



Published in final edited form as:

Cogn Behav Neurol. 2009 December ; 22(4): 229–235. doi:10.1097/WNN.0b013e3181b7f3b1.

Response bias for picture recognition in patients with Alzheimer's disease

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Abstract

Objective—To investigate whether changing recognition stimuli from words to pictures would alter response bias in patients with Alzheimer's disease (AD).

Background—Response bias is an important aspect of memory performance in patients with AD, as they show an abnormally liberal response bias compared to healthy older adults. We have previously found that despite changes in discrimination produced by varying the study and test list length, response bias remained remarkably stable in both patients with AD and older adult controls.

Methods—Patients with mild AD and healthy older adults underwent two separate study-test sessions of pictures and words. For both pictures and words, increasing study-test list lengths were used to determine whether bias changed as a factor of discrimination or task difficulty.

Results—Consistent with apriori hypotheses, healthy older adults showed increased discrimination and shifted to a more liberal response bias for pictures compared to words. In contrast, despite their higher level of discrimination for pictures, patients with AD showed a similar response bias for both pictures and words. Bias was consistent across varying study-test lengths for both groups.

Conclusions—These results suggest that response bias is a relatively invariant factor of an individual with AD that remains liberal regardless of discrimination or stimulus type.

Keywords

Alzheimer's disease; recognition memory; response bias; picture superiority effect

Introduction

Most tests that are available for characterizing the memory problems associated with Alzheimer's disease (AD) quantify memory as a measure of accuracy determined by the number of items that can be correctly remembered. These tests provide only a partial picture of memory deficits because they do not measure factors such as response bias, which is also an important aspect of a patient's performance.

Most recognition memory tests report a corrected measure. The number of baseline false alarms (“old” responses to unstudied items) is subtracted from the total number of hits (correctly recognized studied items). Using this method assigns the same score to a patient who has relatively few hits and a low number of baseline false alarms, as to a patient who has a relatively large number of hits and many baseline false alarms. For example, consider two patients who each receive a score of 6 on the recognition portion of the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) word list memory test¹, a test commonly used in clinical diagnosis of AD in which there are 10 studied and 10 unstudied words. The first patient correctly endorses only 6 of the 10 studied words and none of the unstudied words. The second patient correctly endorses all 10 studied words but also incorrectly endorses 4 of the unstudied words. Do these patients have the same problems with their memory? The answer is likely no. The first patient shows a *conservative response bias*, that is, they responded “old” less than 50% of the time, while the second patient had a *liberal response bias* because they responded “old” greater than 50% of the time. Despite having the same recognition score, these two patients probably have different memory problems, which may be attributable to different anatomical and neurochemical dysfunction. Focusing on discrimination as the sole measure of memory performance would overlook such differences. A more descriptive measure of recognition memory would account for response bias. Memorial response bias and accuracy are both important measures because evidence from earlier research shows that response bias is, for the most part, independent of accurate recollection².

Response bias is a particularly relevant aspect of memory when studying patients with AD, since this population differs from healthy older controls in bias as well as memory accuracy³. In our first study investigating memory and response bias for lists of words, we found that despite changes in discrimination produced by varying the study and test list length, response bias remained remarkably stable in both patients with AD and older adult controls³. In our second study investigating memory and response bias in words, we found that both patients with AD and older adult controls were able to shift their response bias when given an instructional manipulation⁴. Thus, we have shown that while response bias tends to be stable in an individual, it is not invariant, and can be altered by test instructions. In the present experiment we were interested in investigating whether changing the experimental stimuli from words to pictures would alter response bias in patients with AD.

Memory for verbal or written information is critically important in some settings, but memory for pictorial information may generally be more ecologically important. Older adults and patients with AD are constantly faced with new visual information to be remembered so memory performance in the real world depends heavily on memory for such detailed visual information as images, scenes, people, landmarks, and medications. Numerous studies of recognition memory suggest pictures are better remembered compared to words in healthy younger and older adults^{5,6} (for a review, see⁷). Further, our previous work has also shown that despite overall worse memory performance, patients with AD also continue to demonstrate the picture superiority effect⁸. Although this picture superiority effect describes higher discrimination for pictures compared to words, only a few studies have investigated response bias for pictures², and none have compared response bias of pictures versus words in patients with AD. Based on our previous finding that response bias was not affected by changes in discrimination when task difficulty was list length was manipulated³, we hypothesized in the current study that the patients' response bias would not change when discrimination increased as a result of studying pictures compared to words. In contrast, we hypothesized that healthy older adults' response bias would become more liberal with pictures compared to words. Previous work has shown that healthy adults adopt a more conservative response bias when memory judgments become more difficult⁹. Therefore, we expected that as discrimination decreased in the words condition compared to the picture condition, response bias would become more conservative.

Methods

Participants

Twelve healthy older adults and twelve patients with a clinical diagnosis of probable AD were recruited for the study from the Memory Disorders Unit at Brigham and Women's Hospital in Boston, MA, the Geriatric Research, Education, and Clinical Center at the Edith Nourse Rogers Memorial Veterans Hospital, in Bedford, MA, and the Boston University Alzheimer's Disease Center. The healthy older adults (6 male) had a mean age of 73.8 years (range 68-85) and a mean education of 16.8 years. Patients (6 male) had a mean age of 76.9 years (range 66-85 years) and a mean level of education equal to 14.1 years. Independent samples t-tests revealed no significant differences in age among groups [$t(21) = 1.31, p = .203$], but significant differences in education were revealed [$t(21) = 2.21, p = .038$].

In order to better characterize the cognitive deficits of the patient population and to assure that the healthy controls did not demonstrate cognitive impairment, participants completed a battery of standard neuropsychological tests. This battery included the Mini Mental State Exam¹¹, the CERAD Word List Memory Test¹, Verbal Fluency to letters and categories¹², the 15-Item Boston Naming Test¹³, Trails Making B¹⁴, Stroop Color Word Interference Task¹⁵, the Ruff 2 and 7 Selective Attention Test¹⁶, the Rey-Osterrieth Complex Figure Test¹⁷, and Weschler Memory Scale III Logical Memory, Mental Control, and Digit Span¹⁸. Table 1 shows the results of the neuropsychological testing for both groups. Participants without normal or corrected to normal vision and hearing, or with clinically significant depression, alcohol or substance abuse, or traumatic brain damage were excluded, and those who participated were screened for ability to distinguish color. Healthy older adults were also excluded if they demonstrated cognitive impairment on neuropsychological testing or reported having a blood relative with Alzheimer's disease or notable memory impairment. Patients with AD were excluded from the study if they fell outside of the mild range of the disease based on MMSE scores ranging from 20 to 26. Written IRB-approved informed consent was obtained from all participants, as well as from a caregiver if appropriate. Participants were paid \$10/ hour for their participation. One AD patient was dropped from the analysis because her accuracy on the first level of the word test was over 1.5 standard deviations from the mean AD performance (Hit rate = .05, Pr = .00), leaving 11 patients for analysis.

Materials and Procedure

The stimuli used in the current study were derived from previous stimulus sets^{3,5,6}. Word stimuli³ were displayed in Chicago font of about 1 inch size. They appeared in red for level 1 study items, green for level 2 study items, blue for level 3 study items, and in black for test items. Picture stimuli were 320 high resolution clip-art style color pictures of nameable common objects^{5,6}. Stimuli were counterbalanced for condition (word, picture) and study status (old, new).

Participants completed the study at Edith Nourse Rogers Memorial Veterans Hospital, Brigham and Women's Hospital, or in their own homes. They were tested on two paradigms (word paradigm and picture paradigm) programmed with PsyScope software¹⁹ for presentation on Apple G4 laptop computers. Each paradigm consisted of three levels for the patients and two levels for the controls. For the patients, level 1 had 10 study and 20 test items, while level 2 had 20 study and 40 test items, and level 3 had 40 study and 80 test items. For the controls, level 1 has 80 study items and 160 test items, and level 2 had 160 study items and 320 test items. Each test phase was composed of 50% studied and 50% unstudied items. All stimuli were counterbalanced across study and test, and across the three levels. Paradigm order was counterbalanced so that half of the participants completed the word paradigm first and half completed the picture paradigm first, with a median time of 82 days between paradigm

administrations. Participants sat approximately 24 inches from the screen and gave verbal responses, which the experimenter entered in the computer.

During the study portion of each condition, participants were asked to make like/dislike judgments of the stimuli and to remember the stimuli for a subsequent memory test. Study stimuli were presented for 2500 ms each and were followed by the question, "Do you like this item?" Healthy older adult participants were then prompted to button press to signify their like/dislike judgment, while AD subjects reported their judgments aloud to an experimenter. To assure that subjects remained engaged during the study phase, they were asked to read the words aloud or name the pictures. There was a 500 ms pause between each study trial. The study phases were followed by a one-minute delay during which participants worked on number puzzles or simple math problems. Test stimuli were each presented for 1.5 s, followed by the question, "Is this item old or new?" Healthy older adults were prompted to button press to signify their old/new judgment, while AD subjects reported their judgments aloud and had responses input by the experimenter. Subjects were asked to hold their old/new response until the question appeared immediately following stimulus presentation. The test phases were self-paced. The process was then repeated for the remaining levels. The levels progressed forward in sequential direction (shortest to longest) for half the subjects and in backward direction for the other half. There were no differences in discrimination for words [$F(1, 22) = 1.48, p = .236$] or pictures [$F(1, 22) = 1.65, p = .213$] as a result of paradigm direction. When the shortest level was presented first, the average d' for words was .88 and the average d' for pictures was 2.60. When the longest level was presented first, the average d' for words was .68 and the average d' for pictures was 2.11. The neuropsychological tests were always administered following the paradigms.

Results

Analyses were performed to evaluate differences in memory performance and response bias between the word and picture conditions. Because patients with AD were near ceiling on Level 1 (10 study items / 20 test items), the level was not included in the analyses. Therefore, two levels will be analyzed for both the healthy older adults and patients with AD. Further, due to group differences in education, each of the analyses below were performed with education as a covariate.

True and False Recognition

To compare true and false recognition between groups, we performed a repeated measures ANOVA with the factors of Group (older adults, AD), Condition (words, pictures), Item Type (hits, false alarms) and Level (1, 2). The ANOVA revealed effects of Group [$F(1, 20) = 14.11, p = .001, \eta^2 = .43$] and Item Type [$F(1, 20) = 9.83, p = .005, \eta^2 = .34$], as well as interactions of Condition and Group [$F(1, 20) = 7.03, p = .016, \eta^2 = .27$], Item Type and Group [$F(1, 20) = 11.68, p = .003, \eta^2 = .38$], Condition and Item Type [$F(1, 20) = 21.99, p < .001, \eta^2 = .54$], and Condition, Item Type, and Group [$F(1, 20) = 14.35, p = .001, \eta^2 = .43$]. Follow-up analyses revealed that across the two levels, healthy older adults showed a significantly greater hit rate for words [$t(21) = 2.34, p = .029$], but not for pictures [$t(21) = 1.474, p = .155, \text{Cohen's } d = .60$] compared to the patients. In contrast, across the two levels the patients with AD showed a higher number of false alarms for both words [$t(21) = 3.92, p = .001$] and pictures [$t(21) = 3.91, p = .001$]. Within-subjects analyses revealed that the healthy older adults demonstrated a greater hit rate for pictures compared to words [$t(11) = 7.68, p < .001$] and a greater false alarm rate for words compared to pictures [$t(11) = 3.66, p = .004$]. The patients with AD showed a similar pattern. Patients demonstrated a greater hit rate for pictures compared to words [$t(10) = 3.63, p = .005$] and a greater false alarm rate for words compared to pictures [$t(10) = 3.87, p = .003$].

Discrimination (d') and Response Bias (C)

In addition to true and false recognition, discrimination and response bias were analyzed using the measures d' and C provided by Snodgrass and Corwin². Greater d' indicates greater discrimination; 0 indicates chance performance. Positive values of C indicate a conservative response bias, negative values indicate a liberal response bias, and 0 indicates a neutral bias. Because these measures are undefined when the proportion of responses equals 0 or 1, all responses were converted using the formulas provided by Snodgrass and Corwin^{2*}. To compare groups on discrimination (d'), we performed a repeated measures ANOVA with the factors of Group (older adults, AD), Condition (words, pictures), and Level (1, 2). The ANOVA revealed an effect of Group [$F(1, 20) = 12.37, p = .002, \eta^2 = .37$], such that discrimination was better for healthy older adults compared to patients with AD. There were also an effect of Condition [$F(1, 20) = 14.64, p < .001, \eta^2 = .42$] revealing that discrimination was better for pictures than for words, and Level [$F(1, 20) = 12.57, p = .002, \eta^2 = .37$], such that discrimination was better for level 1 compared to level 2. The ANOVA also revealed an interaction of Condition and Group [$F(1, 20) = 14.27, p = .001, \eta^2 = .42$] because healthy older adults appeared to have a greater improvement in discrimination when switching from words to pictures [$t(11) = 15.12, p < .001$] than patients with AD [$t(10) = 5.87, p < .001$].

To compare groups on response bias (C), we performed a repeated measures ANOVA with the factors of Group (older adults, AD), Condition (words, pictures), and Level (1, 2). The ANOVA revealed an effect of Group [$F(1, 20) = 13.40, p = .002, \eta^2 = .41$], such that healthy older adults demonstrated an overall more conservative response bias than patients with AD. The ANOVA also revealed an interaction between Condition and Group [$F(1, 20) = 4.70, p = .042, \eta^2 = .20$]. Follow-up t-tests show that healthy older adults demonstrated a significantly more conservative response bias for words than pictures [$t(11) = 3.28, p = .007$], whereas there was no difference in response bias for the two conditions for patients with AD [$t(10) = 0.12, p = .908$].

Correlations

To gain insight into the liberal response bias of the patients, we performed correlations between the average of the bias measure C for words and pictures and several of the standard neuropsychological tests of cognitive functions (Table 1). Because a total of 10 comparisons were performed, using the Bonferroni correction to avoid type I error, we adjusted our α to .05 divided by 10 or .005, indicating that only correlations with a P value of $< .005$ would be considered significant. To avoid a type II error and ignoring potentially meaningful results with small N , however, we will also comment on correlations with a P value of $< .05$. For the patients, two correlations showed marginal or trends toward a correlation at the .05 level. The average C for words showed a marginal correlation with CERAD word list recognition ($r = .598, p = .052$), and the average C for pictures showed a trend towards correlation with CERAD word list memory encoding ($r = .562, p = .072$). There were no significant correlations for the older adults group.

Discussion

Previously we have shown that despite changes in discrimination produced by varying the study and test list length, response bias remained stable in patients with AD and older adult controls³, and that both older adults and patients with AD were able to shift their response bias when given an instructional manipulation⁴. In the present experiment we were interested in investigating whether changing the experimental stimuli from words to pictures would alter

*Because d' and C are undefined when the proportion of responses equals 0 or 1, all responses were converted using the formulas provided by Snodgrass & Corwin (1988): $H = (\#hits + 0.5)/(\#studied\ items + 1)$; $FA = (\#false\ alarms + 0.5)/(\#unstudied\ items + 1)$.

response bias in patients with AD. Our results were clear. Despite showing large changes in their discrimination when picture stimuli were used instead of words, and in contrast to healthy older adults who shifted to a more liberal bias with pictures, response bias did not change for the AD patients.

In contrast to the patients, the healthy older adults in the current study became more liberal in the picture condition, and shifted to a more neutral response bias. These results are consistent with previous work in understanding criterion shifting and decision making in recognition memory⁹. It has been shown that healthy adults adopt a more conservative response bias when memory judgments become more difficult^{9, 20}. Based on the behavioral data from the present study, the word condition was more difficult compared to the picture condition, and subsequently bias for the healthy older adults was more conservative for words than for pictures. Hirshman⁹ hypothesized that individuals use a metacognitive strategy, known as the range model, to estimate the endpoints of a range of old/new judgments by recalling a few study items at test, and then placing their criterion as some point of proportional distance between the estimated old and new endpoints. This metacognitive strategy may be possible for healthy older adults, but not for patients with AD. Indeed, it has been commonly reported that patients with AD are impaired in the use of metacognitive and metamemory strategies (see ^{21, 22} for reviews).

The present study provides the second set of results demonstrating a consistent liberal response bias for patients with AD. Budson, Wolk et al.³ showed that response bias remained stable in patients and healthy controls despite different lengths of study and test lists of words, and the present results demonstrate that response bias remains relatively stable regardless of whether word or picture stimuli are to be remembered. In combination these results suggest that response bias is a relatively stable property of an individual with AD; that is, although it can be modified, individuals appear to have a “set point” to which they gravitate. Figure 1 shows how each individual patient's response bias changed with the different stimulus types. Although a certain degree of variability is present, in general those with a conservative bias to words showed a conservative bias to pictures, those with a liberal bias to words showed a liberal bias to pictures, and those with a neutral bias to words showed a neutral bias to pictures.

It is important to note that although response bias in patients with AD was not altered by changes from word to picture stimuli, some stimulus changes do alter response bias. Windmann and Kutas²³ found that emotional words led young adults to show a more liberal response bias compared to neutral words. Budson, Todman et al.²⁴ expanded this finding to healthy older adults, and also found that patients with AD showed trends in the opposite direction—a more conservative response bias with emotional compared to neutral words. We find it quite interesting that recognition response bias is altered when comparing emotional to neutral words, but not when comparing words versus pictures. Budson, Todman et al.²⁴ suggested that, at least for emotional stimuli, Alzheimer's pathology in the amygdala in particular may be related to these patients' response bias, perhaps because amygdala activation has been associated with one's confidence in a memory²⁵, which in turn may affect decision criteria.

The pictures used in the present study were in color with a high level of details—very different than the abstract semantic information conveyed by words alone. This rich information contained in the pictures was able to significantly increase the discrimination of the patients, while not altering their bias (Figure 2). One possible explanation for this dissociation between discrimination and bias is that these two aspects of episodic memory are modulated by different neural systems with different anatomical bases. Supporting this idea, in an fMRI study Miller, Handy, Cutler, Inati, and Wolford²⁶ found that activations associated with bias were observed in lateral cerebellum, lateral parietal lobe, and dorsolateral prefrontal cortex, whereas activations associated with discriminations were observed in anterior and medial prefrontal

cortex. Highlighting the importance of the frontal lobes, the results of an ERP study²⁷ suggested that response bias is related to a top-down control process mediated by prefrontal cortex, which may be important in the setting of a criterion level. Thus, criterion setting leading to particular response biases may be related to specific activity of particular regions of prefrontal cortex.

The findings of this study, while answering some questions, raise a number of others that may be addressed by future studies. One question is why individuals show different underlying tendencies toward a response bias set point? Budson, Wolk et al.³ suggested that the degree of Alzheimer's pathology was one determinant in a patient's bias, with those patients with a greater degree of pathology showing a more liberal bias. Although the relative burden of pathology may be the most important factor in patients with AD (explaining 79% of the variance of the response bias data in the patients in that study [based upon r^2]), pathology would not of course explain why healthy individuals may also differ in their response bias. A number of recent studies have focused on trying to identify the factors involved in understanding individual differences. Many different theories have been proposed to explain various kinds of individual differences, including psychodynamic²⁸, strategic²⁹, and biochemical³⁰. A study of individual differences in response bias that includes an examination of subjects' underlying cognitive ability in several neuropsychological domains and the strategies that subjects use would help us to begin to understand why response bias is relatively invariant despite dramatic changes in stimuli and discrimination. Improved understanding of response bias will in turn improve our understanding of episodic memory function and dysfunction.

Acknowledgments

This material is the result of work supported with resources and the use of facilities at the Edith Nourse Rogers Memorial Veterans Hospital in Bedford, MA. This research was supported by National Institute on Aging grants K23 AG031925 (BAA), R01 AG025815 (AEB), and P30 AG13846.

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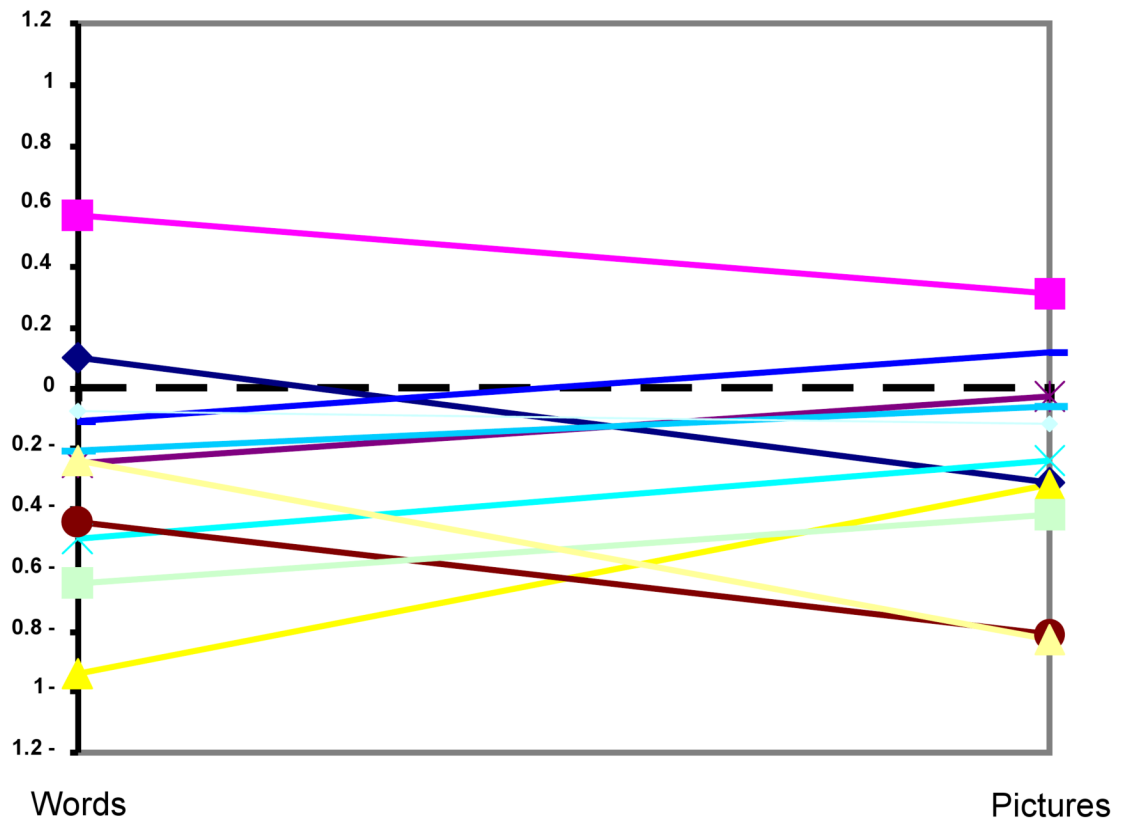


Figure 1. Average response bias (C) of Alzheimer's patients for words and pictures
 Individual average C values for the 2 levels of the word test compared to average C for the 2 levels of the picture test. Colored lines connect the C scores for individual participants for each condition.

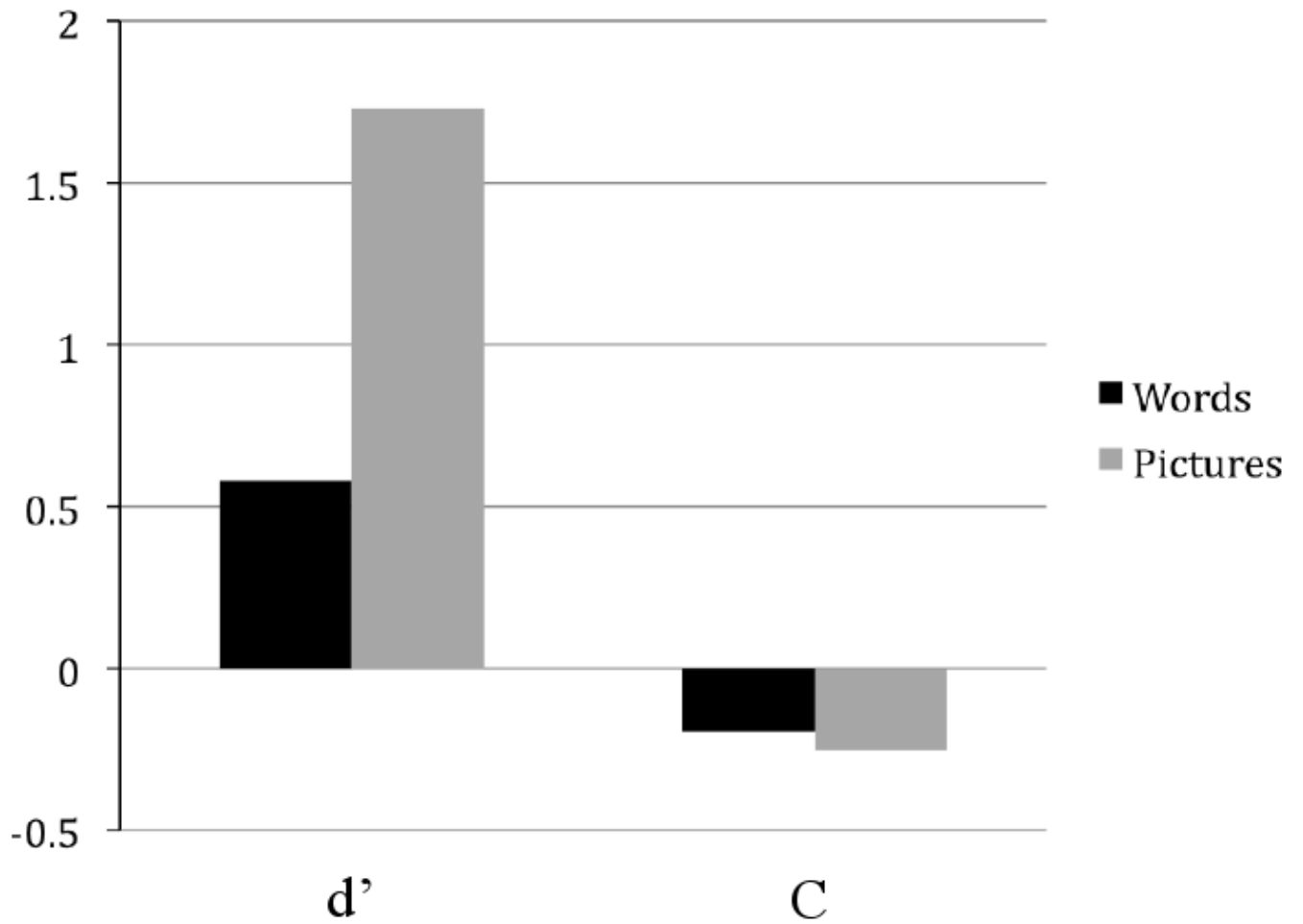


Figure 2. Patient discrimination (d') and response bias (C) for words and pictures
Average d' and C for patients with AD on the word and picture tests.

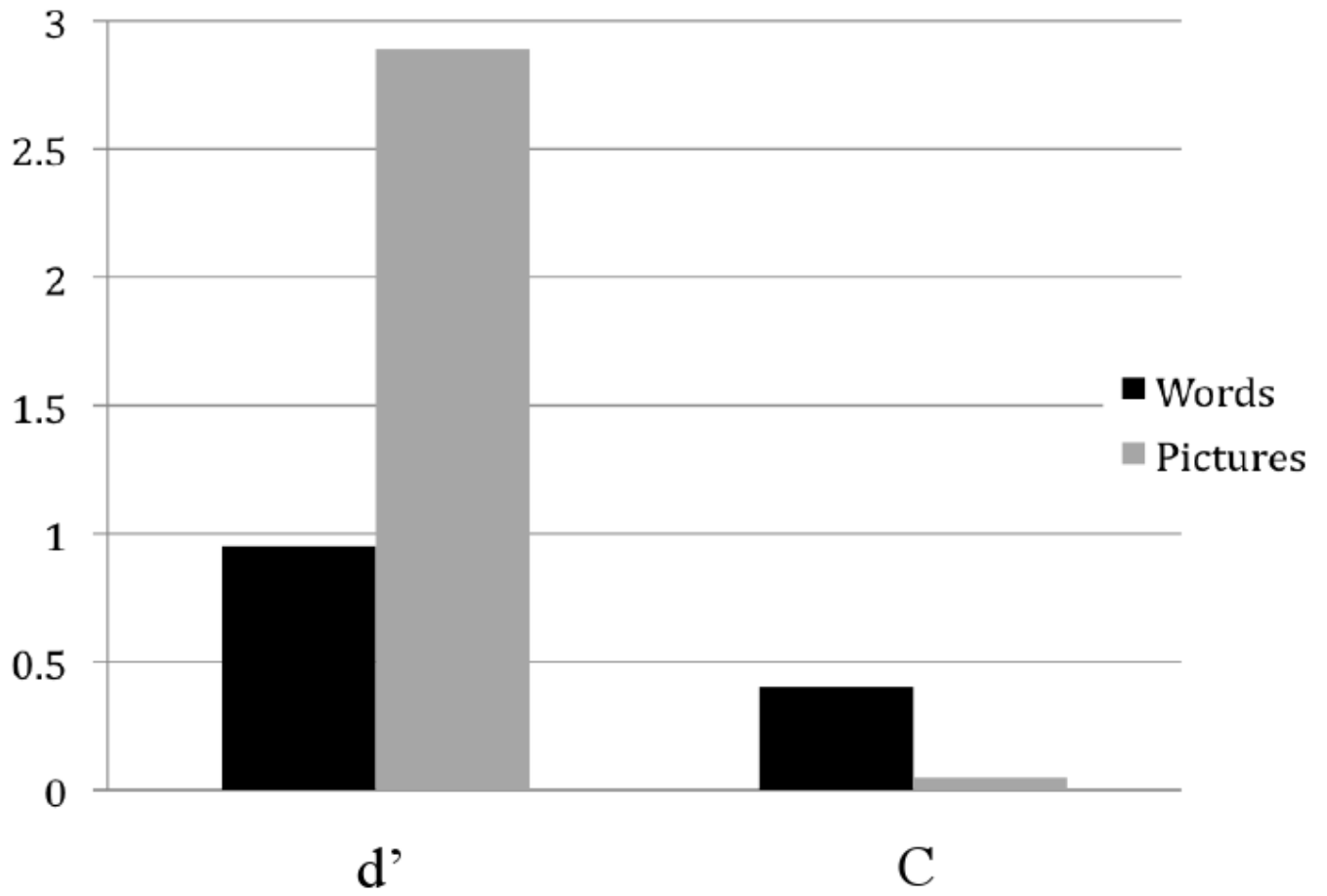


Figure 3. Older adult discrimination (d') and response bias (C) for words and pictures
Average d' and C for healthy older adults on the word and picture tests.

Table 1
Results of the neuropsychological tests

Test	Mean (SD)	Mean (SD)
	AD Patients	Controls
Global cognition score		
MMSE (Folstein et al., 1975)	25.45 (4.0)	29.63 (0.7)
Verbal fluency (Spreen & Benton, 1969)		
Letters (FAS)	28.64 (13.2)	42.64 (14.2)
Categories (animals, fruits, vegetables)	29.64 (13.4)	46.45 (10.4)
Memory (CERAD; Morris et al., 1989)		
Word List Memory	8.36 (4.9)	20.16 (3.1)
Word List Recall	0.73 (1.2)	6.25 (1.7)
Word List Recognition	5.27 (2.7)	9.58 (0.7)
Forward Digit Span (Wechsler, 1997)	5.73 (2.6)	7.33 (1.1)
Boston Naming Test-15 (Mack et al, 1992)	10.67 (3.5)	13.33 (2.9)
Color Word Interference Task (Stroop, 1935)	36.73 (18.2)	80.18 (25.2)
Logical Memory (Wechsler, 1997)		
Recall I	17.3 (13.6)	40.1 (10.8)
Recall II	4.8 (7.5)	22 (6.2)
Recognition	19.3 (4.1)	38 (1.1)
Mental Control (Wechsler, 1997)	18.81 (3.5)	24.14 (3.6)
Trails Making B (Adjutant General's Office, 1944)	250.45 (120)	84.61 (25.9)

Note: The results of Boston Naming Test and Logical Memory were not available for one AD patient.

Table 2
Proportions of hits and false alarms for pictures and words (SD)

	Hits			False Alarms			
	Level 1	Level 2	AVG	Level 1	Level 2	AVG	
Words	AD	0.69 (.13)	0.66 (.16)	0.68 (.15)	0.45 (.18)	0.50 (.21)	0.48 (.20)
	Controls	0.54 (.18)	0.55 (.16)	0.55 (.17)	0.20 (.16)	0.21 (.14)	0.21 (.15)
Pictures	AD	0.85 (.16)	0.81 (.15)	0.83 (.16)	0.29 (.21)	0.32 (.18)	0.31 (.19)
	Controls	0.92 (.06)	0.88 (.10)	0.90 (.08)	0.08 (.04)	0.07 (.04)	0.08 (.04)

Table 3
Discrimination (d') and response bias (C) for words and pictures (SD)

	d'			C		
	Level 1	Level 2	AVG	Level 1	Level 2	AVG
Words						
AD	0.68 (.59)	0.48 (.44)	0.58 (.52)	-.18	-.21	-.20
Controls	1.00 (.28)	0.91 (.25)	0.96 (.27)	.42	.40	.41
Pictures						
AD	1.86 (.92)	1.61 (.99)	1.74 (.96)	-.25	-.26	-.26
Controls	2.98 (.57)	2.84 (.58)	2.91 (.58)	-.01	.08	.05

Table 4
Correlation between average C for words and pictures and standard neuropsychological tests

Test	r			
	AD		OC	
	Words	Pictures	Words	Pictures
Global cognitive functioning				
MMSE	-.173	-.177	.185	-.310
Verbal Fluency				
Letter fluency	-.392	-.262	-.111	.399
Category fluency	.035	-.304	.002	.354
Memory				
Word list memory encoding	.141	.562	.143	.070
Word list recall	.168	.477	-.346	-.242
Word list recognition	.598	.534	-.283	-.113
Executive				
Trails B	.193	.427	-.396	-.339
Mental Control	.344	-.280	-.463	.094