 7.32$ $p < .01$. There was no interaction.

Recognition

The control group was more accurate than the amnesic group in recognizing what words had been presented together in the study phase, $t(22) = 3.32$, $p < .01$. Further, the control group exhibited explicit memory for study-phase associations by selecting correct old choices more often than incorrect recombined choices, $t(11) = 5.16$, $p < .001$. The amnesic group, however, failed to reliably select old choices more often than recombined choices, $t(11) = 1.71$, $p > .10$, and thus did not demonstrate explicit memory for study-phase associations between unrelated words.

DISCUSSION

Amnesic patients showed intact priming not only for single words (recombined vs. new pairs) but also for new associations between unrelated words presented together in the study phase (old vs. recom-

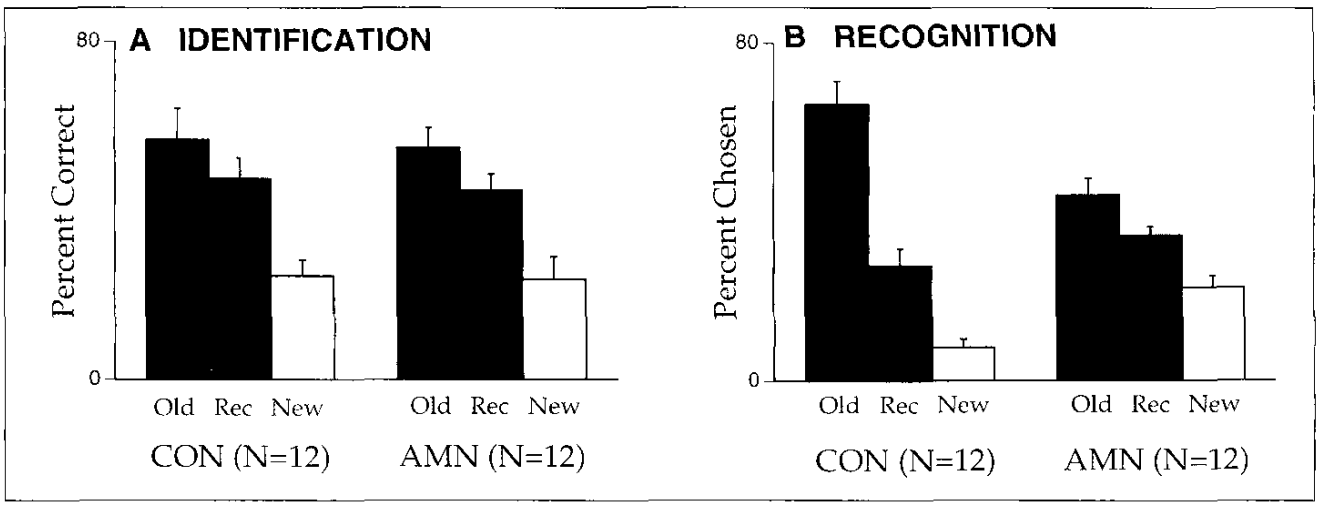

Fig. 1. Implicit and explicit memory performance with old, recombined (Rec), and new test items by control (CON) and amnesic (AMN) participants. Brackets show standard error of the mean. The two graphs show (a) the percentage of word pairs identified correctly at threshold duration and (b) the percentages of three kinds of recognition choices. Old choices are correct.

bined pairs). When analyzed alone, the amnesic group demonstrated reliable priming for new associations. Priming for new associations in the present study may have been more robust than that found by Musen and Squire (1993) because there were more amnesic patients (12 vs. 8 patients), more word pairs per test list (60 vs. 30 word pairs), and more study presentations (two vs. one presentation). Following identical study conditions, amnesic patients showed an overall explicit memory deficit for study-phase words, and a specific explicit memory deficit for associations between unrelated words presented together in the study phase (a failure to reliably select more old than recombined choices). These results meet the criteria for demonstrating a clear dissociation in amnesia between normal implicit memory for new associations between unrelated words and impaired explicit memory for those associations.

Priming for the identification of single words at threshold duration has been well characterized as visual-perceptual in nature (e.g., Jacoby & Dallas, 1981). Amnesic patients have shown intact identification priming for words, pronounceable pseudowords (Haist, Musen, & Squire, 1991), and unpronounceable letter strings (Keane, Gabrieli, Noland, & McNealy, 1995). In addition, amnesic patients exhibit intact priming for novel nonverbal stimuli (e.g., Gabrieli, Milberg, Keane, & Corkin, 1990). The same kinds of implicit memory mechanisms may mediate perceptual priming for visual associations between letters in novel letter strings, between components of novel nonverbal stimuli, and between unrelated words seen together. Lesion evidence indicates that occipital neocortex may mediate such priming for words (Gabrieli, Fleischman, Keane, Reminger, & Morrell, 1995) and for pronounceable pseudowords (Keane, Gabrieli, Mapstone, Johnson, & Corkin, 1995). The same visual neural system may mediate the priming of new associations demonstrated in the present study.

Amnesic patients, however, exhibit impaired priming for new associations between unrelated words on other visual-perceptual tasks that yield normal single-word priming in amnesia. Amnesic patients show little or no implicit memory for new associations by the word-stem completion measure (Cermak et al., 1988; Schacter, 1985; Shimamura & Squire, 1989), a measure of priming that appears to depend on explicit memory mechanisms in normal participants (e.g., Bowers & Schacter, 1990; Graf & Schacter, 1985). With the same word-identification measure used in the present study, amnesic patients showed no priming for new associations between words presented sequentially at test (Paller & Mayes, 1994). Perhaps the implicit new association underlying visual priming must be formed in a single percept of simultaneously presented words, and cannot be accessed across two sequential percepts. Current theories cannot account for why some priming tasks allow for the expression of implicit new associations, but other priming tasks do not.

The present results provide unambiguous evidence that priming for new associations between pairs of spatially distinct and semantically unrelated stimuli can be intact in patients with global amnesia. The results do not favor the idea that implicit memory mechanisms are, in general, poorly suited for fast learning of new associations between separately presented words (Musen & Squire, 1993). The question for future research is no longer whether implicit memory mechanisms can represent new associations without support from explicit memory mechanisms: They can. The questions now are what distinguishes implicit memory processes that do or do not make new associations and how implicit and explicit associations differ in nature.

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REFERENCES

Bower, G.H. (1996). Reactivating a reactivation theory of implicit memory. *Cognition and Consciousness, 5,* 27–72.

Bowers, J.S., & Schacter, D.L. (1990). Implicit memory and test awareness. *Journal of Experimental Psychology: Learning, Memory, and Cognition, 16,* 404–416.

Cermak, L.S., Bleich, R.P., & Blackford, S.P. (1988). Deficits in the implicit retention of new associations by alcoholic Korsakoff patients. *Brain and Language, 7,* 312–323.

Cermak, L.S., Talbot, N., Chandler, K., & Wolbarst, L.R. (1985). The perceptual priming phenomenon in amnesia. *Neuropsychologia, 23,* 615–622.

Cohen, N.J., & Squire, L.R. (1980). Preserved learning and retention of pattern-analyzing skill in amnesia: Dissociation of knowing how and knowing that. *Science, 210,* 207–210.

Gabrieli, J.D.E., Fleischman, D.A., Keane, M.M., Reminger, S.L., & Morrell, F. (1995). Double dissociation between memory systems underlying explicit and implicit memory in the human brain. *Psychological Science, 6,* 76–82.

Gabrieli, J.D.E., McGlinchey-Berroth, R., Carillo, M.C., Gluck, M.A., Cermak, L.S., & Disterhoft, J.F. (1995). Intact delay-eyeblink classical conditioning in amnesia. *Behavioral Neuroscience, 109,* 819–827.

Gabrieli, J.D.E., Milberg, W., Keane, M.M., & Corkin, S. (1990). Intact priming of patterns despite impaired memory. *Neuropsychologia, 28,* 417–427.

Graf, P., & Schacter, D.L. (1985). Implicit and explicit memory for new associations in normal and amnesic subjects. *Journal of Experimental Psychology: Learning, Memory, and Cognition, 11,* 501–518.

Graf, P., Squire, L.R., & Mandler, G. (1984). The information that amnesic patients do not forget. *Journal of Experimental Psychology: Learning, Memory, and Cognition, 10,* 164–178.

Haist, F., Musen, G., & Squire, L.R. (1991). Intact priming of words and nonwords in amnesia. *Psychobiology, 19,* 275–285.

Jacoby, L.L., & Dallas, M. (1981). On the relationship between autobiographical memory and perceptual learning. *Journal of Experimental Psychology: General, 110,* 306–340.

Keane, M.M., Gabrieli, J.D.E., Mapstone, H.C., Johnson, K.A., & Corkin, S. (1995). Double dissociation of memory capacities after bilateral occipital-lobe or medial temporal-lobe lesions. *Brain, 118,* 1129–1148.

Keane, M.M., Gabrieli, J.D.E., Noland, J.S., & McNealy, S.I. (1995). Normal perceptual priming of orthographically illegal nonwords in amnesia. *Journal of the International Neuropsychological Society, 1,* 425–433.

Kucera, H., & Francis, W.N. (1967). *Computational analysis of present-day American English.* Providence, RI: Brown University Press.

Milner, B. (1962). Les troubles de la memoire accompagnant des lesions hippocampiques bilaterales [Memory impairments associated with bilateral hippocampal lesions]. In *Psychologie de l'hippocampe* (pp. 257–272). Paris: Centre National de la Recherche Scientifique.

Moscovitch, M., Winocur, G., & McLachlan, D. (1986). Memory as assessed by recognition and reading time in normal and memory-impaired people with Alzheimer's disease and other neurological disorders. *Journal of Experimental Psychology: General, 115,* 331–347.

Musen, G., & Squire, L.R. (1993). On the implicit learning of new associations by amnesic patients and normal subjects. *Neuropsychology, 7,* 119–135.

Paller, K.A., & Mayes, A.M. (1994). New association priming of word identification in normal and amnesic subjects. *Cortex, 30,* 53–73.

Schacter, D.L. (1985). Multiple forms of memory in humans and animals. In N. Weinberger, J. McGaugh, & G. Lynch (Eds.), *Memory systems of the brain: Animal and human cognitive processes* (pp. 351–379). New York: Guilford Press.

Shimamura, A.P., & Squire, L.R. (1984). Paired associate learning and priming effects in amnesia: A neuropsychological study. *Journal of Experimental Psychology: General, 113,* 556–570.

Shimamura, A.P., & Squire, L.R. (1989). Impaired priming of new associations in amnesia. *Journal of Experimental Psychology: Learning, Memory, and Cognition, 15,* 721–728.

Wechsler, D. (1981). *Wechsler Adult Intelligence Scale-Revised* [manual]. New York: Psychological Corp.

Wechsler, D. (1987). *Wechsler Memory Scale-Revised* [manual]. New York: Psychological Corp.

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