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Response bias and response monitoring: Evidence from healthy older adults and patients with mild Alzheimer's disease

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Abstract

Patients with Alzheimer's disease (AD) often exhibit an abnormally liberal response bias in recognition memory tests, responding “old” more frequently than “new.” Investigations have shown patients can to shift to a more conservative response bias when given instructions. We examined if patients with mild AD could alter their response patterns when the ratio of old items is manipulated without explicit instruction. Healthy older adults and AD patients studied lists of words and then were tested in three old/new ratio conditions (30%, 50%, or 70% old items). A subset of participants provided estimates of how many old and new items they saw in the memory test. We demonstrated that both groups were able to change their response patterns without the aid of explicit instructions. Importantly, AD patients were more likely to estimate seeing greater numbers of old than new items, whereas the reverse was observed for older adults. Elevated estimates of old items in AD patients suggest their liberal response bias may be attributed to their reliance on familiarity. We conclude that the liberal response bias observed in AD patients is attributable to their believing that more of the test items are old, and not due to impaired meta-memorial monitoring abilities.

Keywords

recognition memory; Alzheimer's disease; response bias; monitoring

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1. Introduction

One of the hallmark and earliest symptoms of Alzheimer's disease (AD) is impairment in episodic memory. Patients with AD show a decline in their ability to retain new information, which can be demonstrated easily with neuropsychological tests like the California Verbal Learning Test (CVLT; Woods, Delis, Scott, Kramer, & Holdnack, 2006) or the CERAD word list memory test (Morris et al., 1989). Additionally, recent longitudinal work following groups of initially healthy older adults that either developed or did not develop AD found that more qualitative aspects of memory performance such as intrusion errors and response bias may be very useful in identifying preclinical AD (Schmid, Taylor, Foldi, Berres, & Monsch, 2013). Performance on memory tests produce a recognition score which can be useful in making a clinical diagnosis, but examining more subtle aspects of a patient's performance can provide additional information.

Patients with AD often demonstrate an abnormally liberal response bias (Balota, Burgess, Cortese, & Adams, 2002; Bartok et al., 1997; Snodgrass & Corwin, 1988). Response bias quantifies the tendency to either respond in a predominantly liberal (i.e., endorsing “old” frequently) or conservative (i.e., endorsing “old” infrequently) direction in recognition memory tests. Budson and colleagues (2006) demonstrated that the abnormally liberal response bias seen in patients with AD can be dissociated from their poor discrimination and thus reflects additional information about their impairment. In this experiment, discrimination between the two groups was equated by presenting study-test lists of increasing length. When healthy older adults studied 160 words and then were tested on 320 words (160 old, 160 new), their discrimination did not significantly differ from patients with AD when they studied 10 words and were tested on 20 words (10 old, 10 new). Even though their discrimination levels were matched, the patients with AD maintained a liberal response bias while the healthy older adults maintained a conservative response bias. The healthy older adults still showed a conservative response bias even with poor discrimination. Importantly, response bias remained constant across the discrimination levels for both patients with AD and the older controls indicating that while list length had a significant effect on discrimination, it was not related to bias.

Given that many studies have found an abnormally liberal response bias in patients with AD despite different experimental stimuli and conditions (Beth, Budson, Waring, & Ally, 2009; Budson, Wolk, Chong, & Waring, 2006; Deason, Hussey, Ally, & Budson, 2012; Waring, Chong, Wolk, & Budson, 2008), one important question that arose was whether patients with mild AD were capable of altering their response bias. Waring and colleagues (2008) directly examined whether patients with mild AD could shift their response bias if provided with specific instructions. In their experiment, participants were presented with a recognition memory test composed of 50% old and 50% new words, but participants were instructed that either 30% or 70% of the words were old. Although the AD patients were more liberal than healthy older adults, both groups were able to shift their response bias to the same extent in response to the instructions. That patients with AD can shift to a more conservative (or at least more neutral) response bias with external direction suggests that, given the proper support, patients with mild cognitive impairment (MCI) due to AD and mild AD might be able to reduce their false recognition and improve their memory by shifting to a more

conservative response bias. Indeed, patients exhibited a modest reduction in false alarm rates when shifting to a more conservative response bias (from a mean of .52 in the 70% old condition, to a mean of .42 in the 30% old condition). However, patients with AD were not able to improve their discrimination, which had been the case for amnesic patients with medial temporal lobe damage when tested with a similar paradigm (Verfaellie, Giovanello, & Keane, 2001).

Typically, in experiments looking at shifting response bias either only instructions or both instructions and underlying distributions are used to create the conditions. Both of these manipulations are providing explicit direction to the participant of how to properly shift their response patterns. In this study, we wanted to investigate whether healthy older adults and patients with mild AD dementia could change their response patterns appropriately without explicit direction – based purely on the underlying old/new distribution. If patients with AD can shift their response pattern as a result of subtle cues from structure of the test itself, then that preserved ability to shift could possibly be used to aid patients' performance in real-life situations.

Potentially, the liberal response bias in patients with AD may be related to disruption of the frontal cortex. Patients with frontal lobe lesions show increased false recognition in some instances (Budson et al., 2002; Parkin, Bindschaedler, Harsent, & Metzler, 1996; Schacter, Curran, Galluccio, Milberg, & Bates, 1996), but not in others (Verfaellie, Rapcsak, Keane, & Alexander, 2004; Hwang et al. 2007). In one study, patients with focal lesions in the left posterior dorsolateral prefrontal cortex demonstrated a liberal response bias that resulted in an increased level of false recognition (Alexander, Stuss, & Fansabeddian, 2003). There has also been evidence in patients with AD that decreased brain volume in the frontal cortex is correlated with a more liberal response bias (Kramer et al., 2005). However, several studies have failed to find correlations between measures of response bias and neuropsychological assessments related to executive functioning in patients with AD (Budson et al., 2006; Deason et al., 2012).

In the present study, we were interested whether the abnormally liberal response bias in patients with AD is related to problems in meta-memorial monitoring of response patterns, therefore offering more evidence that the liberal response bias is due to frontal lobe impairment. Meta-memory refers to one's own awareness of their memory abilities. There has been extensive study of meta-memory and metacognitive monitoring abilities in healthy older adults suggesting that some aspects of monitoring are preserved in healthy aging (for a review see Hertzog & Dunlosky, 2011). Memory monitoring and meta-memory processes have been related to the processing of the prefrontal cortex (Chua, Schacter, Rand-Giovannetti, & Sperling, 2006; Maril, Simons, Mitchell, Scwartz, & Schacter, 2003; Schnyer, Nicholls, & Verfaellie, 2005) and disruptions of the frontal cortex in healthy aging has been linked to declines in monitoring abilities (Dulas & Duarte, 2011). Additionally, there is a mixed literature examining these abilities in patients with Alzheimer's disease (Dodson et al., 2011; Gallo, Cramer, Wong, & Bennett, 2012; Halamish, McGillivray, & Castel, 2011; Souchay, 2007; Thomas, Lee, & Balota, 2013). In their study examining metacognitive monitoring in patients with AD, Dodson and colleagues (2011) concluded that both impaired retrieval and impaired evaluative processes lead to disruptions of memory

monitoring in AD patients compared to healthy older adults. These findings suggest that there might be a relationship between impaired monitoring and the liberal response bias in patients with AD.

If individuals are not provided with explicit instructions that indicate changes in the ratios of old/new items, then to correctly shift response criterion individuals need to have insight and be able to monitor their responses. For example, although healthy older adults may become more conservative in their responding after saying, “yes,” seven times in a row, the AD patient— not remembering the prior seven responses—may be just as likely to say “yes” again. Healthy older adults may be able to shift their response based on their overall pattern of responses, whereas patients with mild AD may be responding old/new based on an item-by-item basis. Potential differences in the ability to monitor responses might be leading to differences in response bias (and abilities to shift response bias) between healthy older adults and patients with mild AD. To examine this possible explanation, for a subset of our participants, we asked participants how many old and how many new items they had seen at the halfway point and at the end of the recognition test phase.

We predicted that healthy older adults would be able to shift their responding successfully when the underlying ratio of old and new items shifted and that they would also be able to successfully monitor their patterns of responses. Based on prior literature, we expected patients with AD to be more liberal overall than healthy older adults and, thus, perhaps less likely to shift their response patterns to match the underlying old/new ratio conditions or be aware of their response patterns due in part to frontal lobe impairment.

2 Method

2.1 Participants

Twenty-five healthy older adults (12 male) and 29 patients (18 male) with a clinical diagnosis of probable AD were recruited for this study. Healthy older adults were recruited from online and community postings in the Boston area. In addition, some of the healthy older adults were also spouses and friends (but not blood relatives) of the AD patients who participated in the study. Patients with probable mild AD met criteria described by the National Institute on Aging and Alzheimer's Association workgroup criteria (McKhann et al., 2011) and were recruited from the Boston University Alzheimer's Disease Center (BU ADC). These patients were each assessed and diagnosed by a neurologist or neuropsychologist and were otherwise healthy. Participants were screened for clinically significant depression, alcohol or drug use, past stroke, traumatic brain injury, or other neurologic disorder. All participants were native English speakers and had normal or corrected to normal vision. The study was approved by the human studies committees of VA Boston Healthcare System, Boston, MA, the Edith Nourse Rogers Memorial Veterans Hospital, Bedford, MA, and Boston University, Boston, MA. Written informed consents were obtained from all participants and from their caregivers when appropriate. Participants were paid $10/hour for their participation.

The healthy older adults and patients with AD completed a brief neuropsychological battery in a 45-minute session either directly following the experimental session or on a separate

date. This battery included the MMSE (Folstein, Folstein, & McHugh, 1975), CERAD Word List Memory Test (Morris et al., 1989), Trail Making Test B (Adjutant General's Office, 1944), Verbal fluency to letters and categories (Monsch et al., 1992), and the short form Boston Naming Test (Mack, Freed, Williams, & Henderson, 1992). Table 1 presents demographic and neuropsychological data for the participants.

Although the average age of the AD patients was 2 years older than the older adult controls, this difference was not significant ($F(1,52) = 1.38$, $p = .25$, $\eta_p^2 = .026$). There was no significant difference in years of education reported between patients with AD and healthy older adults ($F(1,52) = 1.36$, $p = .25$, $\eta_p^2 = .026$). Patients with AD were in the very mild or mild dementia stage of the disease based upon their performance on the MMSE (mean = 25.86, range = 17-30). Older controls scored significantly higher than AD patients on the MMSE ($F(1,52) = 24.83$, $p < .001$, $\eta p^2 = .323$), CERAD immediate recall ($F(1,52) = 50.11$, $p < .001$, $\eta_p^2 = .491$), CERAD delayed recall ($F(1,52) = 87.34$, $p < .001$, $\eta_p^2 = .627$), CERAD recognition ($F(1,52) = 23.93$, $p < .001$, $\eta p^2 = .0315$), lexical fluency (FAS: $F(1,52) = 8.04$, $p < .01$, $\eta_p^2 = .134$), and categorical fluency (CAT: $F(1,52) = 17.57$, $p < .001$, $\eta_p^2 = .253$). Older adults were also faster to complete the Trail Making Test Part B ($F(1,52) = 34.01$, $p < .001$, $\eta_p^2 = .382$) and had fewer errors on the 15-item Boston Naming Test than the patients with AD ($F(1,52) = 7.51$, $p < .01$, $\eta_p^2 = .126$).

2.2 Materials

The stimuli were 414 words, four to eight letters in length with Kucera-Francis frequencies between 10-700, generated from the University of Western Australia MRC Psycholinguistic Database (http://www.psy.uwa.edu.au/MRCDataBase/uwa.mrc.htm). We used 36 of these words as “filler” words during the study phase and the remaining 378 words were divided into six lists of 63 words counterbalanced by word length and frequency. Assignment of lists to experimental conditions was counterbalanced across participants. Words were presented in 48-point bold Verdana font in the center of the screen at both study and test.

2.3 Procedure

The experiment consisted of three sessions each one week apart. Participants completed one study-test block in each session. There were no overlapping stimuli between the three study-test blocks. Each study phase consisted of 75 words with 6 filler words at the beginning and the end to counteract primacy and recency effects. In the study phases, each word was presented for 2000 ms with a 500 ms interstimulus interval. Participants were instructed to read each word aloud and to remember them for a subsequent memory test. After the study phase, there was a 10-minute delay during which participants worked on a number search or on math problems.

In all three sessions the test phase consisted of 90 words, but the ratio of studied/unstudied words was different each session. During the first session, all participants were presented with 50% studied words and 50% unstudied words (45 old words/45 new words). During the second session, the test phase consisted of either 70% studied words and 30% unstudied words (63 old words/27 new words) or 30% studied words and 70% unstudied words (27 old words/63 new words). The third session consisted of either the 70% studied or 30% studied

condition depending on what had been presented in the second session. The order of the 70% and the 30% conditions were counterbalanced across participants. Participants were not informed of the change in ratio and were given the same instructions each session. In the test phases, participants were instructed to respond "old" if the word had been presented before or "new" if the word had not been presented previously. The test word remained on the screen until participants responded.

For a subset of the participants (12 healthy older adults and 17 patients with AD), we interrupted them halfway through the test phase (after seeing 45 words) and asked two questions: "How many OLD items have you seen? How many NEW items have you seen?" After recording their answers, the experimenter would then continue the test phase after reminding the subject of the instructions. The same two questions were asked at the end of the test phase and participants were instructed to report the number of items they had seen since the last set of questions. The timing of these two interruptions was kept constant across the participants.

3. Results

3.1 Raw Number of "old" responses

To verify the impact of the ratio manipulation, we also analyzed the total number of the raw number "old" responses by ratio condition. A repeated-measures ANOVA was conducted using a between-subjects factor of group (healthy older adults vs. patients with AD) and within-subjects factors of ratio condition (30%, 50%, 70%) for the raw number old responses (see Figure 1). There was a significant main effect of group [$F(1, 52) = 11.79$, $p < .01$, $\eta_p^2 = .185$]. Overall, patients with AD made a greater number of "old" responses ($M = 50.35$) compared with healthy older adults ($M = 39.88$). A significant main effect of ratio condition was observed [$F(2, 104) = 21.39$, $p < .001$, $\eta_p^2 = .292$]. Pair-wise comparisons revealed that there were a greater number of "old" responses in the 70% condition ($M = 50.60$) compared to both the 50% condition ($M = 44.37$) and the 30% condition ($M = 41.54$) [$t(53) = 3.87$, $p < .001$ and $t(53) = 6.93$, $p < .001$, respectively]. There was also a trend toward a greater number of old responses in the 50% condition compared to the 30% condition [$t(53) = 1.86$, $p = .068$].

A group by ratio condition interaction was observed [$F(2, 104) = 3.31$, $p < .05$, $\eta_p^2 = .060$]. Additional one-way ANOVAs were conducted on ratio condition within each group. For healthy older adults, there was a main effect of ratio condition ($F(2, 48) = 22.94$, $p < .001$, $\eta_p^2 = .489$). Pair-wise comparisons revealed that there were a higher number of "old" responses in the 70% condition ($M = 46.8$) compared to both the 50% condition ($M = 39.08$) and the 30% condition ($M = 33.76$) [$t(24) = 3.92$, $p = .001$ and $t(24) = 7.21$, $p < .001$, respectively]. There was also a greater number of old responses in the 50% condition compared to the 30% condition [$t(24) = 2.63$, $p = .015$] In patients with AD, the main effect of ratio condition was also significant [$F(2, 56) = 4.16$, $p = .021$, $\eta_p^2 = .129$]. The number of "old" responses was higher in the 70% condition ($M = 53.86$) than in the 30% condition ($M = 48.24$) [$t(28) = 3.43$, $p = .002$]. There was a trend toward higher "old" responses in the 70% compared to the 50% condition [$M = 48.93$; $t(28) = 2.0$, $p = .056$], but no difference was found between the 30% and 50% conditions ($t < 1$).

3.2 Hit and False Alarm rates

A repeated-measures Analysis of Variance (ANOVA) was conducted using a between-subjects factor of group (healthy older adults vs. patients with AD) and the within-subjects factor of ratio condition (30%, 50%, 70%) for hit rates. No main effect of group was observed ($F < 1$). There was no main effect of ratio condition [$F(2,104) = 1.90$, $p = .155$, $\eta_p^2 = .035$] or ratio by group interaction ($F < 1$]). A repeated-measures ANOVA was also conducted on false alarm rates. There was a main effect of group ($F(1, 52) = 28.15$, $p < .001$, $\eta_p^2 = .351$). Patients with AD showed higher false alarm rates compared with healthy older adults (OCs: $M = .215$, ADs: $M = .431$). No main effect of ratio condition [$F(2,104) = 2.30$, $p = .105$, $\eta_p^2 = .042$] or a ratio condition by group interaction ($F < 1$) was observed. Hit and false alarm rates are in Table 2.

We conducted additional analyses to determine if hit and false alarm rates differed between participants that were not interrupted, and those that were interrupted. We conducted a repeated-measures ANOVA with the same factors as the prior analyses, but included an addition between-subjects factor of interruption condition (Interruption vs. No Interruption). For hit rates, we did observe a main effect of interruption condition [$F(1, 50) = 4.138$, $p = .047$, $\eta_p^2 = .076$] with higher hit rates for the no interruption condition ($M = .719$) than for the interruption condition ($M = .634$). There was also a trend towards a group by interruption condition interaction [$F(1, 50) = 3.33$, $p = .074$, $\eta_p^2 = .062$]. There was no interruption condition by ratio condition interaction or three-way interaction ($Fs < 1$).

For false alarm rates, we did not observe a main effect of interruption condition, nor did we observe group by interruption condition or interruption condition by ratio condition interactions ($Fs < 1$, $p > .1$). There was also no three-way interaction ($F < 1$). Additionally, we examined the effect of ratio condition order as well as potential differences between the first and second halves of the test phase. No main effects or interactions were found for either hit or false alarm rates.

3.3 Discrimination and Response Bias

We examined discrimination and response bias using signal detection theory parameters, d' and C as well as Pr and Br (Macmillan & Creelman, 2005; Snodgrass & Corwin, 1988). High values of d' and Pr indicate greater discrimination. Response bias, measured by C or Br, can be either conservative (less likely to respond old; indicated by positive values of C and lower values of Br) or liberal (more likely to respond old; indicated by negative values of C and higher values of Br). In these analyses, we also included first vs. second half of the recognition test to track if performance changed as the test progressed.

A repeated-measures ANOVA was conducted using between-subjects factors of group (healthy older controls versus patients with AD) and within-subjects factor of ratio condition (30%, 50%, 70%) and half of the recognition test for discrimination (separately for d' and Pr). There was an overall main effect of group [$F(1,52) = 19.853$, $p < .001$, $\eta_p^2 = .276$] with healthy older adults showing better discrimination than patients with AD. There was no main effect of ratio condition or test half, nor was there a group by ratio condition or group by test half interaction ($ps > .1$). The same pattern was shown when Pr was used instead of

d' [Group: F(1,52) = 16.61, p < .001, η_p^2 = .242; see Figure 2a]. Using Pr, there was an interaction between test half and group [F(1, 52) = 4.40, p < . 05, η_p^2 = .0 78]. Post-hoc t-tests showed that the two groups were numerically trending in opposite directions, but no significant effects.

Analogous repeated-measures ANOVAs were conducted for response bias (using C and Br). There was a main effect of group [F(1, 52) = 12.09, p < . 01, η_p^2 = . 189] with patients showing a more liberal response bias (C = -0.16) compared to healthy older adults (C = 0.20). There was no main effect of ratio condition or test half, nor were there interactions with group (ps > .1). A slightly different pattern emerges when the Br response bias calculation was used. In addition to the main effect of Group [F(1,52) = 11.75, p < . 01, η_p^2 = . 184], there was also a significant main effect of Ratio [F(2,104) = 3.61, p < . 05, η_p^2 = . 065; see Figure 2b]. Participants were significantly more liberal in the 30% condition (Br = . 53) than in the 70% condition [Br = .47; t(53) = 2.87, p < .01] and marginally more liberal than in the 50% condition [Br = .49; t(53) = 1.85, p = .070]. There was no difference in response bias between the 50% and 70% condition (t < 1). There was also no main effect of test half nor significant interactions with test half or group.

3.4 Interruption Response Count Analysis

For a subset of the participants, we collected their answers to the questions *"How many OLD items have you seen? How many NEW items have you seen?"* at the midpoint of the test phase and again at the end of the test phase for each condition. As a reminder, each condition had a total of 90 items. There were 27 old items in the 30% condition, 45 old items in the 50% condition, and 63 items in the 70% condition.

To examine these data, we first conducted a repeated-measures ANOVA with a between-subjects factor of group (healthy older adults versus patients with AD) and a within-subjects factor of response (old versus new), ratio condition (30%, 50%, 70%) and time point (midpoint or end of test phase) examining the reported counts subjects provided (see Figure 3). There was a significant interaction between response and group [$F(1,27) = 8.55$, $p < .01$, $\eta_p^2 = .241$]. This interaction is likely due to the fact that whereas healthy older adults reported that there were more new ($M = 109$) than old items ($M = 70$) [$t(11) = 3.09$, $p < .05$] across the three sessions, patients with AD showed tendencies in the opposite direction, and reported numerically greater old ($M = 91$) than new items ($M = 71$) [$t(16) = 1.41$, $p = .178$]. There was also an interaction between response and ratio condition [$F(2,54) = 6.10$, $p < .01$, $\eta_p^2 = .184$]. To follow up on this interaction, we conducted a repeated-measures ANOVA with a within-subjects factor of ratio condition (30%, 50%, 70%) for the number of old responses [$F(2,56) = 4.68$, $p < .05$, $\eta_p^2 = .143$] and then separately for the new responses (*ns*; $p = 0.15$). There were more old items reported in the 70% studied condition than in the 50% studied condition [$t(28) = 3.48$, $p < .01$]. There was a marginal interaction between ratio condition and subject group [$F(2,54) = 2.93$, $p = .062$, $\eta_p^2 = .098$]. This interaction is likely due to patients with AD reporting more items seen in the 30% condition ($M = 60$ responses) than in the 50% condition ($M = 48$ responses) [$t(16) = 2.21$, $p < .05$] and reporting marginally more items seen in the 70% condition ($M = 54$ responses) than in the

50% condition [$t(16) = 2.04$, $p = .059$] whereas healthy older adults reported similar number of items seen in all ratio conditions ($ps > .15$).

There was no main effect of the time point of the question in the experiment and this variable did not significantly interact with other factors. Interestingly, there was also no main effect of participant group.

4. Discussion

Patients with very mild and mild AD dementia showed similar hit rates but increased false alarm rates when compared to healthy older adults. This finding was expected, as patients with AD consistently show elevated false alarm rates in recognition memory tests (Budson, Daffner, Desikan, & Schacter, 2000; Snodgrass & Corwin, 1988). Additionally, patients with mild AD showed an overall more liberal response bias compared to healthy older adults (Budson et al., 2006). Even though the patients with mild AD had overall lower discrimination, both groups showed similar rates of discrimination across the three ratio conditions (Table 2 and Figure 2a). *The lack of an interaction between group and ratio condition for either discrimination or response bias suggest that healthy older adults and patients with mild AD responded similarly to the change in proportion of old/new items.*

Our findings suggest that patients with mild AD do not show an additional decrement in performance when the underlying old/new ratios are manipulated without externally provided instruction. Overall, patients with mild AD did show lower levels of discrimination and more liberal response bias compared to healthy older adults, but these differences remained consistent across ratio conditions. The shift in response patterns shown by the patients with AD in our experiment also argues against the explanation that the abnormally liberal response bias typically found in these patients is due to a type of “response perseveration.” If this were the case, then the patients should have shown a more dramatic shift (either liberal or conservative) depending on which type of item occurred most frequently.

Participants demonstrated a more liberal response bias in the 30% condition than in both the 50% and 70% ratio conditions. In the current experiment, all participants experienced the 50% old/new recognition test in their first session. Potentially this created an expectation for a similar old/new distribution in the two subsequent sessions. As participants progress through the 30% condition and realize they are responding primarily “new”, they may change their criterion accordingly to a more liberal response pattern overall. While we could not detect a shift in response bias when the test phase was divided into halves, the more liberal response bias in the 30% condition does suggest that both patients with mild AD and healthy older adults are monitoring their response patterns and using this information to inform their criterion placement.

In addition to examining overall response patterns, for a subset of the participants we also gathered their subjective report at two points in the experiment of how many old and new items they had encountered. In particular, we wanted to know whether patients with mild AD are showing a bias to simply responding “old” to items, which may not necessarily be

related to memory (e.g., having a liberal response bias irrespective of their memory impairment), or whether the AD patients really believe that more old items have been presented. If patients with AD were simply more prone to respond “old” in any memorial context (perhaps due to poor response inhibition due to frontal lobe dysfunction), we would not expect it to influence the item estimates in the old/new interruption question. In contrast, if the patients actually believe that more items are old (and are able to maintain this information), then they should report higher numbers of old versus new items when asked at the end of the experiment.

Both healthy older adults and patients with mild AD reported seeing a similar number of items overall, but the old/new distribution of these responses varied. Across all three ratio conditions, healthy older adults reported seeing significantly more new items than old items whereas patients with mild AD showed non-significant tendencies toward the opposite pattern (Figure 3). The pattern of subjective reports from the healthy older adults and patients with mild AD corresponded with each groups’ overall response bias tendency. Healthy older adults reported more new items and showed an overall more conservative response bias, whereas patients with mild AD numerically reported more old items and showed a more liberal response bias.

Both frontal and parietal cortex have been related to response bias, and both these areas are disrupted in the neurodegenerative progression of Alzheimer's disease (Braskie, Toga, & Thompson, 2013; McKee et al., 2006; Whitwell, 2010). As reviewed previously, studies examining frontal lesion patients have suggested that the increase in false recognition in these patients establishes a relationship between the frontal cortex and response bias (Alexander, et al., 2003; Budson et al., 2002; Parkin, et al., 1996; Schacter et al., 1996). When examining AD patients, decreases in brain volume in the frontal cortex correlated with response bias, whereas decreases in hippocampal volume correlated with recognition accuracy (Kramer et al., 2005). Neuroimaging findings have indicated a relationship between response bias and areas of the parietal and frontal cortex (Miller, Handy, Cutler, Inati, & Wolford, 2001; O'Connor, Han, & Dobbins, 2010). Changes in response bias have been associated with changes in activations in lateral parietal cortex and dorsolateral prefrontal cortex (Miller et al., 2001). O’Connor and colleagues (2010) showed activity in inferior parietal cortex correlated with changes in response bias but not with memory accuracy. Dobbins, Jaeger, Studer, and Simons (2012) found that patients with damage to the lateral parietal cortex were unable to integrate external cues to adapt their response patterns when compared to healthy controls and patients with frontal lesions. Evidence suggests that intact functioning of both the frontal and parietal areas may be necessary for establishing and successful adaptation of the response criterion.

Our findings provide evidence that despite their tendency towards a liberal response bias, patients with mild AD dementia do retain some insight into their response patterns. Patients’ insight into their memorial response patterns may be related to relatively intact meta-memorial abilities. Several studies examining meta-memory have found evidence that patients perform similar to healthy controls on tasks measuring meta-memory (Bäckman & Lipinska, 1993; Gallo, Cramer, Wong, & Bennett, 2012; Moulin, Perfect, & Jones, 2000; Schmitter-Edgecombe & Seelye, 2011). As reviewed previously, Waring et al. (2008) found

that patients could shift their response bias when given more detailed instructions about the memory test. However, in the current study, patients were not told to respond in any specific manner. Changes in response bias likely reflect patients' ability to evaluate the conditions of a memory test (e.g., the memorability of items, the ratio of old to new items, their performance on prior and current memory testing, etc.), and to adjust their responding in recognition memory tests accordingly. These abilities most likely rely on an interaction between frontal, parietal, and temporal regions.

The current data indicate that patients can monitor the subjective sense of what they studied in order to try to predict how many items they actually studied. This preserved monitoring ability provides evidence that the liberal response bias observed in patients is not solely an impairment of frontally mediated decision-making in memory tests. Rather, patients' liberal response bias might be due, in part, to their over-reliance on certain memory mechanisms. Dual process theories of recognition memory suggest that two independent processes contribute to accurate recognition decisions: *recollection,* which is utilized in specific recall of an event with context/details, and *familiarity,* which is a more general sense of having encountered an event/item before without recall of the specific context (Yonelinas, 2002). Evidence has shown that patients with AD are severely impaired on their use of recollection, and as a consequence, they mainly rely on familiarity for their memory judgments (Balota et al., 2002; Hudon, Belleville, & Gauthier, 2009; Knight, 1998; Koivisto, Portin, Seinelä, & Rinne, 1998; Smith & Knight, 2002; Wolk & Dickerson, 2011; Wolk et al., 2005; Wolk, Dunfee, Dickerson, Aizenstein, & DeKosky, 2011). While familiarity is not entirely spared in patients with AD, it is better preserved than recollection (Ally, Gold, & Budson, 2009; Ally, McKeever, Waring, & Budson, 2009; Embree, Budson, & Ally, 2012; Westerberg et al., 2006). Prior work has suggested that an over-reliance on familiarity may contribute to the abnormally liberal response bias shown by AD patients (Deason, Hussey, Ally, & Budson, 2012). In the current study, patients with AD are likely unable to use recollection to inform their estimates of old and new items. Patients may have a general sense of familiarity that they studied many old items, but cannot use recollection to reject (and disqualify) new items as being old. Patients can monitor elements of a memory test, but impairments in their recollection abilities limit the accuracy of their estimates. This finding is similar to previous work, suggesting that patients can engage in various forms of strategic retrieval monitoring, but impairments in recollection limit how well they can implement such strategies (Budson, Dodson, Daffner, & Schacter, 2005; Gallo, Sullivan, Daffner, Schacter, & Budson, 2004).

The results of this study also have implications regarding findings from prior investigations into the rate of false memory in patients with AD. These studies, in general, have demonstrated that patients with AD have a higher rate of false memory, especially when gist-information is strengthened (e.g., Balota et al., 1999; Budson, Daffner, Desikan, & Schacter, 2000; Budson, Desikan, Daffner, & Schacter, 2001; Budson, Sullivan, Daffner, & Schacter, 2003; O'Connor et al., 2015; Gallo et al., 2006). Memory test lists used in these studies are often composed of an unequal number of items, usually split into a third of old items, a third of unstudied critical lure items, and a third of unrelated new items. By default, memory tests in these studies favor "new" responses more frequently than "old" responses, or in other words, they numerically bias individuals to respond more conservatively. *As demonstrated in the current study, patients' performance is similar to healthy older adults*

when the underlying ratio of old and new items are modified. Although false memory studies favor conservative responding, AD patients in false memory studies tend to exhibit a more liberal response bias relative to healthy controls (for a review, see Budson et al., 2006). The current data supports the assertion that patients' liberal response bias, to a large extent, is due to the reliance on familiarity.

The results of this study provide more information about the nature of the liberal response bias in patients with mild AD. We demonstrated that patients are able to respond similar to healthy older adults to differing ratios of old and new items in a memory test without requiring explicit instructions. Further, we discovered that patients tend to provide greater estimates of having seen more old than new items in memory testing. Combining these two findings leads us to conclude that the liberal response bias observed in patients with mild AD is directly attributable to their believing that more of the test items are old, and not due to impaired meta-memorial monitoring abilities. Thus, these patients' liberal response bias is likely due to their impairments in recollection, leading to familiarity-based false recognition of individual items. Most likely this impairment results from a disruption of a combination of brain regions rather than reflecting impairment isolated to either the temporal or frontal cortex.

Given the prior evidence and the current data, future studies can examine additional methods and strategies to leverage patients' ability to shift their response bias based on the underlying memory test composition, and their intact meta-memory. Determining strategies and interventions to help patients shift to a more conservative response bias may reduce their rate of false memories, enabling patients to live more independent and fulfilling lives.

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Highlights

-Older adults and AD patients were tested with differing ratios of old/new items.

-Both groups showed similar performance without explicit instruction.

-Subset of subjects asked to estimate count of old/new items seen on test.

-AD patients reported more old items than new.

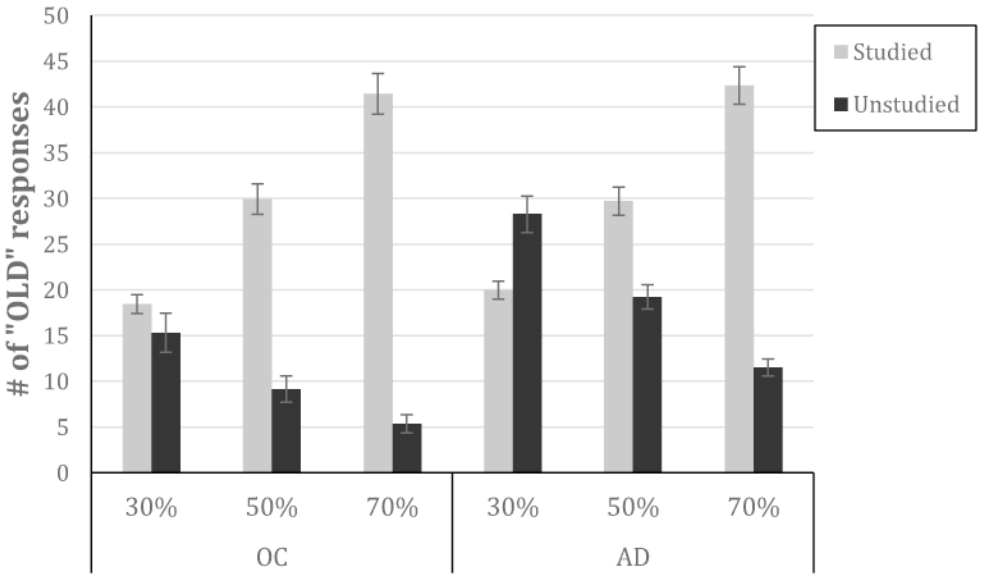

Figure 1.

Raw number of “old” responses for both healthy older adults and patients with mild AD. In the 30% condition, participants could make a total of 27 “old” responses to studied items, and 63 “old” responses to unstudied items. In the 50% condition, participants could make a total of 45 “old” responses to both studied and unstudied items. In the 70% condition, participants could make a total of 63 “old” responses to studied items and 27 “old” responses to unstudied items. Error bars are standard errors.

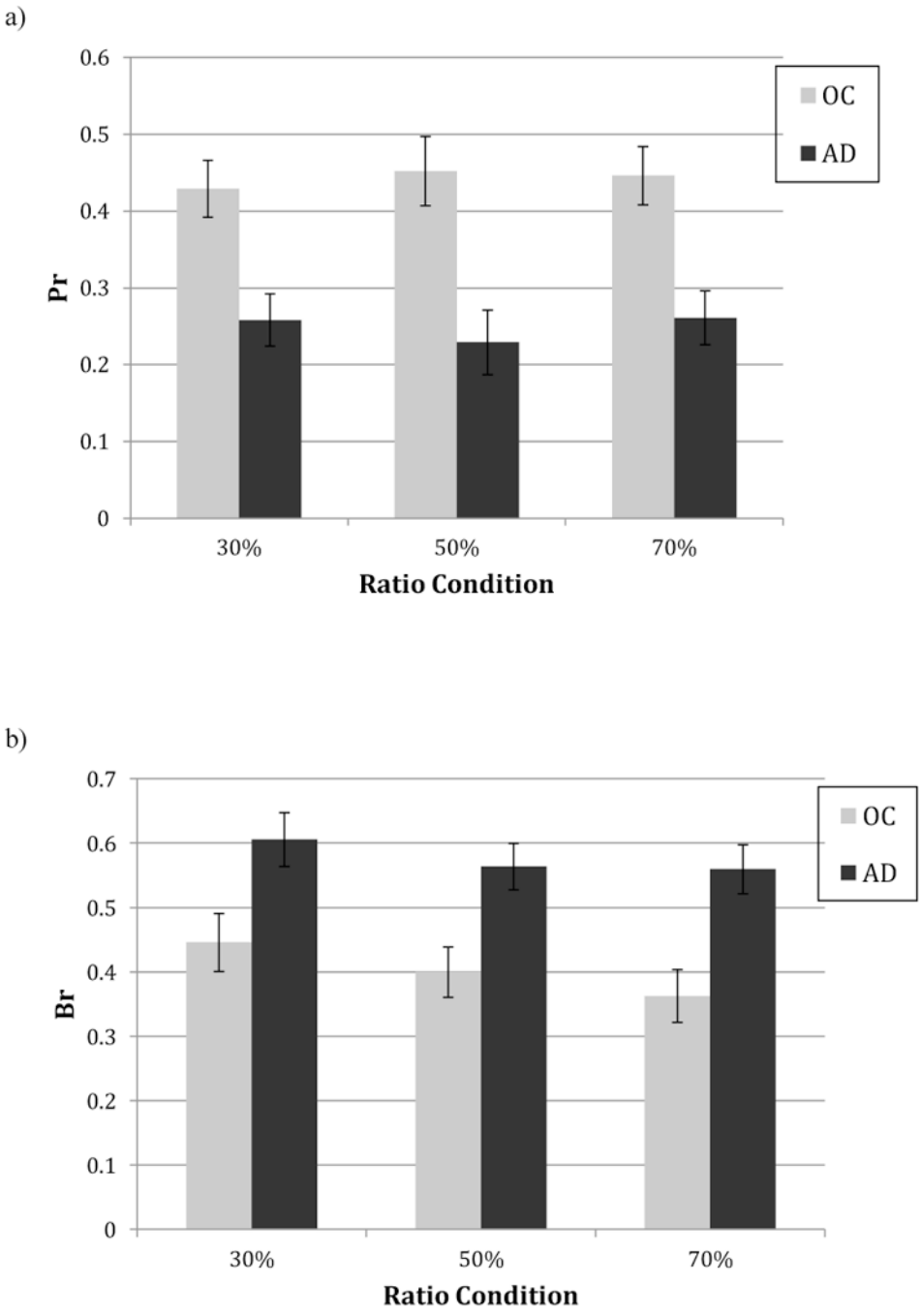

Figure 2.

a) Discrimination (Pr) performance for both healthy older adults and patients with mild AD.) Response bias (Br) performance for healthy older adults and patients with mild AD. Error bars are standard errors.

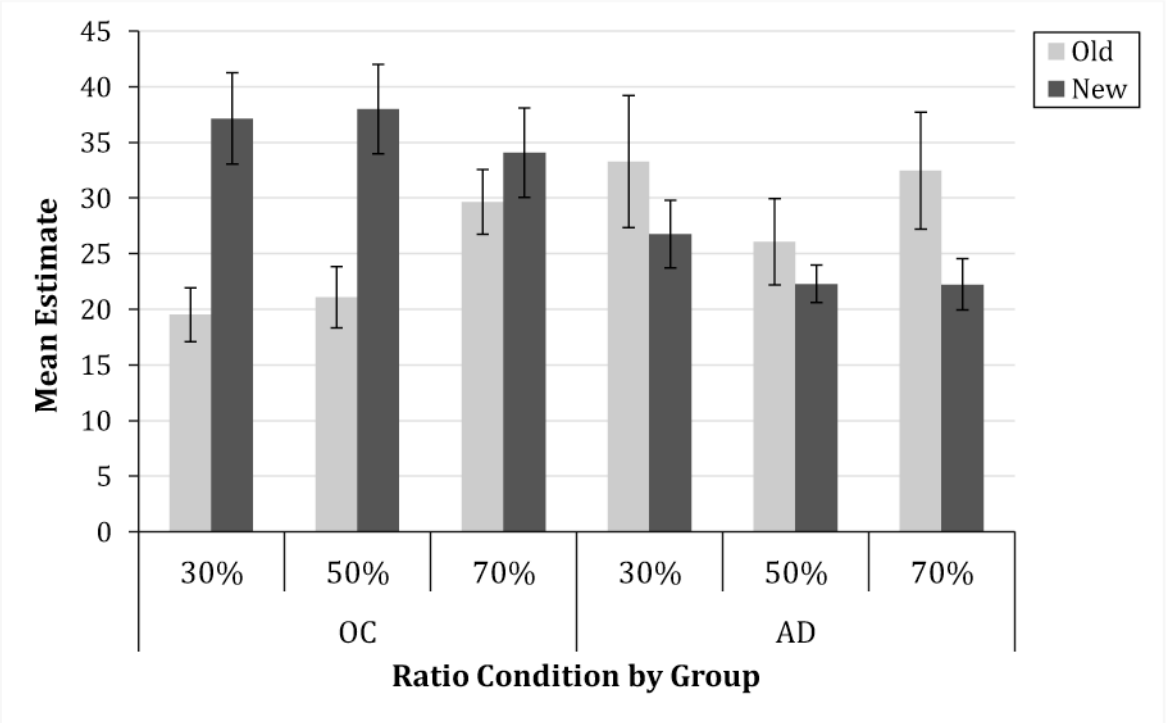

Figure 3.

Subjective reported old/new responses for both healthy older adults and patients with mild AD. The mean estimate reflects the total count of old/new items reported across both sets of questions (one at the midpoint of the experiment and one at the end). Accurate report would be 45 old/45 new items in the 50% condition, 27 old/63 new items in the 30% condition, and 63 old/27 new items in the 70% condition. Error bars are standard errors.

Table 1
Demographic and Neuropsychological data for participant groups

Test	Older Adults Mean (SD) n=25	Patients with AD Mean (SD) n=29
Age	77.16 (6.26)	79.21 (6.50)
Years of Education	16.68 (1.95)	15.90 (2.82)
MMSE	29.28 (1.06)	25.86 (3.28)
CERAD		
Immediate	21.00 (5.67)	11.83 (3.76)
Delayed	7.48 (1.90)	2.34 (2.11)
Recognition	9.72 (0.46)	7.10 (2.64)
Trails-B	79.56 (32.27)	198.62 (100.57)
FAS	46.62 (12.12)	36.07 (14.15)
CAT	44.68 (10.71)	31.24 (12.57)
BNT-15		
No cue	14.20 (1.12)	12.52 (2.89)
Semantic cue	0.12 (0.33)	0.07 (0.37)
Phonemic cue	0.56 (0.77)	1.24 (1.22)

Table 2

Hit and False Alarm rates for participant groups by ratio condition

	Older Adults		Patients with AD	
Ratio Condition	**Mean Hit (SD)**	**Mean False Alarms (SD)**	**Mean Hits (SD)**	**Mean False Alarms (SD)**
30%	.68 (.22)	.24 (.17)	.72 (.16)	.45 (.17)
50%	.67 (.18)	.20 (.13)	.66 (.19)	.43 (.18)
70%	.66 (.15)	.20 (.17)	.68 (.18)	.41 (.20)