# Memory for emotional stimuli in patients with Alzheimer's disease

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### Abstract

Although a hallmark of Alzheimer's disease (AD) is memory impairment, there is speculation that recall may be enhanced when an emotional component is associated with an event. The current study aims to assess whether patients with AD would recall emotionally laden material better than neutral stimuli. DSM-IVdiagnosed AD patients with mild to moderate dementia, as well as groups of young and elderly healthy controls, participated in this study. All subjects were administered three word lists for three trials each. The words were positive, negative, or neutral in valence and matched for concreteness, emotionality, and pleasantness. As expected, the controls performed significantly better than the AD patients. Importantly, the pattern of recall for the emotions was different, such that both control groups recalled all emotions equally, whereas the AD patients recalled significantly more negative words than positive or neutral. These findings of improved immediate memory for emotional material in AD lends support to the

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Steven G. Potkin, MD, Department of Psychiatry and Human Behavior, University of California, Irvine, California. notion that mnemonic functions are differentially affected in the disease.

Key words: Alzheimer's disease, memory, emotional memory, dementia, neuropsychology, amygdala

#### Introduction

While a cardinal feature of Alzheimer's disease (AD) may be memory impairment, the domain of memory is not itself a unitary construct. In fact, numerous types of mnemonic functions have been found to rely upon different neuroanatomical substrates, and these functions are affected by different central nervous system disease conditions.<sup>1</sup> In AD, the primary memory deficit involves the actual encoding of explicit declarative material that is based primarily upon the integrity of the hippocampal region.<sup>2</sup> Other types of memory that have been found to be aberrant in AD, generally as the disease progresses, include recognition memory, contextual memory, temporal memory, and the primacy effect.<sup>3</sup> Some forms of memory, such as procedural memory, skill learning, lexical priming, and the recency effect, rely on regions other than the mesial temporal region (e.g., basal ganglia, frontal cortices) and have been found to be relatively less deficient in AD.4,5

One area of memory that clinicians and caregivers of AD patients assume to be relatively unimpaired is memory of emotional events. Until recently, there has been little empirical research assessing this domain of memory. Several new studies have assessed memory of emotional events in AD by retrospectively analyzing patients' recall for a past natural disaster. Ikeda et al.<sup>6</sup>

Table 1. Raw recall means (standard deviation) for AD patients and controls on immediate condition				
Group	Total recall	Total +	Total -	Total neutral
AD patients (N = 25)	28.0 (6.7)	8.2 (3.4)	11.2 (3.6)	8.6 (3.2)
Young controls (N = 27)	81.3 (15.0)	26.8 (6.0)	26.6 (5.7)	27.4 (5.7)
Elderly controls (N = 19)	59.4 (14.0)	19.8 (5.6)	20.9 (4.8)	19.2 (5.6)

found that AD patients were better at recalling an emotional event (such as the Kobe earthquake) than a relatively neutral event (such as an MRI). Recall of an earthquake—an extremely traumatic event—does not necessarily imply that this finding could be generalized to enhanced recall for less emotionally charged stimuli. Moreover, a subsequent MRI study on these patients found that the propensity to recall the emotional event correlated with amygdala volume.<sup>7</sup> Taken together, there seems to be preliminary evidence for an increased recall for emotional material in AD that may be related to amygdala integrity.

To our knowledge, there have been no prior studies specifically and prospectively assessing emotional memories in AD. Thus, the aim of the present study was to assess whether patients with AD would recall emotionally laden material better than neutral stimuli.

# Materials and methods

#### Subjects

This study included 25 patients diagnosed with probable DSM-IV AD, with mild to moderate dementia (mean age = 75, sd = 7.4; mean years of education = 13.2, sd = 2.0). The mean Mini-Mental State Examination score for patients was 21 with a standard deviation of 2.3. Controls consisted of two cohorts, stratified by age: 27 young controls (mean age = 23.8, sd = 10.8; mean years of education = 15.4, sd = 1.8) and 19 elderly controls (mean age = 70.1, sd = 7.5; mean years of education = 12.7, sd = 1.8). All patients were voluntary research subjects at the University of California, Irvine, Medical Center and provided informed consent prior to participation.

#### Materials

Three word lists, each comprised of 15 words for the young controls and 12 words for the elderly controls and AD patients, were developed from Brown and Ure.<sup>8</sup> Each word had positive, negative, or neutral emotional connotations (e.g., friend, hate, and thermometer, respectively). The lists were constructed by the author Fleming by matching lists and valences according to the

means for item frequency, concreteness, emotionality, and pleasantness. Equal numbers of each class of words were interspersed throughout the lists and matched for order to control for primacy and recency effects. We decided to use 15 words for the young control group and 12 for the elderly control group and AD patients based on analysis of pilot data that suggested that these numbers minimized ceiling and floor effects for each group.

#### Procedure

Subjects were presented with three 15- or 12-word lists (lists A, B, and C), each of which was administered for three trials, so that the testing session consisted of a total of 9 trials and either 135 or 108 words. Subjects were instructed to repeat each word as it was read to them, in order to maintain their attention as well as to ensure that the test item had been heard correctly. At the end of each trial, subjects were asked to recall as many items as possible without regard to order. All recall responses, including intrusions, were recorded, but only correct responses were counted in the recall scores.

#### Results

Table 1 shows the mean total recall scores for the AD patient and control groups. An analysis of variance of 3 (diagnosis) by 3 (emotion type) revealed significant differences in the total number of words recalled by the groups [F(2,68) = 110.3 p < 0.001]. Post-hoc analysis revealed that both control groups recalled significantly more words than the AD patients (p < 0.001) and that the young control group recalled significantly more than the elderly control group (p < 0.001).

The effect for emotion type was also significant [F(2,136) = 3.8, p = 0.02], indicating that the negative words were recalled significantly more than the positive or neutral words. There was also a significant interaction effect [F(4,136) = 2.8, p = 0.02]. A post-hoc Scheffe analysis revealed that within the AD group, the patients recalled significantly more negative than positive or neutral words. Such results were in contrast to the two control cohorts, which recalled emotional classes equivalently.

# Discussion

The major finding of this study was that patients with AD demonstrated better immediate recall for emotionally laden stimuli than recall for neutral stimuli. To our knowledge, this is the first prospective investigation to provide objective evidence for the clinical observation that patients with AD are able to remember emotionally laden events more than non-emotional material.

Several caveats are in order. One must consider the possible role of mood in the AD patients' enhanced recall for negative stimuli when compared to controls. It has been shown that, when depressed, people often pay increased attention to the negative stimuli in their environment. Such selective focus may lead to increased retention of negative emotion words, as was shown by the AD patients in this study. However, it should be noted that, based upon mood ratings made by a physician at the time of testing, none of the AD subjects were judged as clinically depressed. A self-administered measure (e.g., the Beck Depression Inventory) may have been more sensitive to subjectively experienced depression, but since such data were not obtained at the time of testing, the role of mood cannot be completely excluded.

Studies of animals and human beings have noted the role of the amygdala in emotional memory.9 An illustration of the role of the amygdala in human memory can be inferred from the study of individuals with Urbach-Wiethe disease, a neurological disease that involves selective damage to the amygdala. It has been demonstrated that individuals with this disease are differentially impaired at learning emotional material versus neutral material.<sup>10,11</sup> Moreover, a recent PET study further implicated the amygdala in emotional memory as Cahill et al.<sup>12</sup> found the right amygdala metabolism to be correlated with recall of emotional material. In addition to the neural circuitry involved in emotional memory, there is evidence that the noradrenergic system is involved in the recall of emotional memory, as it has been demonstrated that the administration of a beta-blocker-propranololcan block the retention of emotionally laden material.<sup>13</sup>

It is important to note that this study assessed memory *immediately* rather than after a delay. This was done because the AD patients were not able to recall a significant amount of material after a delay (even one as short as 10 minutes). This memory paradigm differs from the design commonly used in prior investigations, in which recall for emotional memory is assessed after 24 hours. In contrast to the present study, these investigations generally found that healthy individuals recall emotionally enhanced stimuli better than they do neutral stimuli. The

difference between these findings may be explained by the use of different delay intervals. In fact, we have found that, following 24-hour delays, both young and elderly controls do indeed retain emotional material better than neutral (Fleming et al., in preparation). We further speculate that there may actually be some evolutionary advantage to not becoming overwhelmed by emotion simultaneously with the emotion-provoking event (so as not to interfere with survival instincts) but rather only after a delay when it is important (and perhaps more convenient) for the organism to retain and recall significantly charged emotional events.

From a therapeutic perspective, these findings of improved memory for emotional material in AD lend support to the usage of contextual manipulations aimed at increasing memory function in these patients.

# References

1. Perani D, Bressi S, Cappa SF, et al.: Evidence of multiple memory systems in the human brain: a FDG PET metabolic study. *Brain*. 1993; 116(Pt 4): 903-919.

2. Libon KJ, Bogdanoff B, Cloud BS, et al.: Declarative and procedural learning, quantitative measures of the hippocampus, and subcortical white alterations in Alzheimer's disease and ischaemic vascular dementia. *J Clin Exp Neuropsychol.* 1998; 20(1): 30-34.

3. Becker JT, Wess J, Hunkin NM, et al.: Use of temporal context information in Alzheimer's disease. *Neuropsychologia*. 1993; 31(2): 137-143.

4. Simon E, Leach L, Winocur G, et al.: Intact primary memory in mild to moderate Alzheimer disease: indices from the California Verbal Learning Test. *J Clin Exp Neuropsychol*. 1994; 16(3): 414-422.

5. Hirono N, Mori E, Ikejiri Y, et al.: Procedural memory in patients with mild Alzheimer's disease. *Dement Geriatr Cogn Disord*. 1997; 8(4): 210-216.

6. Ikeda M, Mori E, Hirono N, et al.: Amnestic people with Alzheimer's disease who remembered the Kobe earthquake. *Br J Psychiatry*. 1998; 172: 425-428.

7. Mori E, Ikeda M, Hirono N, et al.: Amygdalar volume and emotional memory in Alzheimer's disease. *Am J Psychiatry*. 1999; 156(2): 216-222.

8. Brown WP, Ure DM: Five rated characteristics of 650 word association stimuli. *Br J Psychol.* 1969; 60(2): 233-249.

9. LeDoux JE: Emotional memory systems in the brain. *Behav Brain Res.* 1993; 58(1-2): 69-79.

10. Markowitsch HJ, Calabrese P, Wurker M, et al.: The amygdala's contribution to memory—a study on two patients with Urbach-Wiethe disease. *Neuroreport*. 1994; 5(11): 1349-1352.

11. Adolphs R, Cahill L, Schul R, et al.: Impaired declarative memory for emotional material following bilateral amygdala damage in humans. *Learn Mem.* 1997; 4(3): 291-300.

12. Cahill L, Haier RJ, Fallon J, et al.: Amygdala activity at encoding correlated with long-term, free recall of emotional information. *Proc Natl Acad Sci USA*. 1996; 93(15): 8016-8021.

13. Cahill L, Prins B, Weber M, et al.: Beta-adrenergic activation and memory for emotional events. *Nature*. 1994; 371(6499): 702-704.