

Selection Ability in Alzheimer's Disease: Investigation of a Component of Semantic Processing

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Selection ability (selecting a response from several competing semantic and/or lexical representations) was tested in 21 participants with Alzheimer's disease (AD) and 28 control participants to help clarify the nature of semantic impairments in AD. Selection demands were manipulated in 3 tasks (lexical fluency, comparison, and verb generation). In each, high-selection conditions required response selection from competing alternatives, whereas low-selection conditions had a reduced need for selection. Patients with AD were disproportionately impaired on the high-selection conditions of all tasks, even when this condition was easier. Selection deficits on verb generation were evident only relative to nonspeeded controls. Overall results indicate impaired semantic selection abilities in AD, which may contribute to poor performance on some semantic tasks.

It is widely agreed that impairment of semantic memory frequently accompanies Alzheimer's disease (AD; e.g., Chan, Butters, & Salmon, 1997; Martin, 1992; Nebes, 1989; Salmon, Butters, & Chan, 1999). This impairment is thought to underlie poor performance on a number of tasks by patients with AD, even in the early stages of the disease. For example, patients with AD have difficulty naming objects and typically make disproportionately more semantic errors, that is, calling an object by the name of its superordinate category (e.g., *animal* for *dog*), or by the name of another exemplar within a category (such as *peach* for *pear*), than do older control participants (e.g., Hodges, Salmon, & Butters, 1991; Lukatela, Malloy, Jenkins, & Cohen, 1998). They also perform poorly on verbal fluency tasks (e.g., Mickanin, Grossman, Onishi, Auriacombe, & Clark, 1994; Randolph, Braun, Goldberg, & Chase, 1993; Troyer, Moscovitch, Winocur, Leach, & Freedman, 1998), with some evidence that the deficit is worse on semantic fluency than phonemic fluency (e.g., Mickanin et al., 1994; Pasquier, Lebert, Grymonprez, & Petit, 1995). On word-picture matching tasks participants with AD have difficulty when the nontarget distractors belong to the same semantic category as the target but have no difficulty when the distractors belong to different semantic categories, even when they are perceptually similar to the target (e.g., Chertkow, Bub, & Seidenberg, 1989).

In addition to the multitude of findings demonstrating poor performance by patients with AD on tasks that tap semantic memory, there are also some findings that seem to indicate preserved semantic memory. For example, although patients with AD perform poorly when asked to rank attributes related to a concept in order of importance (48% accurate), they are very accurate (95%) at identifying whether or not attributes are related to a concept (Grober, Buschke, Kawas, & Fuld, 1985). Furthermore, if the task simply involves deciding whether an attribute is related to a concept or not, individuals with AD have faster reaction times to high-importance attributes than low-importance attributes, indicating that their knowledge of the relative importance of different attributes of a concept is intact (Nebes & Brady, 1990). These and other findings, including demonstrations of preserved semantic priming in some studies (e.g., Nebes, Martin, & Horn, 1984; Ober, Shenaut, Jagust, & Stillman, 1991), have led a number of investigators to argue that patients with AD do not, in fact, have a loss or degradation of semantic knowledge but rather have impaired retrieval or other attentionally mediated processes involved in accessing this knowledge (e.g., Nebes, 1992; Ober & Shenaut, 1995).

Nebes and colleagues (e.g., Nebes & Brady, 1988, 1990, 1991; Nebes & Hallighan, 1995, 1996, 1999) have produced many findings that indicate intact semantic memory, and on the basis of this work they have formulated one alternative interpretation of the underlying impairment in AD. They have shown that the degree of impairment shown by patients with AD on tests of semantic memory is keenly dependent on the attentional demands of semantic retrieval. For example, whereas patients with mild-to-moderate AD perform well below normal on sentence completion tasks in which the missing word is relatively unconstrained (e.g., "They went to see the famous ____"), their performance approaches normal when the sentence provides strong contextual constraint (e.g., "Father carved the turkey with a ____"; Nebes, Boller, & Holland, 1986). In another demonstration Nebes and Hallighan (1999) showed that patients with AD can make accurate inferences based on the semantic context provided by a sentence, even if these involve objects they cannot name. Patients were presented with a sentence containing the name of a concrete category and were asked to select which of four pictures of members of the category

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This research was supported by National Institutes of Health Grants R01-AG14082 and R01 MH60414, the Searle Scholars Program, and University of Auckland Research Committee Grant 3442143. We thank Phil Wood of the Memory Clinic at North Shore Hospital, New Zealand, for his assistance with this project and Gavin Pilkington for assistance with recruiting participants. We also thank Irene Kan for her invaluable assistance with the implementation of the semantic selection tasks. We thank Karalyn Patterson for her helpful comments. Finally, we are grateful to all individuals who kindly volunteered to participate in this study and generously gave their time.

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was appropriate to the meaning of the sentence. The sense of the sentence was always consistent with a low-dominant member of that category. For example, for “The fireman picked up a tool to break down the door of the burning house,” the four drawings of category exemplars were screwdriver, chisel, ax, and pliers. Patients with AD were highly accurate (mean of 86%) even if they were unable to name the target object, and even more accurate (mean of 93%) for items they could name. Nebes and Hallighan (1999) reasoned that these two types of findings—preservation of the ability to retrieve semantic knowledge in some tasks or conditions, and poor performance when external constraint is low and internal attentional control is required—both imply that the problem is not one of semantic memory per se but one of attention-demanding processing of semantic memory.

In sum, two main claims have been made about the fate of semantic memory in mild-to-moderate AD. The simplest and most straightforward claim is that semantic memory is degraded. The alternative claim is that attention to semantic memory or, equivalently, attention-demanding retrieval from semantic memory, is impaired. It is, of course, possible that both impairments coexist.

The present study was conducted in an attempt to clarify the nature of the semantic processing impairment in AD and, in particular, the role of what Nebes and colleagues (e.g., Nebes, 1997; Nebes & Hallighan, 1999) have called *attentional processing* (and others have called *controlled* or *effortful processing*), by applying a set of concepts and tasks originally developed for investigations of semantic memory using functional neuroimaging. The main promise of this approach is that it will begin to integrate our understanding of semantic memory phenomena in AD within a theoretical framework that is emerging in the neuroimaging literature. That is, we can establish whether certain components of semantic processing, which have been operationalized and localized in imaging studies of healthy participants, are impaired or spared in AD. On the face of things, there may be a direct correspondence between the so-called “selection” process first studied in functional magnetic resonance imaging (fMRI) experiments, and the “attentional” processing described by Nebes and colleagues (e.g., Nebes, 1997; Nebes & Hallighan, 1999). In order to examine this possible correspondence, we adapted the tasks used to assess selection for use in behavioral studies with the AD population.

The concept of selection was originally developed in the course of reconciling certain inconsistencies in the functional neuroimaging literature on retrieval of semantic knowledge. Most studies involving semantic retrieval showed activation of the left inferior frontal gyrus (IFG), but a sizable minority did not. When the differences between the two sets of studies were scrutinized, it became apparent that the tasks yielding prefrontal activation required more than mere access of semantic memory; they required a relatively high degree of selection among competing sets of associated semantic and/or lexical representations. The tasks that did not activate prefrontal cortex were relatively free of this requirement.

To test the hypothesis that the selection demands of the semantic tasks determined whether or not prefrontal cortex is activated, Thompson-Schill, D’Esposito, Aguirre, and Farah (1997) identified three different semantic memory tasks from the functional neuroimaging literature and for each created versions with high- and low-selection demands. The three tasks, verb generation, sim-

ilarity judgment (comparison), and classification, were quite different from one another on the surface, whereas the high- and low-selection pairs within a task differed minimally on the surface. Nevertheless, the pattern of regional brain activation, and in particular the activation of the left IFG, correlated with the selection demands rather than the task.

Desmond, Gabrieli, and Glover (1998) also argued that left prefrontal cortex is associated with response selection on the basis of increased fMRI response on a word stem completion task for items for which there were many possible completions (e.g., STA____) compared with items with few possible completions (e.g., PSA____). Unfortunately participants failed to complete the stems for many items on the low-selection task ($M = 83\%$ compared with 99% for stems in the high-selection task). Because the design did not permit exclusion of trials in which participants did not produce a response, the diminished fMRI signal in the low-selection condition may simply result from lower response in the prefrontal cortex on trials in which no word was successfully retrieved. This caveat aside, however, the findings of Desmond et al. are certainly consistent with Thompson-Schill et al.’s (1997) account of selection demands.

Given the similarity between the ways in which attention-demanding retrieval (Nebes, 1997) and selection (Thompson-Schill et al., 1997) have been described, the question is raised whether the two processes are the same. That is, does the operationalization used for selection reveal the same dissociation in patients with AD as in the brain activation patterns of healthy participants? Although the early stages of AD are generally thought to involve medial temporal and posterior pathology, executive dysfunction is a common finding in the mild-to-moderate stages of the disease, and thus, through direct or indirect mechanisms, anterior regions of the brain are likely affected (e.g., Butters, Lopez, & Vicker, 1996; Collette, Van der Linden, & Salmon, 1999; Helkala et al., 1996; Reid et al., 1996). Studies using positron emission tomography have also typically shown that in AD the lowest glucose metabolic rates are found in regions near the hippocampus and extending into the temporo-parietal cortex but that there are also significant reductions in small areas of the frontal lobes (e.g., Johannsen, Jakobsen, & Gjedde, 2000; Herholz et al., 1999; Stein, Buchsbaum, Hof, Siegel, & Shihabuddin, 1998).

In the present study we administered three experimental tasks (lexical fluency, comparison, verb generation), each of which assesses selection ability by manipulating the relative selection demands in two conditions. Before we explain the precise nature of the manipulations in each task, it is important to clarify exactly what is meant by selection ability and selection demands. What common mechanism underlies the manipulation of selection demands across tasks that are very different on the surface? When a stimulus in any selection task is presented, it will activate many associated representations. The amount of competition between these representations, with regard to guiding an appropriate response, is key to modulating selection demands. Competition between representations could be increased (hence creating a high-selection condition) in a number of ways. First, the amount of conflict between activated representations will influence competition. The manipulation of selection demands in the comparison task (described below) is an example of this type of effect. Second, the degree of constraint in the set of representations activated by a

stimulus will also influence the level of competition between representations. The manipulation of selection demands in the fluency and generation tasks (also described below) are examples of this effect. In other words, the mechanism common to tasks that investigate selection ability is manipulation of the amount of competition among activated representations.

In this study the three experimental tasks are very different on the surface (just as in the neuroimaging study of Thompson-Schill et al., 1997), whereas the high- and low-selection pairs within each task differ only minimally on the surface. Two of the tasks, lexical fluency and verb generation, are production tasks, which differ in that one is constrained to have only a single response and the other has multiple responses. Selection demands in both of these tasks are modulated by manipulating the amount of constraint on the potential response, or responses, to the target stimuli. In the fluency task, the low-selection condition involves constraints on possible responses that can be generated in the minute provided by specifying the first two letters of words to be generated (*Fl*, *Ap*, and *St*). In contrast, the high-selection condition (in which words to be generated are specified by only a single letter, *F*, *A*, and *S*) provides much less constraint on possible responses and thus increases competition among activated representations. Similarly, in the verb generation task (Thompson-Schill et al., 1997), the low-selection condition again involves constraints on possible responses by including only nouns that have either few associated verb responses or a clearly dominant verb response. In contrast, nouns in the high-selection condition have many appropriate associated responses, thus increasing competition between activated representations.

The third task, the comparison task (Thompson-Schill et al., 1997), differs from the first two tasks as it does not require production per se. Selection demands are modulated by manipulating the amount of conflict between activated representations. In this task participants must compare a target word to two probe words and decide which probe is most similar (see Figure 1). In the low-selection condition the task is to pick which of two probe words is most similar in meaning to the target. A key feature of the low-selection condition is that almost any way of thinking about the stimuli would lead one to the same answer. The participant is free to attend to any dimension because they all point in the same direction. In other words, there is no conflict between activated representations. In the high-selection condition participants are forced to attend to only a single dimension and must do so to select

the correct answer, as the incorrect answer is always similar to the target in other ways. For example if the target item was *dime*, and the two choices were *quarter* and *penny*, the penny is more similar to the dime in size but the quarter is more similar in color. This creates a conflict among the representations activated by the target word.

In summary, in the high-selection conditions of all three tasks there is greater competition among semantic representations activated in response to target stimuli than occurs in the low-selection condition of that task. If patients with AD have a selection impairment, they should perform disproportionately worse on the high-selection condition of each task compared with control participants.

Method

Participants

The AD group comprised 21 individuals (10 female, 11 male), who ranged in age from 53 to 89 years ($M = 75.43$, $SD = 8.83$), recruited from the Memory Clinic of North Shore Hospital, Auckland, New Zealand. All had a diagnosis of probable AD as defined by the National Institute of Neurological Disorders and Stroke Work Group (McKhann et al., 1984). Individuals were excluded if they had a history of cerebrovascular accident, head injury, neurological disorders (other than AD), cardiovascular disease, chronic alcoholism or drug abuse, or psychiatric illness. No participants were using neuroleptic medications, and all had normal general medical, neurological, and blood chemistry screening tests. Participants were also required to have normal corrected eyesight, to be fluent English speakers, and to be in the mild-to-moderate stages of the disease process, as assessed by scores on the Mini-Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975). The lower cutoff used for moderate impairment was 10 out of 30. Mean score on the MMSE for participants with AD was 20.76 ($SD = 2.81$), with a range of 15 to 24. Twenty-six individuals volunteered for the study, but 4 were excluded because they scored below the lower MMSE cutoff score, and 1 was excluded because of visual problems.

Twenty-eight healthy older volunteers (16 female, 12 male), who ranged in age from 53 to 89 years ($M = 73.21$, $SD = 8.63$), composed the control group. The same criteria as described above were applied to control participants. The exception was a score of 24 out of 30 or better on the MMSE as the cutoff for inclusion as a control participant to screen for individuals with undiagnosed clinical impairments (e.g., Cullum, Smernoff, & Lord, 1991; Galasko et al., 1990). Mean score on the MMSE was 29.5 ($SD = 4.91$). Participants were recruited from a variety of community-based social organizations for older people. Thirty-two healthy volunteers were tested, but the first 4 participants served as pilot participants before methodological details were finalized, leaving a total of 28 participants.

Written informed consent was obtained from all participants or caregivers when appropriate. Demographic characteristics of the AD and control groups are presented in Table 1. The groups did not differ significantly in terms of sex, $\chi^2(1, N = 49) = 0.44$, $p = .51$; age, $t(47) = 0.88$, $p = .38$; or years of education, $t(47) = 1.57$, $p = .12$. As expected, a significant difference between MMSE scores was observed, $t(47) = 10.43$, $p < .01$.

For two of the three experimental tasks (comparison and verb generation), the 28 control participants were allocated to one of two control groups. One was administered tasks at the same rate as the AD group (i.e., trial duration of 20 s), whereas the other group (speeded control group) received a speeded presentation of the two tasks (i.e., trial duration of 5 s for both tasks). The aim of the faster presentation was to increase task difficulty in line with task difficulty for the AD group and thus control for the possibility that any group differences result purely from differences in the varying overall difficulty of the conditions for AD and control participants.

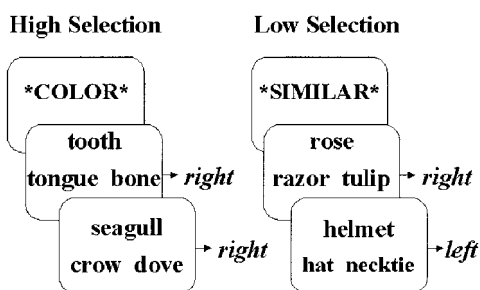


Figure 1. Comparison task: sample stimuli from the comparison task. In the high-selection condition participants made comparisons between the target word and probe words according to a particular dimension, in this example, color. In the low-selection condition the comparison between the target and probe words was according to global similarity.

Table 1
Demographic Characteristics of Alzheimer's Disease (AD) and Control Groups

Characteristic	AD				Control			
	No.	<i>M</i>	<i>SD</i>	Range	No.	<i>M</i>	<i>SD</i>	Range
Sex (male, female)	11, 10				12, 16			
Age (years)		75.43	8.83	53–89		73.21	8.63	53–89
Education (years)		12.38	2.06	9–19		11.43	2.13	8–16
MMSE score ^a		20.76	2.81	15–24		29.5	4.91	24–30

Note. MMSE = Mini-Mental State Examination.

^a Maximum score = 30.

The three groups were not significantly different from each other on the demographic variables of sex, $\chi^2(2, N = 49) = 0.44, p = .80$; age, $F(2, 46) = 0.47, p = .63$; or years of education, $F(2, 46) = 2.05, p = .14$. A significant difference between the groups on MMSE scores, $F(2, 46) = 72.99, p < .01$, was observed, with post hoc least significant differences tests demonstrating a difference between the AD group and the two control groups (speeded and nonspeeded, $p < .01$) but not between the two control groups ($p = .55$).

Materials

Lexical Fluency Task

This task is based on the commonly used verbal fluency task, the Word Fluency test (FAS; Spreen & Strauss, 1998). The high-selection condition involved the standard administration of the FAS task, namely, asking participants to produce as many words as possible that start with a particular letter (*F, A, S*) in 60 s. Responses must exclude proper nouns, numbers, and repetitions of a word with a different suffix. In the low-selection condition there were again three trials, but participants had to produce as many words as possible within 60 s that start with the letters *Fl, Ap, and St*. Thus, the number of potential responses (and hence the number of competing responses) is constrained by specifying the first two letters with which words must start.

Comparison Task (Thompson-Schill et al., 1997)

Stimuli. Participants were required to compare a target word to two probe words and decide which probe was most similar. In the high-selection condition, participants picked which of the probe words was most similar to the target along a specified dimension (color, function, or shape). In the low-selection condition participants picked which of the two probe words was most similar in meaning to the target (i.e., the comparisons were based on global similarity). There were 108 experimental trials, 54 low selection and 54 high selection (see Figure 1 for examples).

Procedure. Experimental trials were presented in alternate blocks of 18 high- and 18 low-selection trials. In the high-selection blocks, dimensions were grouped so that within a given block, attribute judgments were made about only one dimension. Two demonstration trials and up to six practice trials preceded each block of experimental trials. On each trial a fixation point “+” was followed by simultaneous presentation of the target and two probes on a computer screen. Participants were instructed to “decide which of the two lower words is most like the top word,” according to either color, function, or shape (high selection), or in overall similarity (low selection). In the high-selection condition, the target dimension appeared above the experimental stimuli to reduce the memory demands of the task. The stimuli remained on the screen either until the participant responded or for a maximum of 20 s for the AD and nonspeeded control groups, and for a maximum of 5 s for the speeded control group. Participants were allowed to rest between, or if necessary within, blocks and to

resume testing at their own pace. Participants responded by stating the word they thought was most similar. In this task no feedback was given.

Verb Generation Task (Thompson-Schill et al., 1997)

Stimuli. Participants were required to generate a verb related to a visually presented noun. In the high-selection condition, items were nouns with many appropriate associated responses without any clearly dominant response. In the low-selection condition, items were nouns with few associated responses or with a clearly dominant response. For example, the verb *row* is one of a number of possible responses generated to the noun *boat* (high selection). However, the verb *play* is a dominant response generated to the noun *piano* (low selection).

The stimuli were 96 concrete nouns (Kucera–Francis frequency range from 0 to 591, *Mdn* frequency = 32; word length range from 3 to 8, *Mdn* = 4) divided into two groups on the basis of verb generation data from two independent groups of participants ($n = 30$ and $n = 50$). Participants were asked to generate a verb from each noun. A ratio of the relative frequency of the most common completion to the relative frequency of the second-most-common completion was calculated as a measure of response strength. On the basis of these data, two groups of 48 nouns were created so that nouns in the high-selection group (response strength ratio range from 1.0 to 3.0, *Mdn* = 2.0) differed from nouns in the low-selection group (response strength ratio range from 5.0 to 50.0, *Mdn* = 13.34) in terms of response strength ratio, $t(94) = 13.85, p < .01$, but not word frequency, $t(94) = 0.76, p = .45$. (Statistics were performed on the cube root of ratio and frequency.) In this study two of the original 96 nouns (*yarn* and *cane*) normed on American participants were removed from the stimulus set because there was concern that common usage of these words differed in New Zealand. This left 47 high-selection items and 47 low-selection items.

Procedure. Each trial began with a fixation point, “+”, followed by a randomly selected noun from either the high- or low-selection group, presented centrally on a Macintosh G3 PowerBook (active-matrix color display, with a screen size of 1024 × 768 pixels and a graphics resolution of 72 × 72 dots per inch). Participants were instructed to say a word that described either “what the object does or what you do with the object.” The noun remained on the screen until the participant responded, or for a maximum of 20 s if no response was given for the AD and nonspeeded control groups, or for a maximum of 5 s for the speeded control group. Prior to the experimental trials a set of 16 practice trials was presented, with 2 of these demonstration trials performed by the experimenter. The experimental trials were divided into three blocks of 32 stimuli; participants were allowed to rest between, or if necessary within, blocks and resume testing when they were ready. Practice trials were repeated if necessary for the AD group before the second and third blocks of experimental trials. If a participant made an inappropriate response (e.g., a nonverb response), the error was noted but the instructions for the task were repeated. Responses were recorded on tape for later scoring.

Procedure

Ethical approval was obtained from the Auckland Ethics and the University of Auckland Human Subjects Ethics Committees. Each testing session was conducted in the same manner for all participants. In an initial interview (that for participants with AD also included a family member) demographic and biographical information was obtained. The MMSE was then administered, followed by the experimental tests. Instructions were repeated as many times as was necessary before and during tasks. Breaks occurred whenever requested or if the researcher judged that the individual was becoming fatigued. Participants were offered the opportunity to spread the testing over two sessions. Overall, the number, length, and timing of breaks varied a great deal among the participants, with participants with AD taking many more breaks and an extra session in which to complete the testing. In each case the second session took place within 1 week of the first session.

Results

To investigate whether individuals with AD were differentially impaired on the high-selection conditions of the three selection tasks, performances were analyzed using repeated measures analyses of variance (ANOVA), with group (AD and control groups) a between-subjects factor and selection (high, low) a within-subjects factor. The error data for two of the tasks (comparison and verb generation) were also analyzed to determine whether there were different patterns of errors in the three groups that performed these tasks. Once again, repeated measures ANOVAs were used, with group (AD, speeded control, and nonspeeded control) a between-subjects factor and selection (high, low) and error type (incorrect response, nonresponse) within-subjects factors. On the comparison and verb generation tasks, any significant interactions involving the three-level factor, group, were further investigated by computing the interaction for each pairing (i.e., AD and nonspeeded, AD and speeded, and nonspeeded and speeded) and testing this against the error term from the original analysis.

Lexical Fluency Task

Figure 2 shows the mean number of correct responses in the high- and low-selection conditions of the lexical fluency task for

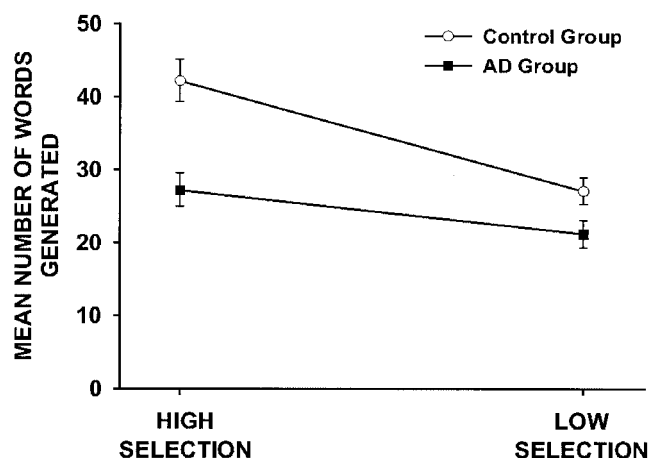


Figure 2. Mean number of words (\pm SE) produced on the high- and low-selection conditions of the lexical fluency task by Alzheimer's disease (AD) and control groups.

the AD group and the control group ($n = 28$). As the order of the high- and low-selection conditions was counterbalanced across participants, the repeated measures ANOVA also had order as a between-subjects factor. There was, however, no main effect of order, $F(1, 45) = 0.81, p = .37$, and no significant interaction between order and selection level, $F(1, 45) = 1.01, p = .32$. There was a significant main effect of group, $F(1, 47) = 334.89, p < .01$, with the control group ($M = 34.61, SD = 14.80$) producing a greater number of words overall than the AD group ($M = 24.21, SD = 10.09$). There was also a significant main effect of selection, $F(1, 47) = 73.80, p < .01$, with more words produced on the high-selection ($M = 35.73, SD = 15.31$) than the low-selection condition ($M = 24.57, SD = 9.70$). In other words the high-selection condition on this task was easier than the low-selection condition, in contrast with the relative difficulty of the selection conditions on the other two tasks. If the group with AD is disproportionately affected by selection demands, there should be a significant interaction between group and selection. This interaction was, in fact, significant, $F(1, 47) = 12.03, p < .01$, with the AD group producing differentially fewer responses on the high-selection condition. Furthermore, 29% of the AD group (6 of 21) produced more words on the more difficult low-selection condition than they did on the high-selection condition, whereas only 4% of control participants (1 of 28) showed this pattern. A chi-square test confirmed that a significantly greater number of participants with AD showed this pattern of responding than did control participants, $\chi^2(1, N = 49) = 6.13, p = .03$.

Comparison Task

Figure 3 shows the mean number of correct responses in the high- and low-selection conditions for the AD and two control groups on the comparison task. There was a significant main effect of group, $F(2, 46) = 9.50, p < .01$, with participants with AD the least accurate ($M = 44.76, SD = 8.47$), followed by the speeded control participants ($M = 47.68, SD = 7.32$), then the nonspeeded control participants ($M = 48.36, SD = 5.25$). Post hoc Tukey's honestly significant difference (HSD) tests revealed a significant difference in accuracy between the AD group and both control groups (AD and nonspeeded, $p < .01$; AD and speeded, $p = .01$), but no significant difference between the two control groups ($p = .77$). A significant main effect was also found for selection, $F(1, 46) = 349.61, p < .01$, with performance on high-selection trials ($M = 40.31, SD = 5.42$) less accurate than performance on low-selection trials ($M = 52.94, SD = 1.25$).

Regarding the question of interest, the key interaction, Group \times Selection, was significant, $F(2, 46) = 6.30, p = .01$. Tests of simple interaction revealed significant Group \times Selection interactions for both the AD and nonspeeded control groups, $F(1, 46) = 11.64, p < .01$, and the AD and speeded control groups, $F(1, 46) = 5.1, p < .05$, but not between the nonspeeded and speeded control groups, $F(1, 46) = 1.11, p > .10$. Although these findings indicate that the AD group performed differentially worse on the high-selection condition, interpretation of these data are made difficult by the near ceiling effects in the low-selection condition ($M = 53/54$) of all three groups. In an attempt to clarify whether this significant interaction remains when performance on the low-selection condition is below ceiling, we removed all participants who scored a perfect 54/54 on the low-selection condition from

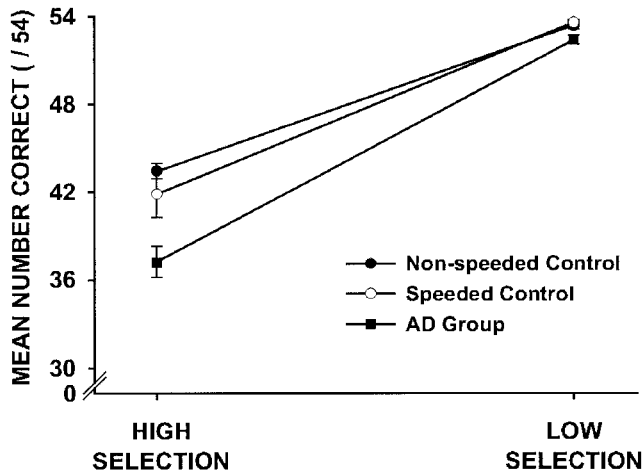


Figure 3. Mean number of correct responses ($\pm SE$) on the high- and low-selection conditions of the comparison task by Alzheimer's disease (AD) and control groups.

each of the three groups. This left a total of 16 participants with AD and 6 control participants in each of the two control groups. As there was no significant difference in the performance of the two control groups, they were combined, giving $n = 12$. Analysis of these data revealed a significant main effect of group, $F(1, 26) = 12.62, p < .01$, and a significant main effect for selection, $F(1, 26) = 225.83, p < .01$. As before, the Group \times Selection interaction was significant, $F(1, 26) = 9.03, p < .01$. Figure 4 shows the mean number of correct responses in the two selection conditions after removing all participants with perfect scores on the low-selection condition. The significant interaction shows no signs of reducing, although it must be acknowledged that the manipulation only reduced performance on the low-selection con-

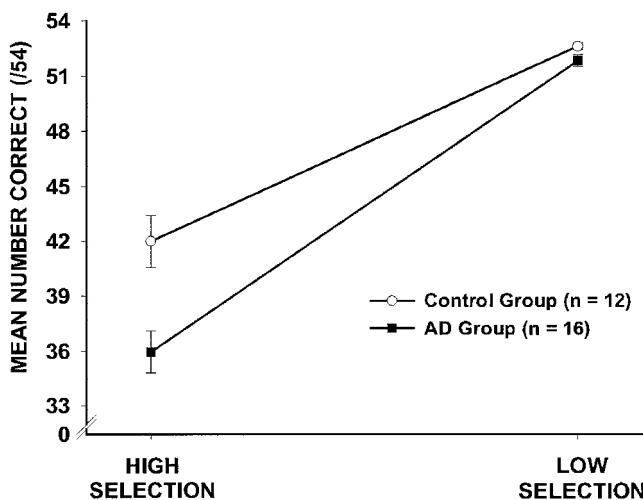


Figure 4. Mean number of correct responses ($\pm SE$) on the high- and low-selection conditions of the comparison task by modified Alzheimer's disease (AD) and control groups (without individuals performing at ceiling).

dition by a small amount (mean accuracy of 96%). Unfortunately, removing further participants left an insufficient group size for analysis.

Errors on this task were one of two types: incorrect responses (selecting the wrong probe word) or nonresponses (failing to provide any response within the time allowed). A significant main effect of error type was found $F(1, 46) = 131.20, p < .01$, with more incorrect answers made ($M = 5.77, SD = 6.36$) than nonresponses ($M = 1.30, SD = 2.51$). A significant interaction was found between error type and group, $F(2, 46) = 14.71, p < .01$, but this was superseded by a significant three-way interaction among selection, error type, and group, $F(2, 46) = 13.93, p < .01$ (see Figure 5). Tests of simple interaction were conducted for each group pairing according to error type. For incorrect responses, significant interactions between group and selection were found for the AD and the nonspeeded control group, $F(1, 46) = 10.95, p < .01$, and for the AD and speeded control group, $F(1, 46) = 29.45, p < .01$, but not for the nonspeeded and speeded control groups, $F(1, 46) = 3.74, p > .05$. In other words, the effect of the high-selection condition on incorrect responding was relatively greater for the AD group than the two control groups. For nonresponses, the only significant group by selection interaction was between the two control groups, $F(1, 46) = 10.99, p < .01$. The speeded group made differentially more nonresponses on the high-selection condition relative to the nonspeeded control group only.

Verb Generation Task

Correct responses on the verb generation task included single verbs and verb phrases. If a word was used that could be either a verb or a noun, the response was marked as correct (e.g., *doll-dress, bell-sound*). There was a significant main effect of group, $F(2, 46) = 5.91, p < .01$, with participants with AD the least accurate ($M = 40.02, SD = 6.57$), followed by the speeded control participants ($M = 43.21, SD = 3.51$), then the nonspeeded control participants ($M = 45.14, SD = 2.38$). Post hoc Tukey's HSD tests

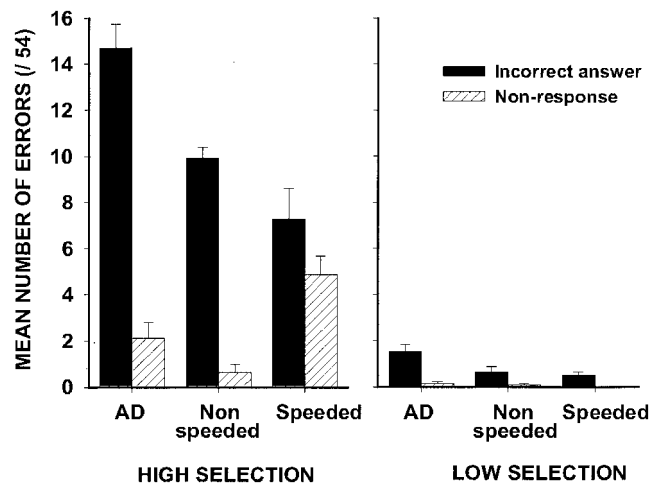


Figure 5. Mean number of incorrect responses and nonresponses ($\pm SE$) on the high- and low-selection conditions of the comparison task by Alzheimer's disease (AD) and control groups.

revealed a significant difference between the AD group and the nonspeeded control group ($p = .01$), but no significant difference between the nonspeeded and speeded control groups ($p = .50$), or between the AD group and the speeded control group ($p = .11$). A significant main effect was also found for selection, $F(1, 46) = 45.21, p < .01$, with performance on high-selection trials ($M = 40.90, SD = 5.50$) less accurate than performance on low-selection trials ($M = 43.90, SD = 4.67$). The critical Group \times Selection interaction was significant at the .05 level, $F(2, 46) = 3.20, p = .05$. Tests of simple interaction revealed a significant interaction between the AD and nonspeeded control group, $F(1, 46) = 6.34, p < .05$, but not between the AD and speeded control group, $F(1, 46) = 0.65, p > .1$, or the nonspeeded and speeded control groups, $F(1, 46) = 2.44, p > .1$ (see Figure 6). In other words, the AD group performed differentially worse on the high-selection condition than nonspeeded control participants (the control participants who performed the task under the same conditions as the patients with AD) only. The two control groups did not differ significantly in their patterns of responding.

On this task three error types were possible. Task errors resulted from failing to follow the task instructions, such as reading the noun presented rather than generating a word to that noun. As very few were made by any of the three groups, these were not included in the analysis. Incorrect responses were a nonverb response such as a noun or adjective. A nonresponse was the failure to produce any response in the time allowed. A significant main effect of error type was found, $F(1, 46) = 7.39, p = .01$, with more incorrect responses made ($M = 2.99, SD = 3.79$) than nonresponses ($M = 1.53, SD = 2.63$). No significant interaction was found between selection, error type, and group, $F(2, 46) = 1.22, p = .30$ (see Figure 7), but there was a significant interaction between error type and group, $F(2, 46) = 11.71, p < .01$. Tests of simple interactions revealed that the speeded control group made differentially more nonresponses relative to incorrect responses compared with both the AD group, $F(1, 46) = 23.42, p < .01$, and the nonspeeded group, $F(1, 46) = 7.06, p < .05$. The interaction between the AD and nonspeeded control group was not significant, $F(1, 46) = 3.72, p > .05$.

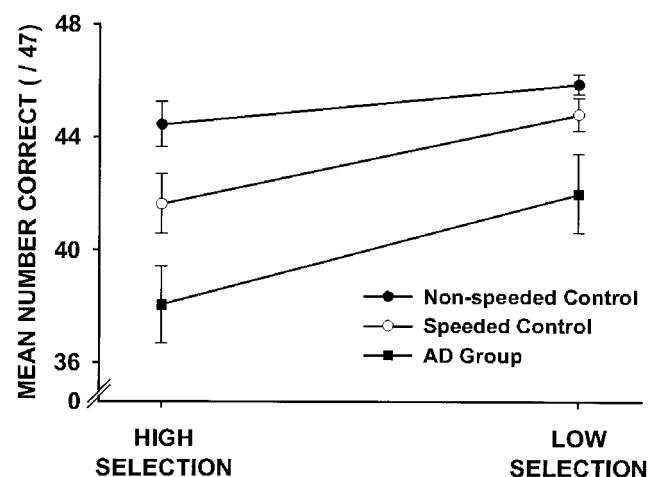


Figure 6. Mean number of correct responses ($\pm SE$) on the high- and low-selection conditions of the verb generation task by Alzheimer's disease (AD) and control groups.

Discussion

Patients with AD were differentially impaired on the high-selection condition of all three selection tasks administered. In other words, on these tasks they showed disproportionate deficits when the condition placed high demands on the ability to select relevant information from a number of competing alternatives. This finding was not simply because high-selection conditions are always more difficult; in the lexical fluency task the high-selection condition was easier than the low-selection condition, yet the AD group was differentially impaired on this easier condition. Furthermore, on this task a number of patients with AD actually generated more words on the more difficult low-selection condition than they did on the high-selection condition (whereas only 1 control participant did this). Performance on this task, therefore, provides strong support for the hypothesis that individuals with AD have an impairment in selection ability.

Patient performance on the comparison task is also consistent with this claim, although it could be argued that these data are ambiguous because of the ceiling effects for all groups in the easier low-selection condition. When we removed all participants who performed without error on the low-selection condition, the crucial group by selection interaction was undiminished and remained significant, although this manipulation was not able to eliminate totally the ceiling effects. Converging evidence for a selection impairment comes from the analysis of error types in this task, in which patients with AD made predominantly selection errors, that is, responses based on the irrelevant dimension of similarity, and they made these errors relatively more in the high-selection condition. Although control participants also made selection errors, they did so at a much lower rate, in both absolute terms and relative to nonresponse errors. Thus, performance on the comparison task provides moderate support for the claim that patients with AD are impaired when semantic retrieval places high demands on selection.

Consistent with the two other tasks, the verb generation task also revealed disproportionate impairment for patients with AD in the high-selection condition relative to the performance of the nonspeeded control participants. On this task, however, speeding up the task for control participants produced a pattern of performance on the two selection conditions that fell between that of the patients with AD and the nonspeeded controls and did not differ reliably from either. In other words, patients with AD showed a selection impairment relative to control participants who performed the task under identical conditions, but not relative to control participants who had only 5 s to respond to each stimulus. However, the speeded control participants made a greater proportion of nonresponse errors than both of the other groups, suggesting that the effect of speeding the task, at least to the degree used in this study, was to make it difficult to generate any response to items in the allowable time regardless of selection condition. Certainly speeding up control participants so that they make errors at a rate more comparable to that of participants with AD does not simply produce the same pattern of responses and selection impairment as seen in AD. Overall, these results on the verb generation task are consistent with a selection impairment in AD but provide only moderate support for the claim because of the performance of the speeded control group. On the basis of the totality of data presented for the three tasks, however, we can say that

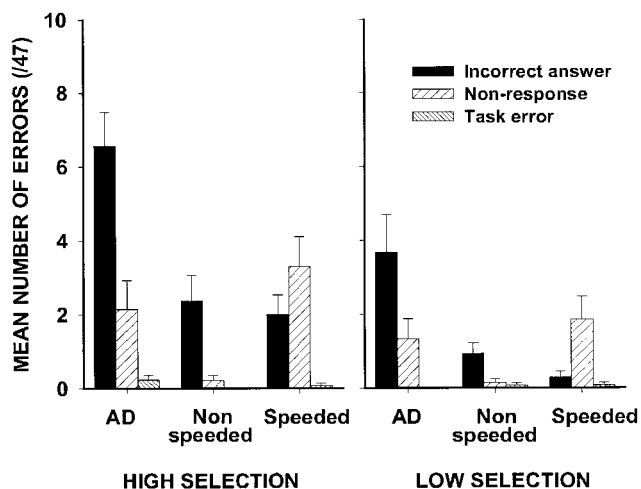


Figure 7. Mean number of incorrect responses and nonresponses (+ SE) on the high- and low-selection conditions of the verb generation task by Alzheimer's disease (AD) and control groups.

there is some clear evidence for a semantic selection impairment in AD, along with other consistent but less clear findings.

Manipulation of selection demands within a task can influence task difficulty. In this study, for example, the high-selection conditions of two tasks (comparison task and verb generation task) were more difficult for participants when accuracy was the dependent measure. As noted above, however, the high-selection condition on the third task (lexical fluency) was less difficult than the low-selection condition. Thus, difficulty does not covary with selection across our three tasks. Although the differences in difficulty between high- and low-selection conditions were not equated across the three tasks, there is no doubt that in the key task for this issue, namely, lexical fluency, control participants provided significantly more responses on the high-selection condition than the low-selection condition ($M = 42.11$, $SE = 2.90$, and $M = 27.11$, $SE = 1.84$, respectively). Overall, these findings illustrate that although increasing selection demands may make a task more difficult, it does not always do so. A priming task used by Thompson-Schill, D'Esposito, and Kan (1999) also increased selection demands but improved behavioral performance. In this task, priming irrelevant information increased selection demands relative to an unprimed condition (by providing competing information about a concept) but decreased difficulty (as evidenced by significantly faster response times and increased accuracy of responses). Although priming irrelevant information improved behavioral performance relative to the unprimed condition, the general facilitatory effects of priming relevant information were reduced by this manipulation, indicating there was a behavior cost of the increased selection requirement.

A neuroimaging study with healthy participants indicated that the left IFG is a critical brain region for semantic selection (Thompson-Schill et al., 1997). This was supported by a study of focally damaged patients that showed that patients with frontal lesions involving the left IFG had a disproportionate impairment on the high-selection condition of the verb generation task (Thompson-Schill et al., 1998). The present results therefore suggest that there is damage or dysfunction that influences functioning

of the left IFG in mild-to-moderate AD. Although the primary neuropathological changes in AD occur predominantly in temporal and parietal regions, at least in the early stages of the disease, subsequently further regions of association cortex are involved, including frontal cortex (Arnold, Hyman, Flory, Damasio, & Van Hoesen, 1991; McKee, Kosik, & Kowall, 1991). Furthermore, even if the characteristic AD pathology of plaques and tangles is not present in frontal cortex, functioning of these regions may be disrupted by damage to the extensive connections between prefrontal cortex and the hippocampal formation (e.g., Goldman-Rakic, 1990). Certainly there is good evidence that early in the disease "executive dysfunction" is seen in the performance of patients with AD (e.g., working memory tasks; generation tasks; tasks involving reasoning, abstraction, and planning; Brugger, Monsch, Salmon, & Butters, 1996; Morris, 1994). Impaired performance on tasks with high selection demands provides another behavioral example indicating dysfunction of prefrontal cortex in AD, in this instance involving left IFG.

The findings of the neuroimaging study with healthy participants (Thompson-Schill et al., 1997), the study of patients with focal lesions (Thompson-Schill et al., 1998), and this study together suggest that other patient groups with frontal pathology or dysfunction might show similar deficits with manipulation of selection demands. For example, individuals with Korsakoff's syndrome, Parkinson's disease, and schizophrenia might show disproportionate impairment under high-selection conditions. In contrast, one would not expect the performance of patient groups with damage to posterior regions of the cortex (e.g., patients with temporal lobectomies) to be disproportionately sensitive to modulation of selection demands.

How does a semantic selection impairment in AD relate to other findings of semantic processing in AD? To our knowledge, this is the first investigation explicitly designed to assess selection abilities in patients with AD. However, other published studies have included experimental manipulations that affect the selection demands in retrieval tasks. Randolph et al. (1993) used different kinds of cues to facilitate fluency performance in an AD population. In an animal fluency task, they either obtained as many animal names as possible in 60 s or provided subcategory prompts (such as *pets* and *jungle animals*) every 15 s. One could view the latter as a low-selection fluency condition, as the smaller the category, the fewer the competing responses. In contrast to our findings on the lexical fluency task, Randolph et al. did not find that provision of these retrieval cues improved the performance of participants with AD. However, the cues required the use of finer grained, subordinate category information, which is thought to be more vulnerable than superordinate categories such as *animal* (e.g., Hodges, Salmon, & Butters, 1992; Troster, Salmon, McCullough, & Butters, 1989), and this may have outweighed the selection benefits in the cued condition. The different timing of the cued and uncued conditions also makes them difficult to compare. The differential benefits of low selection demands may only become evident with longer trial times. In other words, had Randolph et al. used a 60-s trial length for a subcategory of animals, they might have seen relatively better performance on this condition.

Grande, McGlinchey-Berroth, Milberg, and D'Esposito (1996) argued that impairment in selective attention may underlie difficulties of patients with AD on semantic memory tasks. Using a semantic priming task, they showed that patients with AD were

unable to inhibit the activation of irrelevant semantic information. Two pictures were briefly presented to participants, who were instructed to attend to only one of the two, indicated by color. A target word then had to be read as quickly as possible. Whereas healthy control participants showed facilitation only for target items that were names of the attended prime picture, participants with AD showed facilitation from both the attended and unattended pictures. The authors concluded that irrelevant semantic information is activated, either because the initiation of selective attention mechanisms is impaired or because, although initial selection of the prime occurs, patients with AD are unable to minimize the interfering effect of automatically activated information from the unattended prime. Grande et al. claimed these results are consistent with Posner's (1980) suggestion that the processes involved in orienting and attending to external stimuli can also be involved in orienting within the semantic memory system. They further hypothesized that common errors made by patients with AD on semantic tasks such as naming and fluency could be explained by the patients' inability to ignore distracting information, in conjunction with impairment in the ability to disengage and shift attentional resources (Parasuraman, Greenwood, Haxby, & Grady, 1992). Thus, on confrontation naming tasks, patients with AD may activate all relevant associates in semantic memory but be unable to ignore incorrect competing representations that are prepotent (because of either higher frequency or saliency) because of a reduced ability to rapidly disengage and shift attention from an incorrect associate.

Our account of impaired selection abilities would make similar predictions but for different reasons. We would argue that selection mechanisms are invoked either when the correct response is not the prepotent one (as in the naming example above) or when there is no prepotent response, because there is a need to select among competing alternatives to guide the response. Impairment of selection mechanisms (which depend on working memory to mediate response selection based on the weighting of active information) would produce similar errors on general confrontation naming tasks. Unfortunately, the tasks used in this study do not distinguish between these two hypotheses clearly.

Another alternative account of the underlying semantic impairment in AD is the *gain-decay hypothesis*, namely, that the time constant of spreading semantic activation is reduced, which causes disruption in the rate and peak levels of activation within the semantic network (Milberg, McGlinchey-Berroth, Duncan, & Higgins, 1999). As a result, semantic representations become more or less available than normal, depending on the time frame in which the information must be processed. This account not only specifies the aspect of semantic retrieval impaired in AD but also, according to Milberg et al., specifies a biologically plausible mechanism consistent with the changes in synaptic connectivity accompanying the development of neuritic plaques and neurofibrillary tangles in the early stages of AD.

Proponents of the gain-decay hypothesis claim it can potentially account for AD performance on implicit and explicit semantic memory tasks. Its ability to account theoretically for the puzzling variability of AD performance on semantic priming tasks (normal semantic priming, reduced priming, and in some cases hyperpriming; e.g., Chertkow et al., 1989; Martin, 1992) is appealing, but claims about performance on explicit semantic memory tasks are most relevant to this study. Within this model the reduced time

constant of activation in AD should cause strong semantic associates to reach threshold sooner and rise to a relatively higher level of activation than weak semantic associates, which will drop below threshold more quickly. Thus, failures are predicted whenever a strong associate competes with a weaker associate (e.g., on confrontation naming tasks responding with a basic-level label, *bird*, rather than the weaker, but more accurate, subordinate-level label, *robin*). Milberg et al. (1999) also predicted that "AD patients will have a reduced probability of responding to weaker learned associations even if these are more contextually appropriate" (p. 653). However, Nebes and Hallighan's (1999) findings appear to contradict this prediction. Patients with AD correctly selected the appropriate category exemplar (from a set of four pictures) based on the semantic context provided by a sentence, even though the sense of each sentence was always consistent with a low-dominant member of that category, and one of the alternative competing responses was always a high-dominant member of the category.

Unfortunately, the selection tasks in our study do not test Milberg et al.'s (1999) hypothesis of semantic impairment in AD. The gain-decay hypothesis predicts failures whenever an inaccurate strong associate competes with a weaker accurate associate on explicit semantic tasks. Although the manipulations we used increased selection demands, we did not systematically make the correct response a relatively weaker associate than other candidate responses. One way in which the two hypotheses differ, however, relates to predictions about the effect of high constraint on responses. According to the gain-decay hypothesis, even if weaker learned associations are more contextually appropriate (i.e., high constraint provided by the semantic context), there will be a reduced probability of responding with these. According to the selection hypothesis, however, high levels of constraint reduce selection demands. Thus, if selection abilities are impaired, conditions of high constraint will result in greater accuracy even for weak semantic associates.

In fact, paradigms demonstrating that the performance of participants with AD is differentially facilitated by semantic constraint relate most directly to our findings of impaired selection abilities in AD. For example, when constraint is high in a sentence completion task, there are fewer possible competing alternatives for the final word or phrase, and the selection demands are therefore low. Conversely, low-constraint sentences place high demands on semantic selection processes. Interpretation of the differential facilitation of performance in participants with AD in high-constraint (and low-selection) conditions has traditionally been that of an intact semantic memory structure and impaired semantic access (e.g., Nebes et al., 1986). Leaving aside the question of whether semantic memory itself is intact, our results and interpretation are very consistent with this position. Indeed, we do not view the selection hypothesis as an alternative to the attention-demanding access hypothesis. The former is a somewhat more specific claim about the nature of the attentional demands that cannot be met in AD, and it has been independently operationalized in a variety of ways in the neuroimaging literature. In addition, we do not conclude that a fundamental impairment in semantic memory per se does not exist in AD. Rather, we suggest only that there is at least one additional impairment, namely, in selection abilities, which in some tasks will interact to further impair performance.

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Received November 6, 2001

Revision received April 14, 2003

Accepted April 29, 2003 ■