False memories in patients with mild cognitive impairment and mild Alzheimer’s disease dementia: Can cognitive strategies help?

Christopher Malone\textsuperscript{a}, Rebecca G. Deason\textsuperscript{b}, Rocco Palumbo\textsuperscript{a,c}, Nadine Heyworth\textsuperscript{a}, Michelle Tat\textsuperscript{a,c}, and Andrew E. Budson\textsuperscript{a,c}

\textsuperscript{a}Center for Translational Cognitive Neuroscience, VA Boston Healthcare System, Boston, MA, USA;

\textsuperscript{b}Department of Psychology, Texas State University, San Marcos, TX, USA;

\textsuperscript{c}Department of Neurology, Boston University Alzheimer’s Disease Center, Boston University School of Medicine, Boston, MA, USA

Abstract

Alzheimer’s disease (AD) is a progressive neurodegenerative disorder that presents predominantly with impairments in learning and memory. Patients with AD are also susceptible to false memories, a clinically relevant memory distortion where a patient remembers an incorrect memory that they believe to be true. The use of cognitive strategies to improve memory performance among patients with AD by reducing false memories has taken on added importance given the lack of disease-modifying agents for AD. However, existing evidence suggests that cognitive strategies to reduce false memories in patients with AD are of limited effectiveness, although these strategies may be useful at earlier stages of the disease. The purpose of this review is to examine experimental findings of false memories and associated memory processes in patients with mild cognitive impairment due to AD and mild AD dementia. Cognitive strategies to reduce false memories in these patient populations are also reviewed. Approaches to clinically relevant future research are suggested and discussed.

Keywords

Alzheimer’s disease; cognitive strategies; Deese–Roediger–McDermott; false memory; mild cognitive impairment

Alzheimer’s disease (AD) is a progressive neurodegenerative disorder characterized by a reduction in learning and memory performance, as well as rapid forgetting of new information. In addition to memory loss, patients with AD also have a higher rate of memory distortions and false memories, in which patients remember an incorrect memory.
that is believed to be true. Although the rate of false memories increase with normal aging and is associated with age-related declines in medial temporal areas (Dewitt & Schacter, 2016), the incidence of false memory among patients with AD is greater than that in normal aging. In fact, research has suggested that false memories can be a more specific indicator of both AD and amnestic mild cognitive impairment due to Alzheimer’s disease (MCI-AD; a precursor diagnosis that has a high rate of transitioning into Alzheimer’s disease) than memory performance alone (Hildebrandt, Haldenwanger, & Eling, 2009). Additionally, a recent longitudinal study has shown that aspects of memory performance like false memories may be particularly useful in identifying preclinical AD (Schmid, Taylor, Foldi, Berres, & Monsch, 2013).

The high incidence of false memories may pose a serious risk to patients as it could result in situations such as thinking that they took their medication when they have not, or believing that they turned their stove off after dinner when they have not. Therefore, cognitive strategies, including repetition, recall-to-reject, and the use of metacognitive heuristics, have been explored as a means to help patients with AD improve discrimination between true and false memories. In the following review, we examine false memories in patients with MCI-AD and mild AD as well as the use of cognitive strategies to reduce false memories, with the goal of providing guidance for future interventions that could improve cognitive function of these patient groups.

**False memories**

False memories are commonly investigated experimentally using the Deese–Roediger–McDermott (DRM) paradigm (Roediger & McDermott, 1995). In a common variant of the DRM paradigm, a participant is presented with a series of semantically associated stimuli (e.g., bed, pillow, dream, nightmare, night). One or more exemplar stimuli from the semantic category are absent during the initial presentation, but in the subsequent recognition memory test, participants commonly endorse having studied the closely associated theme word “sleep” even though this word was not presented during the study session. Some versions of the DRM paradigm use a recall test instead of a recognition test, though this variation is less commonly used in AD research due to impaired recall memory performance.

Roediger and colleagues proposed an activation/source-monitoring theoretical framework to account for false memories in their paradigm (e.g., Gallo, 2010; Roediger, Balota, & Watson, 2001). Although the theme word, or critical lure (e.g., sleep), has not been explicitly presented during the encoding phase, it can still be implicitly activated and processed. During the encoding phase, each word presented is activated, and this activation spreads to semantically associated concepts including the critical lure (Collins & Loftus, 1975). Contrary to externally generated sources (words presented) that potentially have more item-specific information, the critical lures are activated only due to spreading activation of the related words on the list (Johnson, Hashtroudi, & Lindsay, 1993). During the test phase, the participant must monitor the source of the item to correctly determine whether it was previously presented (Israel & Schacter, 1997). If the participant fails to recognize that the item is activated via internally generated spreading of activation (a failure of source monitoring), this item will be endorsed as having been presented and, thus, a false memory.
Another explanation for false memories in the DRM paradigm is based on the fuzzy-trace theory (Cann, Mcrae, & Katz, 2011; Reyna & Brainerd, 1995). This theory is based on the parallel encoding of both gist trace (semantic content) and item-specific trace (verbatim or surface form of the item) during the encoding phase (Brainerd & Reyna, 2002). Item-specific recollection is defined as specific, contextualized, details of a prior experience with an item or event. In comparison, gist memory is defined as the knowledge of the general meaning conveyed by a set of items or experiences (Reyna & Brainerd, 1995; Schacter, Norman, & Koutstaal, 1998). Contrary to the activation/source-monitoring theoretical framework that implies that false memories derive from retrieval-monitoring errors, in the fuzzy-trace theory, false memories are attributed to the gist extraction that occurs during encoding phase while true memory is attributed to the item-specific trace (Brainerd & Reyna, 2002; Brainerd, Wright, Reyna, & Mojardin, 2001). While for presented items both item-specific and gist information are available, for critical lure (new-related item) only gist information is available. Therefore, the participant will rely only on the gist memory when judging the presence/absence of critical lures during the test phase (Colbert & McBride, 2007). The fuzzy-trace theory also assumes that true memory relies on item-specific information and that this type of information decays rapidly over time compared to gist information. It follows that false memories will last longer than true memories (Brainerd, Reyna, & Brandse, 1995).

Much recent work has sought to identify brain networks involved in both true and false memory. Several studies have found that true memory more broadly results from activity in the medial temporal lobe whereas false memory is also associated with activity in the prefrontal cortex (Dennis & Cabeza, 2011; Dennis, Kim, & Cabeza, 2007; Kim & Cabeza, 2006). Recent research has investigated the role of the medial prefrontal cortex (mPFC) in schematic, or gist, memory and the relationship between the medial prefrontal cortex and medial temporal lobe (Andrews-Hanna et al., 2010; van Kesteran et al., 2013; for a review, see van Kesteran, Ruitter, Fernandez, & Henson, 2012). Van Kesteran and colleagues have outlined a framework for this relationship that predicts that damage to the medial temporal lobe will result in problems with memory for specific instances due to its role in binding item and contextual information (Ranganath, 2010), but damage to the mPFC will result in problems relating information to schemas (van Kesteran, et al., 2012). Warren, Jones, Duff, and Tranel (2014) examined false memory performance in patients with lesions to the ventromedial pre-frontal (vmPFC) cortex. Patients with damage to the vmPFC showed lower levels of false recall than healthy controls, suggesting that this area of the prefrontal cortex may be related to processing of the gist information that leads to false memories in the DRM paradigm. Ghosh, Moscovitch, Melo Colella, and Gilboa (2014) also found evidence that patients with damage to the vmPFC had difficulty transitioning and using appropriate schemas. Similar findings by Spalding, Jones, Duff, Tranel, and Warren (2015) suggested that patients with damage to the vmPFC were less influenced by gist memory and, therefore, demonstrated reduced false memories based on prior context than controls.

Neuroimaging and neuropathology studies have established that AD impairs functioning of the hippo-campal formation and entorhinal cortex, as well as connections to other structures important to memory and the disruption of the default network (Buckner, Andrews-Hanna, & Schacter, 2008; Buckner et al., 2005; Hyman, Van Hoesen, Damasio, & Barnes, 1984).
The increase in false memories among patients with AD potentially results from the damage to the hippocampus and, at the same time, some preservation of the mPFC region leading to more reliance on gist, or schema, memory. The pathology of AD is crucial to understanding patient performance on false memory studies and the formation of false memories.

**False memories in Alzheimer’s disease**

Episodic memory decline in Alzheimer’s disease has been well studied, but there has been less investigation into how the disease pathology contributes to false memories (Hildebrandt et al., 2009; Weintraub, Wicklund, & Salmon, 2012). To better understand the impact of AD on false memories, Balota and colleagues presented five groups of participants with six 12-item word lists in the DRM paradigm (Balota et al., 1999). The results revealed that true recall and recognition of the study items had a negative correlation with both age and dementia severity. Impaired recall of studied items, increased unrelated intrusions, and relatively low false-alarm rates were found in both patient groups (i.e., patients with very mild AD and patients with mild AD). However, once the groups were matched for true memory performance, patients with AD were more likely than healthy older adults to falsely recall lures. The authors interpreted this result to mean that susceptibility to false recall is not a simple reflection of a decrease in item-specific recollection.

To further explore these findings, Budson and colleagues sought to determine whether patients with AD are impaired in gist memory as well as item-specific recollection (Budson, Daffner, Desikan, & Schacter, 2000). They presented patients with AD and young and old healthy controls with six 15-word DRM lists across five study–test sessions. After a single stimulus presentation, patients with AD demonstrated lower levels of true recognition, lower levels of false recognitions to related lures, and higher levels of false recognition to unrelated lures than healthy controls. After multiple stimulus presentations, however, patients with AD demonstrated improved true recognition, reduced false recognition of unrelated lures, and increased levels of false recognition to related lures. Healthy older controls demonstrated a pattern of improved true recognition and reduced false recognition of both related and unrelated lures. These results suggest that the influence of gist on memory decisions in patients with AD is initially very weak, but is strengthened with repeated stimulus presentation, and this leads to increased false recognition for the critical lures. Although healthy participants are able to oppose these gist influences with item-specific recollection, patients with AD are less able to combat the influence of gist memory due to poor item-specific recollection.

To further explore the quality of memory impairment among patients with AD, Budson, Todman, and Schacter (2006) designed another experiment to specifically measure the impairment of gist memory in Alzheimer’s disease. In this study, patients with AD and healthy older controls were presented with a series of categorized pictures and were asked during a recognition memory test to identify either whether the test item is the same as an item studied before (item-specific recollection) or whether it belongs to a category of items previously studied (gist memory). Results showed that patients with AD made fewer endorsements of related lures after being asked to decide whether the test item was a member of a previously studied category, suggesting that gist memory is impaired in patients.
with AD. In essence, gist memory is weak and impaired in patients with Alzheimer’s disease; however, it is much less impaired than item-specific memory.

This reliance of patients with AD on the use of gist memory in the DRM paradigm has been replicated in studies using different design manipulations including varying associative strength of study lists in either blocked or mixed presentations (Gallo et al., 2006), pictorial stimuli (Abe, Fuji, Nishio, Izuka, Kanno, & Mori, et al., 2011; Budson, Michalska, et al., 2003), and words (Waldie & Kwong See, 2003). It has also been reported that patients with AD are predisposed to remember gist-based details of narratives after a single reading and to remember significantly fewer item-specific details than healthy controls and MCI-AD patients (Hudon, Belleville, Souchay, Gely-Nargeot, & Chertkow, 2006). This reliance on gist memory was replicated even when patients with AD have been prompted to more deeply encode information and respond according to item-specific knowledge at the expense of gist memory (Pierce, Sullivan, Schacter, & Budson, 2005; Wolk, Gold, Signoff, & Budson, 2009). Overall, these results suggest that processing information more deeply does not improve the ability of patients with AD to determine the source of the information (i.e., source memory), but rather only serves to enhance their gist memory for the material. Patients with MCI-AD have also been found to be relatively reliant on gist memory and prone to falsely recognize stimuli (Plancher, Guyard, Nicolas, & Piolino, 2009; Waldie & See, 2003), and have shown elevated false memories with both words and pictures (Deason, Hussey, Ally, & Budson, 2012), when compared to healthy older controls.

Semantic memory is defined as knowledge about ideas and concepts that are not tied to a personal experience (Manns, Hopkins, & Squire, 2003). For example, an individual may know that Paris is the capital of France but be unable to tell you the context in which they learned this. Patients with AD have semantic impairment that has been shown to correlate with cortical atrophy in the anterior temporal lobe and inferior prefrontal cortex, key areas associated with semantic memory (Joubert et al., 2010). Semantic memory is necessary for the ability to form a gist memory for a collection of semantically related items. Budson and colleagues (Budson, Sullivan, Daffner, & Schacter, 2003) sought to determine whether the initial occurrence of low levels of false recognition in patients with AD was due to a semantic memory deficit, item-specific recollection deficit, or both. In a study design including patients with AD, healthy young adults, and healthy older adults, the authors presented lists of semantic, phonological, and mixed stimuli and then immediately tested recognition memory for the words. All groups demonstrated similar levels of false recognition across all stimulus types, and patients with AD showed lower levels of corrected false recognition (lure false alarms minus unrelated new false alarms) than control groups. This result was thought to be due to reliance on gist memory, rather than purely semantic memory impairment, as dysfunction in the semantic network would result in a lower level of corrected false recognition for semantically related lure items than for phonologically based lure items. In a study examining false memories using a modification of the DRM paradigm, intact semantic priming was found for both healthy older adults and patients with mild or moderate AD (Evard, Colombel, Gilet, & Corson, 2016). Evard and colleagues used a lexical decision task in place of the typical recognition memory test in the DRM paradigm to show preserved priming for the critical lures in AD patients. Therefore, the results of these studies provide further evidence that the pattern of memory performance among patients
with AD is due to reliance upon gist memory or problems with monitoring, as opposed to impaired semantic memory.

The findings from these studies have demonstrated that potentially mild AD pathology in the hippocampus may result in difficulties creating highly contextualized memories (i.e., item-specific recollection), whereas the ability to remember the general meaning of a set of items (i.e., gist memory) is somewhat better preserved, at least early in the course of the disease. The associative strength of the stimuli results in activation of semantic networks strengthening the gist memory for the overarching semantic associates. With repeated stimulus presentation, patients with AD develop a strengthened gist memory for the semantic association, which results in both increased true and false recognition as the patients endorse studied and unstudied items from the target category alike, in contrast to the memory performance of healthy older adults who can use relatively intact item-specific recollection to enhance true recognition and decrease false recognition. Although this is a potential reason for the increased false memories seen in patients with AD, it is important to note that patients with medial temporal amnesia do not show this same pattern of increased false memories (Snodgrass & Corwin, 1988). Thus, the increase of false memories cannot be attributed only to a reliance on familiarity as it could be argued that this is the only memory trace available to amnesic patients.

**Response bias in Alzheimer’s disease**

Patients with AD have been found to endorse unstudied stimuli more frequently than expected in recognition memory tests, which indicates a liberal response bias (Budson, Wolk, Chong, & Waring, 2006). Importantly, patients with AD have been found to have an abnormally liberal response bias even when their discrimination ability is matched to that of healthy controls, by giving healthy controls more difficult study lists. Further, the liberal response bias of patients with AD correlates with their overall episodic memory abilities, which suggests that this response bias may be a direct result of disease progression. Patients with AD have exhibited an increased liberal response bias when presented with both categorized pictures (Budson, Todman, & Schacter, 2006) and emotional pictures (Gallo, Foster, Wong, & Bennett, 2010). Patients with AD exhibit a liberal response bias for both words and pictures, and this effect is consistent even when study lists are made more difficult by increasing the length (Beth, Budson, Waring, & Ally, 2009). Additional studies have also shown that the liberal response bias in patients with AD is present at both immediate and long-delay conditions (Deason, Hussey, Ally, & Budson, 2012).

Budson and colleagues (Budson, Todman, Chong, Adams, Kensinger, & Wright, 2006) examined memory for emotional compared to nonemotional word lists among patients with AD, young controls, and older controls. While both younger and older controls demonstrated increased true recognition for emotional words compared to control lists they also exhibited an increase false recognition of emotional words, suggesting that the emotional quality of the stimulus appeared to elicit a liberal response bias from older and younger controls. Among patients with AD, the emotionality of the stimuli did not improve their true recognition but caused them to engage in a more conservative responding bias.
This study is notable for demonstrating that the distinctive quality of emotional stimuli can reduce both true and false recognition among patients with AD.

Fluency is a measure of the relative difficulty of processing a stimulus, with highly fluent items being more easily processed than a lower fluency stimulus. Prior studies have shown that enhancing fluency can increase the likelihood of endorsing unstudied items (Jacoby & Whitehouse, 1989). Additionally, enhancing conceptual fluency of visual stimuli can shift patients with AD into adopting a more liberal response bias leading to increased true and false recognition (Gold, Marchant, Koustaal, Schacter, & Budson, 2007). Wolk and colleagues (2009) found that patients with AD and healthy controls increasingly relied on fluency cues as their discrimination decreased in a recognition memory test, suggesting that reliance on fluency cues is inversely related to discrimination ability.

There are a number of explanations for the liberal response bias found among patients with AD. Impaired gist memory may result from inefficient activation during encoding, which not only impairs recognition memory for specific items at test, but also impairs the formation of gist memory for studied items (Budson, Todman, & Schacter, 2006; Gallo et al., 2006). The gist memory trace that is formed may, therefore, end up being overly broad, leading to endorsement of items only vaguely similar to the semantic representation formed by healthy older adults. The liberal response bias of patients with AD may be exacerbated by impaired evaluative cognitive processes, which further limit their ability to monitor their memory decisions at test. Therefore, dysfunction in the frontal network may result in impaired ability to engage cognitive processes to evaluate the accuracy of memory decisions and to oppose the influence of gist memory.

Waring and colleagues (Waring, Chong, Wolk, & Budson, 2008) investigated whether it was possible to shift the response bias of patients with AD to be more conservative through an explicit instructional manipulation. Patients with AD and healthy controls were presented with a series of word lists in two separate study/test sessions. In one session, participants were told that 30% of words were old at test and in the other session were told that 70% of words are old, when in reality both lists were 50% old. Both groups were able to use metacognitive information to shift their response criterion to become more conservative when appropriate, though this more conservative response bias did not improve discrimination in patients with AD. Though signal detection theory establishes that response criterion and discrimination are orthogonal in recognition memory decisions (Kantner, Vettel, & Miller, 2015; Macmillan & Creelman, 2004), it would have been desirable to see improved discrimination as well as a shift in response bias. Recently, Deason et al. (2017) further examined whether AD patients could shift their responses patterns appropriately when instead of an explicit instruction as in the Waring et al. (2008) study, they had only the underlying ratio of old/new items to influence their behavior. Participants were not provided with any instructions, but the ratio of old/new items varied between study/test sessions. Both groups were able to adapt their response patterns to the underlying ratio without the aid of explicit instructions. Another interesting aspect of this study was that at two time points in the experiment (halfway and end) the participants were asked to estimate how many old and new items they had encountered. Patients with AD estimated higher numbers of old items than of new items, potentially due to their reliance on more gist-based memory. Further
support for this use of metacognitive information comes from studies that demonstrated that patients with AD could use metamemory to reduce susceptibility to fluency-based memory illusions (Willems, Germain, Salmon, & Van der Linden, 2009), and musical encoding may shift AD patients to a more conservative response bias (Simmons-Stern, Deason, Bradler, Frustrate, O’Connor, Ally, & Budson, 2012).

The effect of emotion on false memories

Emotionally arousing pictures have been found to be more prone to false memory errors in healthy older adults. Gallo and colleagues (Gallo, Foster, Wong, & Bennet, 2010) sought to determine whether emotionally arousing pictures led to increased false recollection in Alzheimer’s patients. They presented patients with AD and healthy controls with either pictures with verbal labels or verbal labels alone. In a subsequent recognition memory test, participants were presented with verbal labels and instructed to only endorse labels that were studied along with a picture and to then rate their confidence for their decision. Both patients and healthy participants incorrectly endorsed verbal labels that had not been studied with pictures, and rated these judgments with medium to high confidence levels. The confidence judgments for falsely recalled items were greater for emotional items than for neutral items, and items with a positive valence elicited the greatest degree of false recall in both patients with AD and healthy participants. It is important to note that this study was designed to reduce the usefulness of familiarity-based memory decision by presenting the verbal labels of both test and lure items so that both sets of labels would elicit a feeling of familiarity during the test period. The authors interpreted these results to show that patients with AD are as similarly susceptible to emotional effect on false memory as healthy controls (Gallo et al., 2006; LeBar et al, 2005).

Fairfield and colleagues sought to determine whether the emotional valence of pictorial stimuli affected the creation of false memories in patients with AD (Fairfield, Colangelo, Mammarella, Di Domenico, & Cornoldi, 2017). Patients with AD and healthy older controls were presented with nine series of 12 pictures with each series depicting the precipitants and results of an unseen action on a routine daily activity (e.g., shopping, meeting a friend, etc), referred to as “scripts.” These picture sequences differed between participants by a single picture, which depicted a positive, negative, or neutral outcome for the script. Participants were asked in an immediate recognition memory task whether they had seen the picture in the encoding task or not. False items in the recognition memory task were designed to assess two different memory errors: whether the unseen action was plausible for the daily activity (i.e., plausible script error), or whether the unseen action was causal to the outcome of the picture (i.e., causal error). Assessing plausible script errors allowed the researchers to determine how well the participants processed each script. Causal errors allowed the researchers to assess whether the emotional valence distorted the participant’s memory for the script. In essence, the researchers sought to determine whether participants could accurately remember the pictorial scripts without falsely recognizing an image coherent with the script but not presented (i.e., a plausible error) or an image that was not presented but explained the outcome of the script (i.e., a causal error). Results revealed that healthy controls had better true memory but committed more causal memory errors than patients with AD, which suggests greater inferential and conceptual processing of the scripts.
Healthy older controls and patients with AD endorsed similar levels of plausible script errors, suggesting an encoding and reliance upon the gist of the scripts in the memory task. Further, patients with AD committed more causal errors for positive and negatively valanced scripts than for neutral scripts, which suggests that their memory for pictorial information is vulnerable to distortions due to emotional valence. This finding that patients with AD demonstrate increased memory errors to emotionally valanced pictures has been replicated when attention at encoding was manipulated (Sava, Paquet, Dumurgier, Hugon, & Chainay, 2016).

Further investigations on the effect of emotion on false memories have used an emotional variant of the DRM paradigm. Using this version of the task, Brueckner and Moritz (2009) revealed that memory performance in patients with MCI-AD and mild AD was characterized by increased false recognition to stimuli with a positive valence, despite recognizing emotions as well as healthy controls. This suggests a breakdown in emotional memory in MCI-AD and AD beyond the experience of normal aging. It should be noted that the AD group in this study was unable to use the emotionality of the stimuli to improve their true recognition compared to neutral stimuli, whereas both the healthy older control and MCI-AD groups were able to (Brueckner & Moritz, 2009).

Overall, emotional content tends to elicit a more liberal response bias in participants, which results in a greater degree of false memories for emotional material than for neutral material (Gallo et al., 2010); however, there is some evidence that patients with AD are instead shifted to a more conservative response bias (Budson, Todman, Chong, et al., 2006). Shifting the response bias of patients with AD may be crucial, as is discussed below, to reducing the rate of false memories experienced by this population.

**Dysfunction of frontal networks**

Previous research has also found increased levels of false recognition in patients with damage to their frontal lobes (Lavoie, Wiloughby, & Faulkner, 2006; Parkin, Binschaedler, Harsent, & Metzler, 1996; Schacter, Curren, Galluccio, Milberg, & Bates, 1996), although there have been important exceptions to this pattern (Verfaellie, Rapcsak, Keane, & Alexander, 2004). This suggests that one possible explanation for the increase in false memories in patients with AD is the pathological changes not only to the hippocampal regions, but also to areas of the frontal cortex, with some researchers hypothesizing that inhibitory control may be especially important (Flanagan et al., 2012). Support for the involvement of cognitive abilities in addition to memory comes from a study in which patients with AD and patients with frontal lobe lesions were found to exhibit similar patterns of false recognition with repeated exposure to study lists (Budson, Sullivan, et al., 2002). The patients with frontal lobe lesion were determined to have intact hippocampus and related medial temporal lobe structures while still demonstrating increased false recognition. These findings suggest that frontal network impairment may contribute to the elevated false recognition in patients with frontal lobe lesions and patients with AD. Although it is difficult to determine which specific frontal network impairments are responsible for the results of this study, the authors posited that the inhibition of prepotent reactions and postretrieval memory decision monitoring (i.e., verification- inhibition mechanisms) are impaired in both...
frontal lobe lesion patients and patients with AD. Further, frontal networks have been implicated as critical to the application of cognitive strategies to reduce false memories (Hwang et al., 2007). However, research attempting to quantify specific frontal deficits in patients with AD has thus far been unsuccessful, with some researchers specifically positing that common neuropsychological measures of frontal lobe functioning may not be specific enough to identify early frontal impairments experienced by patients with AD (Budson, Wolk, et al., 2006; Deason, Hussey, Ally, Budson, 2012).

The relationship between prefrontal cortex (PFC) functioning and false memories is nuanced as the PFC is critical for processing gist information and relating information to schemas (Andrews-Hanna et al., 2010; van Kesteren et al., 2012, 2013). Recent models suggest that the neurobiological underpinnings of semantic memory are spread across diffuse brain regions dependent upon the nature of the information (Binder & Desai, 2011), and that prefrontal regions are recruited more heavily during selection tasks than during retrieval tasks (Martin & Chao, 2001). Impairment to prefrontal regions may either increase or decrease false memory depending upon the nature of the task. False memory is reduced, compared to controls, among patients with prefrontal lesions when task demand emphasizes selection and relating information to gist (Warren et al., 2014), whereas patients with prefrontal lesions may experience higher levels of false memory, compared to controls, when inhibitory and monitoring abilities are emphasized in the task demand, and ability to relate information to gist is relatively preserved (Flanagan et al., 2016). It should be noted that the PFC includes many distinct subregions and structures, which may have different effects on memory or behavior depending on the precise location of the lesion or impairment (Devitt & Schacter, 2016).

Multiple studies have suggested that some degree of frontal impairment in patients with AD contributes to their memory performance at test. Distracted attention during the encoding of modified well-known fairy tales was found to induce more confabulations in patients with AD than in controls (Attali, De Anna, Dubois, & Dalla Barba, 2009). Conceptual fluency has been found to preferentially enhance gist memory, and research has found that patients with AD may be impaired in their ability to monitor their responses and engage postretrieval verification processes to reduce false recognition resulting from enhanced gist memory (Gold et al., 2007). As noted earlier, monitoring processes may depend on intact frontal lobe functioning. Patients have shown a high degree of nonsemantic intrusions in recall memory tests and breakdowns in monitoring processes as a consequence of AD (MacDuffie, Atkins, Flegal, Clark, & Reuter-Lorenz, 2012). The pattern of increasing false recognition of related lures among patients with AD in repeated stimulus presentation studies suggests impaired item-specific recollection-based memory monitoring (Abe et al., 2011). This is also supported by research demonstrating an inability of patients with AD to effectively use recall-to-reject monitoring processes (Gallo, Sullivan, Daffner, Schacter, & Budson, 2004; Pierce, Waring, Schacter, & Budson, 2008).

Frontal network dysfunction is associated with monitoring deficits, and patients with AD have also been found to be impaired in their monitoring abilities. Patients with AD demonstrate impaired monitoring of memory judgments, unrelated to memory performance, in comparison to healthy older adults (Dodson et al., 2011). Patients with AD have also been
found to commit more misattribution errors, compared to healthy controls, which may be a result of an impaired ability to direct and sustain attention to formulate and evaluate memory decisions (i.e., dysfunctional attentional-activation monitoring system; Mitchell, Sullivan, Schacter, & Budson, 2006).

In a closely related phenomenon, patients with AD have been found to be susceptible to the imagination inflation effect (i.e., imagining an event can increase the likelihood of incorrectly responding that the action was performed). O’Connor and colleagues had patients with AD and healthy older controls perform, listen, or imagine action statements (e.g., “fill the pillbox”; O’Connor et al., 2015). Following this section, they had the same participants imagine performing a selection of the action statements from the first section one or more times. After a day delay, they tested their source memory for the statements presented in the first section. Patients with AD were found to falsely remember performing the actions more than healthy controls after being asked to repeatedly imagine the actions. Enhanced source memory, the knowledge of the context in which information was previously encountered, may help reduce false memory as the absence of specific information could serve as a cue that the information was not previously experienced. However, this study provides further evidence for a deficit of source monitoring in patients with AD.

Plancher and colleagues (Plancher et al., 2009) correlated performance on neuropsychological tests with an experimental memory test to explore which other cognitive domains may relate to memory performance. They administered a neuropsychological test battery to young adults, older controls, and patients with AD, and presented them with categorized lists of names of famous people. The participants were then administered a recall and recognition memory test. The memory performance of patients with AD was lower than that of the younger and older controls in both the recall and recognition memory test. Semantic false memories were found to increase with age but not with dementia severity; however, patients with AD were found to produce a much higher number of nonsemantically related intrusions. However, a notable weakness of this study is that the associative strength of the famous names stimuli was determined using a normative sample that was significantly younger and better educated than the experimental sample. This raises the possibility that the results of this study were confounded by both cohort effects and decreased associative semantic network activation during the study phase, which may have depressed the performance of both the older adults and patients with AD. Importantly, the overall assessment of executive functions in this study were found to serve as a mediator of both related and unrelated false memories across groups with greater executive functions resulting in a lower level of false memories. This relationship between measured executive functioning abilities and false memories suggests that intact higher order cognitive abilities (i.e., executive functions) may aid a patient to partially compensate for memory distortions resulting from impaired hippocampal memory abilities.

**Strategies to reduce false memories**

Past research exploring the use of memory strategies in false memory studies have typically tried to enhance either item-specific recollection or gist memory (Budson, Sitarski, Daffner,
item-specific recollection tend to require more cognitive effort to execute effectively as they generally require some form of deeper encoding or manipulation of the stimuli (Budson, Sitarski, et al., 2002; Tat et al., 2016). In contrast, strategies to enhance gist memory require relatively less mental effort as the enhancement of gist memory occurs through additional exposure to related information, rather than mental manipulation of it. In the following section, we discuss the application of a variety of strategies to reduce false memories in patients with AD and how the use of these strategies relates to item-specific recollection and gist memory.

Researchers have examined the use of cognitive strategies to reduce levels of false memory among patients with MCI-AD and AD (see Table 1). The distinctiveness heuristic, one of these potential strategies, is a response monitoring strategy whereby participants make recognition memory decisions based on the unique qualities of a stimulus or event and their expectation of remembering these unique qualities (Dodson & Schacter, 2002). For example, participants are exposed to a series of words, and some of the words are presented with corresponding pictures. In a later recognition memory test, the participants are more likely both to correctly endorse the words that were presented alongside pictures and to correctly reject words that were not studied with pictures (Budson, Sitarsky, et al., 2002). This pattern of performance occurs because the pictures that were presented along with the words conferred an added dimension to the studied material that tends to improve the accuracy of memory judgments. With the distinctiveness heuristic, an individual might say to herself, “the word on the test is spider and it must be a new word, because if I saw a picture of a spider I’m quite sure I would have remembered it!” Although the distinctiveness heuristic and other monitoring strategies have been found to be highly effective strategies among young and old healthy participants (Dodson & Schacter, 2002), the evidence of effectiveness in patients with AD is far more variable (Abe et al., 2011; Budson, Dodson, Daffner, & Schacter, 2005; Budson, Sitarski, et al., 2002; Deason et al., 2017; Pierce et al., 2008).

Budson and colleagues (Budson, Sitarski, et al., 2002) examined the effectiveness of the distinctiveness heuristic to reduce false recognition of semantic associates in patients with AD. They presented patients and healthy older controls with visual words or pictures, accompanied by their auditory labels. Pictures are thought to enhance the distinctiveness heuristic by conveying more distinctive perceptual information than printed words. Older adults were found to have lower levels of false recognition of auditory words paired with pictures than auditory words paired with visual words in this study. However, patients with AD showed a reverse pattern, demonstrating higher levels of false recognition when items were studied with pictures. This result suggests that patients with AD were unable to use the distinctiveness heuristic to reduce false recognition. The authors further found that presenting patients with both visual and auditory stimuli at test shifted their response bias to be more liberal (i.e., patients responded “old” more frequently to both studied and unstudied items).

To further explore this potential metacognitive deficit in patients with AD, Budson and colleagues (Budson, Dodson, Daffner, et al., 2005) presented lists of pictures and corresponding verbal labels and then tested the patient’s memory using verbal labels. This
study employed a repetition-lag paradigm of unrelated items to better control for the influence of gist on memory decisions, not controlled for in previous studies (Budson, Sitarski, et al., 2002). This study used picture stimuli to better separate the effect of distinctiveness, through the deeper encoding of visual and source information. During the study period, participants were presented with either the picture or printed word visually, along with the auditory presentation of the word. The participants were then tested on their memory for the studied items along with 45 new items, all of which repeated at various lag intervals, defined as the number of intervening words presented between repetitions of test items. Participants were informed that no studied items were repeated at test, and so recognizing that the item was repeated should serve as a cue to the participants to not endorse that item. Patients with AD endorsed fewer true items in the picture condition than in the word condition whereas the older adult group endorsed more true items in the picture condition than in the word condition. This suggests that the additional information conferred by pictures aided the healthy group but not patients with AD. The patient group incorrectly endorsed significantly more new and repeated (lag) items than older controls. The results of this study revealed that patients with AD could employ the distinctiveness heuristic to improve their memory for studied items; however, they were limited in their ability to effectively use this strategy because of their impairment in item-specific recollection abilities. This pattern of greater performance of healthy older adults in memory tasks of pictures, in relation to words, when compared to that of patients with AD has been replicated and suggests that the additional information conveyed by pictures aids in retrieval monitoring of healthy participants but not of patient groups (Gallo, Chen, Wiseman, Schacter, & Budson, 2007).

Recall-to-reject monitoring is the use of source or item-specific recollection to oppose familiarity in recognition memory tasks (Abe et al., 2011; Gallo et al., 2004). In a recall-to-reject paradigm, a participant is exposed to a stimulus in one of two contexts and is prompted to use contextual information to enhance their memory decision. For example, if participants study words in a red or blue font, and are subsequently tested and asked to only endorse words studied in a blue font, upon encountering the test word they may think, “I definitely remember studying the word in a red font, so I cannot have studied it in a blue font,” and reject the item. In this example, the participant used the contextual information from the study phase to improve their memory decision at test. Abe and colleagues (2011) sought to evaluate the effectiveness of recall-to-reject monitoring among patients with AD. They presented patients with AD and healthy controls with unrelated pictures either once or three times. In the subsequent recognition memory test, participants were presented with old pictures seen at encoding, similar picture lures, and unrelated new pictures and were asked to indicate which pictures had been seen in the study phase. Repeated presentation increased the hit rate for true old pictures in both groups but increased the false-alarm rate for the similar lure pictures in the AD group alone. The results of this study suggest that patients with AD are impaired in their use of recall-to-reject monitoring to reduce false recognition. Overall, the results from Abe et al. (2011), in addition to those of the previously described study by Budson, Dodson, Daffner, et al. (2005), demonstrate that patients with AD are unable to use stimulus repetition at either study or test to improve discrimination in a recognition memory test.
There is further evidence that patients with AD are unable to selectively use distinctiveness information to improve recall-to-reject monitoring. Pierce and colleagues (Pierce et al., 2008) presented patients with AD and healthy younger and older adults with categorized word lists with/without corresponding pictures and then primed them to either shallowly or deeply encode the stimuli along with an intervening incidental task. They were then tested with a recognition memory test where if they responded “yes” they also had to make a source memory judgment about the item. Younger and older healthy controls were able to improve their source memory judgments in the picture condition but patients with AD were not. The enhanced information conveyed by the pictures improved the source-monitoring ability of older adults but patients with AD were unable to selectively use the enhanced distinctive information of pictures to improve their recall-to-reject monitoring (Pierce et al., 2008).

However, in a recent study, Deason, Nadkarni, and colleagues (2017) found that using a metacognitive strategy that enhanced recall-to-reject monitoring reduced false memories in patients with mild cognitive impairment. In their study, patients with MCI-AD and healthy older adults were presented with a simulated trip to the grocery store where they first studied items in the cupboard (viewed as pictures), then they studied items on their shopping list (viewed as words), and subsequently were tested on a mixture of old (both items from their cupboard and shopping list) and new pictures. In one session, they were simply asked whether they needed to buy each item in the test phase (cupboard = yes, shopping list = no, new = no). In the second session, they were asked a series of questions to highlight the source of the memory for old items and encourage the use of a recall-to-reject strategy. Patients with MCI-AD showed a reduction of false recognition in the test using the metacognitive instructions compared to the standard instructions suggesting that this group benefited from this strategy. The real-world source memory task simulated in this experiment may have enhanced patients’ ability to utilize retrieval monitoring strategies effectively or potentially; patients with MCI-AD may have more metacognitive abilities preserved than in patients with mild Alzheimer’s disease, leading to the differences in findings.

Self-referencing is an approach to improve memory for studied information by relating it to personal experiences or characteristics (Rosa & Gutchess, 2013). Self-referencing has been found to enhance memory through more deeply processing the information and relating it to a high-fluency schema (i.e., the self). Rosa and colleagues sought to determine whether a self-referencing encoding strategy increases false memories through the enhancement of a sense of familiarity to personally salient stimuli in older adults and patients with MCI-AD (Rosa, Deason, Budson, & Gutchess, 2015). Healthy older adults and patients with MCI-AD were presented with two lists and rated each one for either self-descriptiveness or commonness. Results revealed that self-reference increased discrimination among older controls but was not beneficial to patients with MCI-AD. Patients with MCI-AD performed similarly in both the commonness and self-referential conditions, and while their false-alarm rate was higher than that of the older group in both conditions, no difference was found in false-alarm rate between conditions. These results revealed that while patients with MCI-AD were not able to improve their performance through use of a self-referencing strategy, their performance was also not harmed as predicted, through increased familiarity to self-
referential information. A follow-up study examining the use of self-referencing, by patients with MCI-AD and healthy controls, to improve memory for physical objects found that this approach improved the true and source memory among patients with MCI-AD (Rosa, Deason, Budson, & Gutchess, 2016).

Item-specific encoding has been found to effectively reduce false memory of young and old healthy adults in the DRM paradigm (McCabe et al., 2004). Item-specific encoding is an elaborative encoding strategy whereby a participant generates a distinctive feature of an item in order to more deeply encode it. Tat and colleagues (Tat et al., 2016) sought to determine whether this strategy could be used effectively by patients with MCI-AD and mild AD. They presented healthy older adults, patients with MCI-AD, and patients with mild AD with lists of categorized words in the categorized word list (CWL) paradigm. The CWL paradigm is similar to the DRM paradigm but the study lists are composed of taxonomic categories, and the lure words at test are nonpresented prototypical members of the categories. In the item-specific encoding condition, participants were asked either to generate a unique quality of the item (e.g., for “train” to say “coal powered”) or to report a personal connection to the item (e.g., for “train” to say “I took the train to New York last year”). In the relational condition, the participants were asked to determine how each item in the study list was related to each other. Results revealed improved memory discrimination in the item-specific condition, compared to the relational condition, for both the healthy older controls and the MCI-AD groups. Patients with AD were unable to improve their memory performance using item-specific encoding. The authors hypothesized that intact frontal networks are necessary to successfully execute item-specific encoding and that patients with AD were unable to use the strategy because of frontal-executive deficits resulting from mild AD pathology.

In summary, a variety of strategies have been examined to reduce false memories in patients with MCI-AD and AD in false-memory studies. Patients with MCI-AD are often able to use cognitive strategies to improve discrimination (Rosa et al., 2016) and to reduce the risk of errors resulting from impaired memory abilities (Rosa et al., 2015). Patients with MCI-AD can also use such techniques to reduce their gist-based false memories (Tat et al., 2016). When evaluated on the basis of pure memory abilities, subjects with MCI-AD typically perform in the intermediate range between subjects with AD and controls (Hildebrandt et al., 2009). In essence, the available literature appears to suggest that while patients with MCI-AD are impaired on memory tasks, they are generally able to compensate when using cognitive strategies to enhance either memory (item-specific recollection or gist) or monitoring abilities.

In contrast, there is evidence that the use of techniques for enhancing item-specific recollection in patients with mild AD served to enhance their gist memory, rather than improve their item-specific recollection for the studied items (Pierce et al., 2005; Wolk et al., 2009). In some cases, patients with mild AD were able to reduce their unrelated false memories but not gist-based false memories (Budson, Dodson, Daffner, et al., 2005). Another trend in the research is that patients with AD tend to have more difficulty applying strategies effectively and consistently, suggesting that cognitive domains other than memory are impacting their performance on memory tests (Budson, Dodson, Daffner, et al., 2005; Tat et al., 2016).
Conclusion

False memories have been experimentally induced in patients with AD under a vast array of manipulations. With an impaired ability to form highly contextualized memories of the lists of stimuli (i.e., item-specific recollection), patients with AD instead rely on gist representations of studied material for their memory decisions (Budson, Wolk, et al., 2006). This gist memory can be enhanced in patients with AD with repeated stimulus presentation (Budson et al., 2000), and these results have been robustly replicated using a multitude of stimuli types and study manipulations (Gallo et al., 2006; Waldie & See, 2003); however, the strengthening of gist also generally results in higher levels of false recognition as well as true recognition (Budson et al., 2000).

Similar to patients with AD, patients with MCI-AD tend to be overly reliant upon gist memory compared to item-specific memory (Plancher et al., 2009; Waldie & See, 2003). Patients with MCI-AD tended to perform in the intermediate range, in terms of both true and false memory, between patients with AD and healthy older controls across studies. Notably, patients with MCI-AD could generally apply cognitive strategies in order to improve their memory discrimination across studies, suggesting that while their hippocampal memory abilities may be impacted by AD, they still retained other cognitive abilities (e.g., executive functions), allowing them to successfully use cognitive strategies to improve their performance on memory tests, occasionally to a level similar to that of healthy controls (Brueckner & Moritz, 2009; Deason et al., 2017).

In contrast, the existing literature examining approaches to improve memory discrimination in patients with AD has not revealed a consistently effective approach. The use of methods such as the distinctiveness heuristic and recall-to-reject methods, often found to be successful in healthy older adults and in patients with MCI-AD, have largely not generalized to patients with AD (Abe et al., 2011; Budson, Dodson, Daffner, et al., 2005, Budson, Sitarski, et al., 2002; Deason et al., 2017; Pierce et al., 2008). Existing evidence suggests that the most successful methods to improve memory test performance of patients with AD are the use of item-specific encoding and conservative responding (Deason et al., 2017; Tat et al., 2016; Waring et al., 2008), although evidence has suggested that patients with AD employ these methods inconsistently or insufficiently, in comparison to healthy peers.

It is not clear why cognitive strategies appear to be largely ineffective among patients with AD. Strategies to enhance the salience or depth of information processing, such as the distinctiveness heuristic, may be hindered by impaired memory formation resulting from AD (Budson, Sitarski, et al., 2002). However, the use of a strategy more reliant upon frontal executive or metacognitive abilities (i.e., recall-to-reject) was also largely unhelpful, although these functions should have been relatively less impaired than memory processing (Budson, Dodson, Daffner, et al., 2005). It is possible that participants with AD have difficulty consistently applying cognitive strategies at test, but determining whether a participant is trying to apply a strategy, and doing so poorly, or whether they are attempting to apply a strategy at all, is not easily dissociable. Research has identified monitoring and/or verification-inhibitory mechanisms as the most likely frontal impairment early in AD (Dodson et al., 2011; O’Connor et al., 2015), but more research is necessary to isolate the

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contributions of specific frontal impairments. In addition, recent research has implicated the ventromedial prefrontal cortex as critical to the formation of gist memory (Warren et al., 2014), suggesting that frontal impairment early in AD may also contribute to impaired memory for gist information. Future research into false memories in patients with AD should seek to better characterize the frontal executive abilities needed to make effective use of memory strategies and heuristics to better inform patient care.

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References


Table 1.

Effectiveness of cognitive strategies in reducing false memories.

<table>
<thead>
<tr>
<th>Article</th>
<th>Strategy</th>
<th>Patient group</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abe et al., 2011</td>
<td>Recall-to-reject</td>
<td>AD</td>
<td>Not effective</td>
</tr>
<tr>
<td>Budson, Sitarksi, et al., 2002</td>
<td>Distinctiveness heuristic</td>
<td>AD</td>
<td>Not effective</td>
</tr>
<tr>
<td>Budson, Dodson, Daffner, et al., 2005</td>
<td>Distinctiveness heuristic</td>
<td>AD</td>
<td>Limited effectiveness</td>
</tr>
<tr>
<td>Brueckner &amp; Moritz, 2009</td>
<td>Emotional stimuli</td>
<td>MCI-AD, AD</td>
<td>Improved true memory among MCI-AD; not effective among AD</td>
</tr>
<tr>
<td>Deason et al., 2017</td>
<td>Recall-to-reject</td>
<td>MCI-AD</td>
<td>Effective</td>
</tr>
<tr>
<td>Gallo et al., 2004</td>
<td>Recall-to-reject</td>
<td>AD</td>
<td>Not effective</td>
</tr>
<tr>
<td>Pierce et al., 2008</td>
<td>Recall-to-reject</td>
<td>AD</td>
<td>Not effective</td>
</tr>
<tr>
<td>Rosa et al., 2015</td>
<td>Self-referencing</td>
<td>MCI-AD</td>
<td>Limited effectiveness</td>
</tr>
<tr>
<td>Rosa et al., 2016</td>
<td>Self-referencing</td>
<td>MCI-AD</td>
<td>Improved recognition but not source memory</td>
</tr>
<tr>
<td>Simmons-Stern et al., 2012</td>
<td>Distinctiveness heuristic/musical mnemonics</td>
<td>AD</td>
<td>Effective for general content but not specific information</td>
</tr>
<tr>
<td>Tat et al., 2016</td>
<td>Item-specific encoding</td>
<td>MCI-AD, AD</td>
<td>Effective among MCI-AD but was ineffective among AD</td>
</tr>
<tr>
<td>Waring et al., 2008</td>
<td>Metacognitive expectation</td>
<td>AD</td>
<td>Ineffective to improve discrimination</td>
</tr>
<tr>
<td>Wilkins et al., 2009</td>
<td>Metacognitive expectation</td>
<td>AD</td>
<td>Effective to reduce fluency based errors</td>
</tr>
</tbody>
</table>

Note. AD = Alzheimer’s disease; MCI-AD = mild cognitive impairment due to Alzheimer’s disease.