Dissociation Between Two Forms of Conceptual Priming in Alzheimer’s Disease

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Patients with Alzheimer’s disease (AD) and healthy control participants performed 2 conceptual repetition priming tasks, word-associate production and category-exemplar production. Both tasks had identical study-phases of reading target words aloud, had the most common responses as target items, and required production of a single response. Patients with AD showed normal priming on word-associate production but impaired priming on category-exemplar production. This dissociation in AD suggests that conceptual priming is not a unitary form of memory but rather is mediated by separable memory systems.
in AD (Dalla Barba & Goldblum, 1996). Indeed, AD patients’ category-exemplar production priming was normal following nonsemantic processing but impaired following semantic processing (Monti et al., 1996). Thus, intact and impaired priming in AD may parallel the priming dissociations observed in healthy individuals between conceptual production tasks. To be specific, patients with AD who show impaired category-exemplar production priming ought to show intact word-associate production priming for strong associates. We examined this prediction in the present study.

Past studies of patients with AD were inadequate in evaluating this prediction because of methodological issues. First, no previous studies examined priming on category-exemplar and word-associate production in the same group of AD patients. Second, in previous studies the procedures of these two tasks differed in the number of responses that had to be produced at test: Multiple responses were required on category-exemplar production, but a single response was required on word-associate production (but see Brandt et al., 1988). Third, perhaps most important, past studies did not control the associative strength of study-test stimuli: All category-exemplar production studies included only weakly related category-exemplar pairs. It is unknown whether category-exemplar production priming deficits in AD extend to strongly related category-exemplar pairs. Past studies of word-associate production included pairs of intermediate to weak strength (Carlesimo et al., 1995; Huff et al., 1988 - Experiment 3) or a mixture of weak and strong functionally related words and category-exemplar pairs (Salmon et al., 1988). Previous findings of word-associate priming deficits in AD may have resulted from inclusion of weak associates or inclusion of category-exemplar pairs. Thus, it was unknown whether the same AD patients would show impaired category-exemplar priming and intact word-associate priming under conditions that controlled for the strength of relation, the kind of relation, and response requirements.

In the present study, AD and control participants performed word-associate and category-exemplar production tests. Word pairs in both tasks were the first, second, or third most common target responses to the cue words. Both tests required the production of only one response. We expected patients with AD to show intact priming on word-associate production and impaired priming on category-exemplar production.

Method

Participants

Twenty-three patients with a clinical diagnosis of AD and 23 age- and education-matched normal control (NC) participants participated in the present study. All AD patients met clinical criteria for probable AD as outlined by the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer’s Disease and Related Disorders Association (NINCDS–ADRSA) Work Group (McKhann et al., 1984). The NINCDS–ADRSA inclusion criteria for probable AD are a history of progressive cognitive decline with onset between the ages of 40 and 90, impaired episodic memory (operationalized in this study by a score of < 70 on the Delayed Recall subscale of the Wechsler Memory Scale or < 5 on the Delayed Word List Recall measure from the Consortium to Establish a Registry of Alzheimer’s Disease [CERAD]; Morris et al., 1989), and impairment in at least one other cognitive domain. The NINCDS–ADRSA exclusion criteria are disturbed consciousness, history of major psychiatric disorder, and concurrent systemic or neurological illness believed to contribute to cognitive impairment. In addition, participants who were being treated with antidepressant or anxiolytic medications or who had a moderately severe dementia as defined by a score below 17 on the Mini-Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975) were excluded. Control participants either were patient spouses or were recruited from a pool of elderly hospital volunteers. Inclusion criteria were an MMSE score > 26 and a CERAD Delayed Word List Recall score > 6; exclusion criteria were the same as those for the participants with AD. Table 1 shows participants’ demographic and psychometric information.

Design and Stimulus Materials

Each participant performed the study and test phases for a word-associate task and a category-exemplar production task. The order of task administration was counterbalanced across participants in each group.

For the word-associate production, 58 word pairs (56 target items and 2 filler items) were selected using norms of word association (Postman & Keppel, 1970). The first word of each pair was designated as the cue, and the second word was the target (e.g., TUSK–elephant; TUSK was the cue word for word-associate production and elephant was the to-be-produced target). Target words were the first, second, or third most commonly produced associate of the cue word (M = 1.4, SD = .69). The mean absolute frequency of the target words was 108/million (Kacera & Francis, 1967). None of the selected cue and target words was strongly associated with any other cue or target words. The 56 target word pairs were divided randomly into two lists of 28 pairs each. The target words in each list formed two study lists; two filler words appeared at the beginning of each list. One word-associate production test list was constructed by combining the cue words associated with the target words from the two study lists. Thus, the test

Table 1

Demographic and Psychometric Characteristics of Patients With Alzheimer’s Disease (AD) and Normal Controls (NC)

<table>
<thead>
<tr>
<th>Group</th>
<th>Age (years)</th>
<th>Education (years)</th>
<th>MMSE</th>
<th>Delayed memory CERAD</th>
</tr>
</thead>
<tbody>
<tr>
<td>AD (n = 23)</td>
<td>M</td>
<td>76.7</td>
<td>13.3</td>
<td>21.5a</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>4.9</td>
<td>2.9</td>
<td>2.6</td>
</tr>
<tr>
<td>NC (n = 23)</td>
<td>M</td>
<td>73.7</td>
<td>13.3</td>
<td>30.0a</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>6.5</td>
<td>2.7</td>
<td>1.3</td>
</tr>
</tbody>
</table>

Note. Age and education did not differ significantly between AD and NC groups. MMSE = Mini-Mental State Examination; CERAD = Consortium to Establish a Registry of Alzheimer’s Disease. 

a$t(44) = 12.2, p < .0001$; Maximum score on MMSE is 30. 
b$t(35) = 10.6, p < .0001$; Maximum CERAD Delayed Recall score is 10. Scores were available for 17 AD and 20 NC participants. 

Mean Wechsler Memory Scale—Revised Delayed Recall Standard Score for the remaining 6 AD patients was 62.8 ($SD = 4.1$), more than 2 standard deviations below the normal mean of 100 ($SD = 15$). The remaining 3 NC participants were not administered any Delayed Memory test.
list consisted of 56 cue words; two filler cue words appeared at the beginning of the test list. For any given participant, 28 cue words were associates of studied words and 28 were associates of nonstudied words. The order of cue-word presentation was pseudorandomized, with the constraint that there were not more than three consecutive trials of the same type (i.e., studied or nonstudied). Study lists were counterbalanced across participants such that each target item on the test list occurred as studied and nonstudied across participants.

For the category-exemplar production task, 56 cue–target word pairs were formed by pairing a category name with an exemplar that was the first, second, or third \( (M = 1.3, SD = .55) \) most common response to the category name (e.g., \textit{FURNITURE–chair}; Battig & Montague, 1969). In addition, we created two filler cue–target word pairs. The mean absolute frequency of the target words was 88/million (Kucera & Francis, 1967). No selected exemplar was strongly related with other category names or exemplars in the set. Study and test lists were constructed using the same procedure as that described for word-associate production.

**Procedure**

For both word-associate and category-exemplar production tasks, each study-phase trial began with the presentation of a fixation cross for 500 ms, followed by the target word for 2 s. Participants were instructed to read aloud the word on the screen. Immediately following the end of the study-phase, participants performed either the word-associate or category-exemplar production test phases. For word-associate production, each trial began with the presentation of a cue word and participants were asked to respond with the first member of that category that came to mind. The experimenter noted the participant’s response and pressed the space bar to advance to the next trial. For category-exemplar production, participants were presented with a category name and asked to respond with the first member of that category that came to mind. The trial procedure was the same as that for word-associate production. At the end of the test phase, participants took a 5 min break and then performed the study and test phases of the remaining task.

**Results**

For both word-associate and category-exemplar production tests, a response was scored as correct if it matched exactly or was a plural of the target word for each cue–target pair. Table 2 shows participants’ mean performance.

**Baseline Performance**

We conducted \( t \) tests to determine whether baseline production differed in the AD and NC groups. For word-associate production, NC participants produced significantly more nonstudied target words than AD participants, \( t(44) = 3.9, p < .001 \). For category-exemplar production, nonstudied target exemplar production did not differ in the NC and AD participants \( (p = .22) \). Of the nontarget responses, AD participants were more likely to provide incorrect or illegitimate exemplars \( (e.g., \textit{SHIP–carnival}; M = 25\%; \text{range} = 3\%–43\%) \) relative to NC participants \( (M = 17\%; \text{range} = 7\%–30\%), t(44) = 3.3, p < .01 \).

**Repetition Priming**

To determine whether priming differed in the AD and NC groups, the percentage of target responses on word-associate and category-exemplar production tests were submitted to separate repeated measures analyses of variance (ANOVA) with group (AD, NC) as a between-participants factor and item type (studied, nonstudied) as a within-participants factor. Word-associate production priming was obtained because participants produced more studied than nonstudied associates (main effect of item type), \( F(1, 44) = 5.5, p < .05 \). NC participants produced more target associates than patients with AD (main effect of groups), \( F(1, 44) = 18.0, p < .0001 \). This difference reflected baseline rather than group differences in priming because the Group \( \times \) Item Type interaction was not significant \( (p = .91) \).

Category-exemplar production priming was obtained because participants produced more studied than nonstudied exemplars (main effect of item type), \( F(1, 44) = 17.2, p < .0001 \). NC participants produced more target exemplars than patients with AD (main effect of groups), \( F(1, 44) = 19.8, p < .0001 \). This group difference reflected priming differences because the Group \( \times \) Item Type interaction was significant, \( F(1, 44) = 13.4, p < .001 \). Two-tailed \( t \) tests confirmed that this interaction resulted from group differences in the magnitude of priming: NC participants produced significantly more studied than nonstudied exemplars, \( t(22) = 6.5, p < .0001 \). In contrast, patients with AD did not produce more studied than nonstudied exemplars \( (p = .76) \). Thus, significant category-exemplar production priming was obtained in NC but not AD participants.

To compare directly the group differences in priming on the two tasks, we computed priming scores (percentage of studied words produced – percentage of nonstudied words produced) for each participant (see Figure 1). Priming scores were submitted to a repeated measures ANOVA with group (AD, NC) as the between-participants variable and task (word-associate production, category-exemplar production) as the within-participants variable. Overall priming did not differ significantly in the two tasks (main effect of task), \( p = .11 \). NC participants showed more priming than patients with AD (main effect of group), \( F(1, 44) = 6.0, p < .05 \). This difference reflected priming differences as a function of task because the Group \( \times \) Task interaction was significant, \( F(1,
Discussion

We examined repetition priming on two conceptual priming tests, word-associate production and category-exemplar production, in AD patients and age- and education-matched NC participants. Both priming tasks had identical study-phases of reading target words aloud: had the first, second, or third most common responses as target items; and required a single response to be produced at test. Priming did not differ between AD (3.9%) and NC (4.4%) participants on the word-associate production test. In contrast, on the category-exemplar production test, priming was less in the patients with AD (0.9%) than in the NC participants (14.6%). Indeed, patients with AD failed to show significant priming on the category-exemplar production test. Thus, this study shows a dissociation between two conceptual priming tests.

All past studies have found deficits in category-exemplar production priming in AD (Gabrieli et al., in press; Maki & Knopman, 1996; Monti et al., 1996). Those studies used atypical exemplars and required the production of multiple exemplars at test. The present study extends that finding to a category-exemplar test with relatively less demanding production requirements: a single prototypical target exemplar.

Category-exemplar production priming deficits in AD occur following encoding conditions that promote semantic processing. In three studies (including the present), AD patients failed to show significant priming following semantic encoding tasks, such as judging whether a word referred to a man-made or natural entity (Monti et al., 1996) and reading words (Maki & Knopman, 1996; present study). Although making semantic judgments and reading words are different tasks, they may engage common semantic processes that are relevant for category-exemplar production priming because they yield equal amounts of category-exemplar production priming in healthy young participants (Vaidya & Gabrieli, 1998). Encoding tasks that do not engage semantic processes, such as making uppercase-lowercase typecase judgments, yielded intact category-exemplar production priming in the same patients with AD who exhibited impaired priming following semantic judgments (Monti et al., 1996). Thus, semantic encoding deficits appear to underlie category-exemplar production priming deficits in AD.

AD patients, however, showed intact category-exemplar production priming following semantic encoding that required generation from semantic cues (Maki & Knopman, 1996). It is difficult to reconcile this finding because the encoding procedure in that study was not comparable to most studies: If participants failed to generate the target word at encoding, they were prompted repeatedly with phonemic cues and eventually provided the target word. Such an encoding procedure leaves ambiguous the exact basis of the priming, whether it is semantic processing, phonemic rehearsal, or additional cueing at study. When category-exemplar priming is measured under semantic encoding conditions that are equivalent in control and patient groups, it is consistently impaired in AD.

An alternative explanation for the priming impairment in
AD is that priming levels were spuriously elevated in NC participants because they explicitly recalled target exemplars. NC participants’ explicit memory abilities were undoubtedly superior to AD patients. On the basis of past findings, however, it appears that normal participants do not routinely use explicit retrieval to perform category-exemplar production: Magnitudes of category-exemplar priming in control participants are comparable to those in several groups with explicit memory deficits ranging from most severe in global amnesia (Keane et al., 1997), to moderate in schizophrenia (Schwartz, Rosse, & Deutsch, 1993), to mild in normal aging (Light & Albertson, 1989; Monti et al., 1996). Furthermore, it appears unlikely that normal participants in the present study would use explicit retrieval for only one of the two priming tasks. Thus, it is unlikely that group differences in explicit memory contributed to priming differences.

Word-associate production priming was intact in AD. Intact word-associate production priming in AD does not appear to be an artifact of baseline production differences because priming was intact in subgroups of AD and NC participants matched on baseline performance and priming was intact when it was measured relative to baseline performance. This present finding seems to contradict past studies that reported impairments in AD. This discrepancy is illusory, however, because two critical methodological features were unique to our study: (a) inclusion of only strong associates and (b) presentation and reading of only the target word at study. Considering the present findings with past findings, it appears that intact priming in AD is limited to strongly associated word pairs; past studies included relatively weak associates. Indeed, there is reason to expect impaired priming in AD with weak associates: In normal participants, word-associate priming with weak associates is sensitive to semantic encoding (Vaidya et al., 1997). In past studies of patients with AD, word-associate priming was examined after semantic encoding for relatively weakly associated items. Participants were required to elaborate encode word associate pairs (e.g., rate semantic relatedness; but see Brandt et al., 1988—participants heard words and performed a free-recall task before word-associate production). Priming that is enhanced by semantic encoding in normal participants consistently yields deficits in patients with AD. Thus, it is no surprise that prior studies found impaired priming in AD with weak associates following semantic encoding.

Intact word-associate production priming in AD suggests that associative relations among words are relatively preserved in AD because it is these associations that must have been primed in the study-phase. Indeed, Brandt et al. (1988) found that when participants were required to produce four word-associates to a cue word, patients with AD provided fewer absolute numbers of responses but their normative frequency distribution (the number of times a word was produced as the first, second, third, or fourth associate) corresponded closely to that of controls. Furthermore, semantic priming for associatively related words is intact in AD (Ober, Shenaut, & Reed, 1995).

Language deficits in AD, however, led to abnormalities in baseline performance on both word-associate and category-exemplar production tasks. Baseline word-associate production was reduced in AD because of a large number of idiosyncratic and paraphasic responses, an observation that has been noted in other studies (Brandt et al., 1988; Santo Pietro & Goldfarb, 1985). Although baseline category-exemplar production in AD was comparable to controls, participants with AD provided fewer legitimate nontarget responses. Language deficits in AD may have been highlighted by instructions of word-associate production to a greater extent than by those of category-exemplar production because word-associate production instructions do not specify criteria for a legitimate response; any response, even if idiosyncratic, was acceptable. Category-exemplar production instructions, on the other hand, clearly specified criteria for an acceptable response, thereby deterring participants from producing incorrect responses.

The present findings of a neuropsychological dissociation between two conceptual priming tests complements the growing evidence for dissociable conceptual priming mechanisms (Gabrieli et al., in press; Vaidya et al., 1997; Vriezen, Moscovitch, & Bellos, 1995). Dissociations parallel to those in AD are obtained in healthy individuals with two study-phase manipulations—semantic encoding and division of attention. Priming on category-exemplar verification and word-associate production with strong associates is intact in AD (Gabrieli et al., in press; present study) and is unaffected by study-phase semantic encoding (Vaidya et al., 1997) and division of attention (Gabrieli et al., in press; Koriat & Feuerstein, 1976; Light, Prull, & Kennison, 1998). Priming on category-exemplar production is impaired in AD (Monti et al., 1996; present study), enhanced by semantic encoding (Hamann, 1990; Srinivas & Roediger, 1990; Vaidya et al., 1997), and reduced by study-phase division of attention (Gabrieli et al., in press; Light et al., 1998; Mulligan & Hartman, 1996). Furthermore, priming on word-associate production with strong associates is impaired in AD (Brandt et al., 1988; Carlesimo et al., 1995; Huff et al., 1988; Salmon et al., 1988) and enhanced by semantic encoding (Vaidya et al., 1997); it is unknown whether it is reduced by study-phase division of attention. Thus, two classes of conceptual priming tests can now be distinguished on the basis of sensitivity to semantic encoding manipulations, to attentional encoding manipulations, and to cortical degeneration in AD. What principles determine the dependence or independence of a conceptual priming process on semantic encoding, attention, and its vulnerability to AD?

One proposal distinguishes priming processes on the basis of retrieval competition in accessing conceptual knowledge (Vaidya et al., 1997). Access into conceptual memory may be direct such that the test cue guides the retrieval of the...
target word without any or with few competing response alternatives. Such a scenario may occur under two conditions. First, the study-word may be re-presented as the test cue and the participant is required to make some decision about it (e.g., category-exemplar verification, abstract/concrete classification). Second, the study-word may be unitized with the target word rather than identical to it (e.g., SALT—pepper; word associate production with strong associates). Both conditions can be characterized as that of absent response competition because there are no competing responses; either the test cue itself or its coactivated associate is the only target for response. In these two conditions, any study-phase retrieval of the word in response to an encoding task may result in full priming on re-retrieval of that word in the test phase. Any encoding aid in the form of semantic processing or any encoding hindrance in the form of impoverished attention may not add or subtract from such direct priming. Indeed, despite attentional and language deficits in AD (Nebes, Martin, & Horn, 1984; Parasuraman & Haxby, 1993), priming under conditions of absent response competition appears to be spared.

In contrast to conditions that do not elicit response competition, access into conceptual memory may be indirect such that the retrieval cue specifies semantic criteria that initiates competition for retrieval among multiple alternatives. Such a scenario occurs when the test cue is neither the target word nor its unitized associate; rather, it nominally specifies a set of words of which any one is a legitimate response to the test cue (e.g., category-exemplar production or word-associate production with weak associates). Under such conditions of competition, the ultimate retrieval of the target word may depend on whether it was well encoded (e.g., semantically relative to nonsynthetically processed). Furthermore, impoverished attention, either by design or disease, would prevent the target word from being encoded adequately, thereby rendering it disabled to effectively rise well above the competition. Small amounts of priming do occur under impoverished encoding, however, as found on category-exemplar production following divided attention and nonsynthetic levels of processing in healthy participants and patients with AD (Gabrieli et al., in press; Monti et al., 1996).

Advances in functional brain imaging techniques hold promise for characterizing the neural underpinnings of these two putative priming processes. Functional magnetic resonance imaging studies provide preliminary support for the distinction between performance under the presence and absence of response competition: Different patterns of brain activation in the frontal lobes were observed in healthy participants during generation of verbs from nouns with many associated verbs (e.g., WHEEL—turn) relative to few associated verbs (e.g., SCISSORS—cut; Thompson-Schill, D’Esposito, Aguirre, & Farah, 1997) and during completion of items having few possible word completions (e.g., PSY______) relative to those having many possible completions (e.g., MOT______); Desmond, Gabrieli, & Glover, 1998). Past imaging studies of repetition priming indicate that it is characterized by a reduction in brain activation during repeated performance in the same brain regions that were active during initial performance (Buckner, Petersen, Ojemann, Miezin, Squire, & Raichle, 1995; Gabrieli et al., 1996). Therefore, on the basis of results from Thompson-Schill et al. (1997) and Desmond et al. (1998), it appears that the frontal lobes, a site of pathology in AD, may be critically involved in response competition processes that influence conceptual priming.

Thus, at present there is converging evidence from behavioral, neuropsychological, and brain imaging paradigms for the distinction between at least two conceptual processes mediating implicit memory performance. It remains to be seen whether there are further fractionations or more parsimonious classifications of the full complement of conceptual repetition priming processes.

References


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