



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



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ARTICLE INFO

Keywords:

Recognition memory
Alzheimer's disease
Response bias
Monitoring

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 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.

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, Wolk, Chong, and Waring (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.

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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 et al., 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 et al. (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 0.52 in the 70% old condition, to a mean of 0.42 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 (Hwang et al., 2007; Verfaellie, Rapcsak, Keane, & Alexander, 2004). 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, & Fansabedian, 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-memory 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 meta-cognitive 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, Schwartz, & 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 et al. (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/h for their participation.

The healthy older adults and patients with AD completed a brief neuropsychological battery in a 45-min 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

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