Advances in Geriatrics

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Understanding Memory Distortion in Alzheimer Disease

Alzheimer disease (AD) and dementia have a tremendous impact on the VA health care system. As of the 2000 census, there were 5.7 million veterans of the World War II (WWII) era, making up 22% of all U.S. veterans.[1] The median age of these veterans was 76.7 years.[1] Given that about 13% of all individuals aged 65 and older—and nearly 50% of those over the age of 85—have AD,[2] it would be reasonable to conclude that a staggering number of WWII veterans (likely several million) have or are at risk for dementia. Additionally, since age is the largest risk factor for AD, other veteran populations (such as Korean War veterans) will be at risk for dementia in the coming years.

At the Bedford division of the VA New England Geriatric Research, Education and Clinical Center (GRECC), Bedford, MA, much of the work being done has centered around dementia—with a particular focus on AD. Areas of research range from the basic pathology and pathophysiology of AD to clinical considerations in caring for patients with late-stage dementia.

Recently, my colleagues at the Bedford GRECC and I have been working to understand an important but rarely studied aspect of AD: memory distortion. My interest in this topic stemmed from a simple clinical observation—that most of my patients with memory problems due to etiologies other than AD could live independently, whereas the majority of those with memory problems related to mild AD could not. In speaking with patients and caregivers, it became clear that something besides simple "memory loss" (the failure to recall previously learned information) was impairing the patients with AD. Specifically, false memories and memory distortions appeared to be making the use of routines and reminders more difficult for those with AD compared with those who had the same degree of memory loss due to other etiologies.

RECOGNIZING MEMORY DISTORTION

Distortions of memory may involve simple but critical aspects of daily activities, as when someone falsely remembers turning off the stove or taking medications, leading the person to neglect performing these tasks. More dramatic memory distortions may occur when an individual substitutes one person in a memory for another, combines two memories together, or believes that an event that happened long ago occurred recently. These more dramatic distortions may fall under the definition of confabulation—when a person fills a gap in his or her memory with a fabrication that he or she believes to be true.

Clinicians or caregivers of patients with AD sometimes misinterpret a false memory as a psychotic delusion or hallucination. In actuality, though, the patient with AD who claims recently to have seen and spoken with a long-deceased family member is more likely to have experienced a memory distortion than a true auditory and visual hallucination (provided that dementia with Lewy bodies is not present). The same is true for a patient who claims that people are breaking into his or her house and moving his or her belongings around. Distinguishing between memory distortions and true hallucinations or delusions is essential to providing optimal treatment, since memory distortions respond better to memory improving medications than to antipsychotic agents.

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The VHA's Geriatric Research, Education and Clinical Centers (GRECCs) are designed for the advancement and integration of research, education, and clinical achievements in geriatrics and gerontology throughout the VA health care system. Each GRECC focuses on particular aspects of the care of aging veterans and is at the forefront of geriatric research and clinical care. For more information on the GRECC program, visit the web site (http://www1.va.gov/grecc/). This column, which is contributed monthly by GRECC staff members, is coordinated and edited by Kenneth Shay, DDS, MS, director of geriatric programs for the VA Office of Geriatrics and Extended Care, VA Central Office, Washington, DC.

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EXPLORING MECHANISMS FOR SUPPRESSING FALSE MEMORIES

My colleagues and I began our research into memory distortions by creating false memories in the laboratory and determining whether patients with AD could use the same mechanisms to suppress these false memories that healthy, older adults used. One method of creating false memories in the experimental setting is to present an individual with a list of words that are all related to a theme word, which is not itself presented (Figure 1). After studying this list of words, all individuals (even those with healthy cognitive function) have a tendency to falsely recall the theme word on free-recall tests and to falsely recognize it on recognition memory tests.

One way to counter the tendency toward false recognition of theme words is to repeat the procedure several times with the same study and test materials. These repetitions help healthy individuals to develop specific recollection of the particular items studied and, in so doing, to resist the lure of the similar but excluded theme word.

Working with this principle, we conducted two studies: one involving repetitions of study-test trials,[3] and the other involving repetitions of the study list alone followed by a single test.[4] In both studies, as expected, the repetitions allowed healthy, older adult, control participants to develop specific recollection of the items that, in turn, reduced their false recognition. In patients with AD, however, the repetitions served only to build up a general meaning, idea, or gist of the list. As a result, these patients actually increased their incorrect identification of the theme word and, thus, their false recognition.

Another way that healthy individuals can reduce false recognition of related words is by pairing the study words with pictures. Although it might seem logical to attribute this reduction in false recognition to the fact that pictures are remembered better than words, it turns out that the situation is a bit more complex—and more interesting. From an elegant series of experiments, Schacter and colleagues concluded that the majority of the reduction of false recognition is attributable to participants using a rule of thumb or heuristic related to the distinctiveness of the picture.[5]

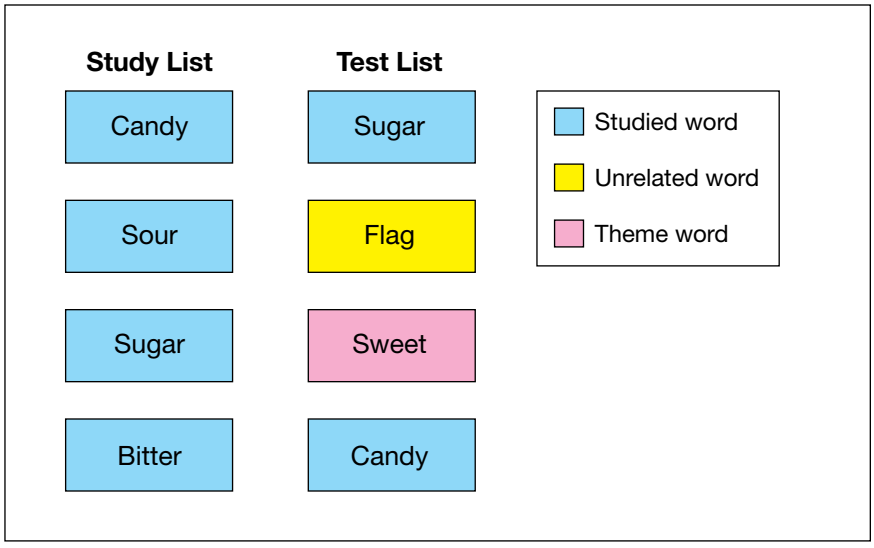

Figure 1. Schematic representation of a false memory paradigm of semantically-related words. The words in the study list are thematically related to the word "sweet," which is not itself included on the list. (Other words used for this list include taste, good, tooth, nice, honey, soda, chocolate, heart, cake, eat, and pie.) On recall or recognition testing, an individual is likely to falsely identify the theme word as a studied word.

The basic idea is that some items or events are so distinctive that, if they had occurred, we would feel 100% certain that we would have remembered them. For example, it might be difficult for you to answer the question, "Did you kill a fly in your office within the past year?" because killing a fly is not a very remarkable or distinctive event. If, however, you were asked the question, "Did you kill a snake in your office within the last year?" chances are that you can confidently answer, "No, I did not, because if I had killed a snake in my office, I'm quite certain that I would have remembered doing it!"

Over the course of three experiments, we investigated whether patients with AD could use this "distinctiveness heuristic" to reduce their false recognition. The results suggested that, while patients with AD are able to employ the distinctiveness heuristic, their poor recall limits how effectively they can use it to reduce false recognition.[6–8]

MEMORY DISTORTION IN THE REAL WORLD SETTING

Studying the frequency of memory distortions and false memories outside of the laboratory can be difficult. The terrorist attacks of September 11, 2001, however, provided such an opportunity. To evaluate both memory and emotions regarding these attacks in patients with AD, patients with mild cognitive impairment, and healthy older adults, we administered a telephone questionnaire to participants from these three

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populations in the initial weeks after the event, three to four months later, and at one year after the event.[9,10]

The questionnaire included personal information questions, such as where participants were and what they were doing when they first heard about the attacks, as well as factual information questions, such as how many planes were involved, what cities they left from, and where they ended up. Other questions asked patients to rate the intensity of their sadness, anger, fear, frustration, confusion, and shock on a scale of 1 to 5 points.

Assuming that participants' answers during the first administration of the questionnaire would be the most accurate, we considered deviations from these answers in future administrations of the questionnaire to represent memory distortions. For example, when asked "How did you first learn about the attacks?" one participant initially responded that she had "overheard two women talking." When answering the question during the second interview, however, the participant responded that she had "[seen] it on TV."

Interestingly, we found that memory distortions were extremely common among all study participants. Even healthy older adults showed a high rate of memory distortions (25%) at three- to four-month follow-up, misremembering personal details such as where they were and whom they were with when they first heard the news.[9] We all have an intuitive sense that our vivid memory for this type of personal information is accurate. Studies such as this demonstrate that, just because a memory is vivid, it does not mean that it is accurate.

For patients with AD, memories were even less accurate. Among these participants, almost half (47%) of the total memories tested were distorted upon second administration of the questionnaire.[9]

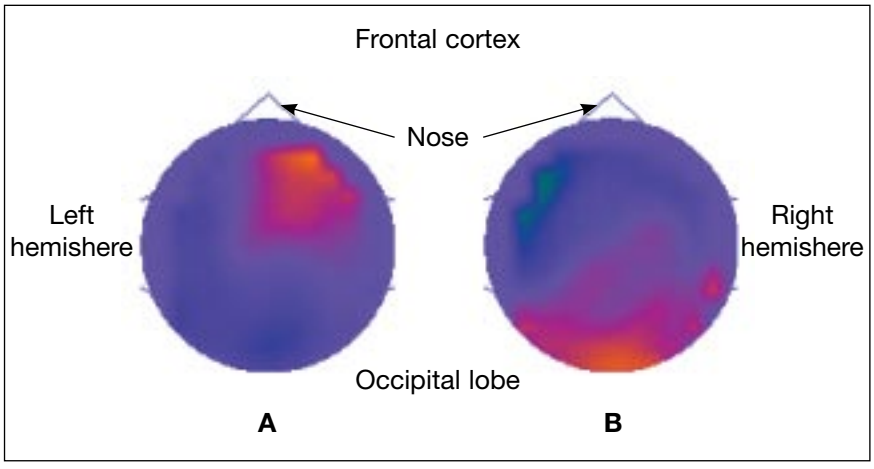

Figure 2. Event-related potential representation of neural activity recorded through 128-channel electroencephalography during memory retrieval in 18 healthy older adults (A) and 18 patients with very mild Alzheimer disease (B). Note the prominent frontal activity in the healthy older adults that is absent in the patients with Alzheimer disease. The occipital activity in these patients may reflect increased visualization in an attempt to compensate for impaired memory processes.

Also notable was the finding that rates of memory failure (defined as a response of "I don't know" or the equivalent) were quite low for all participants at three- to four-month follow-up: 13% in the AD group and 1% in the healthy older adult group.[9] Thus, when it comes to remembering personal information related to large-scale traumatic events, it seems that both patients with AD and healthy older adults are much more likely to misremember information than to say "I don't know."

We also have conducted several studies in the laboratory recently that have real-world significance. In one of these studies, we presented patients with AD and age-matched control participants with statements followed by a label of true or false: for example, "In New York City, the 53 bus will take you uptown: FALSE," or "It takes 32 coffee beans to make a cup of espresso: TRUE." Interestingly, while the patients with AD later correctly remembered that 69% of the true statements were true, they incorrectly remembered that 59% of the false statements were true. By contrast, control participants correctly remembered 77% of the true statements as being true and incorrectly remembered 39% of the false statements as being true.[11]

This finding is quite useful for clinicians and caregivers who communicate regularly with patients who have AD, as it demonstrates that phrasing a statement negatively is likely to result in the patient remembering the opposite of what was intended. Thus, it would be inadvisable to tell a patient with mild AD, "The 53 bus will not take you to your sister's house; take the 67 bus instead." Rather, it's best to use simple and direct phrasing, such as "Take the 67 bus to your sister's house."

POTENTIAL ROLE OF THE FRONTAL LOBES

Part of improving our understanding of memory distortion involves studying the underlying pathophysiology of these problems in patients with AD.

One possibility under consideration is frontal lobe pathology.

We began to test this hypothesis by examining false recognition in patients with anatomic lesions of the brain's frontal lobes due to stroke or tumor resection. We gave these patients and matched control subjects the same repeated study-test trials of related words that we previously had given to the patients with AD.[4] Supporting our hypothesis, the patients with frontal lesions showed high levels of false recognition—even higher than those of the patients with AD.[4]

Some of our newest research uses 128-channel electroencephalography to produce event-related potentials, which provide us with a window into the neural activity of the brain as memories are formed and retrieved. Here, we find that, compared with healthy older adults, patients with very mild AD show vastly reduced frontal lobe activity (Figure 2) (A.E.B, unpublished data, December 2006). Thus, this research also supports the hypothesis that frontal lobe dysfunction may contribute substantially to the high levels of memory distortion in patients with mild AD.

FORGING AHEAD

While our work has been very fruitful thus far, there is still much to learn about memory problems in AD and other dementias. In ongoing studies we continue to explore new ways to help patients with AD reduce their false memories. For example, one line of investigation is examining the question of whether the power of pictures can help to overcome memory impairment in AD, at least to some extent. In addition to comparing these patients' memories for pictures versus words, we are investigating whether the patients can use mental imagery to improve their memory by making their own pictures. In this and other studies, we are working to enable these patients to live richer, more independent lives. ●

Author disclosures

Dr. Budson reports being a member of the advisory board for Neurochem and a member of the speakers bureaus for Pfizer, Eisai, Johnson & Johnson, and Forest Laboratories.

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