Original Research Article

Emotional Working Memory in Alzheimer's Disease Patients

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Key Words

Alzheimer's disease • Emotions • Executive functions • Visuospatial abilities • Working memory

Abstract

Background: Few studies have assessed whether emotional content affects processes supporting working memory in Alzheimer disease (AD) patients. **Methods:** We assessed 22 AD patients and 40 elderly controls (EC) with a delayed matching and non-matching to sample task (DMST/DNMST), and a spatial-delayed recognition span task (SRST; unique/varied) using emotional stimuli. **Results:** AD patients showed decreased performance on both tasks compared with EC. With regard to the valence of the stimuli, we did not observe significant performance differences between groups in the DMST/DNMST. However, both groups remembered a larger number of negative than positive or neutral pictures on unique SRST. **Conclusion:** The results suggest that AD patients show a relative preservation of working memory for emotional information, particularly for negative stimuli.

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Introduction

Emotional information is typically more likely to be remembered than non-emotional information. Experimental studies on emotion have shown that particular qualities of pictures can elicit an emotional response that varies according to the valence (positive and negative) and the level of arousal (from neutral to exciting) of the stimuli [1], i.e. emotionally arousing information can capture attention and activate specialized neural responses (e.g. amygdalar modulation of hippocampal function) [2]. Furthermore, the effects of emotion

can produce both memory enhancement and memory inhibition depending on the level of arousal of an emotional state [3].

In general, the literature shows that declarative memory for emotional stimuli is better than memory for neutral stimuli in both healthy young adults [4–7] and healthy older adults [8]. Although older adults generally have poorer memory than young adults, both age groups remember more about emotional information, such that the overall age discrepancy in memory is less pronounced for highly arousing events [9]. In other words, studies suggest a preserved memory advantage for emotional stimuli in older adults with healthy cognitive aging.

Alzheimer's disease (AD) presents with progressive memory loss and cognitive impairments [10]. Memory loss involves not only difficulty in remembering recent events but also impairments in holding information in mind over short periods of time [11, 12].

Research on emotional memory modulation in AD has shown relatively intact emotional memory enhancement in these patients. In studies exploring memory for negative stories, film clips and real-life emotional events, AD patients showed better declarative memory for the emotional information than for neutral content [13–19], although these findings are not universally accepted [20–22].

One plausible neuroanatomical explanation for reduced emotional memory effects in AD concerns neuropathological changes in the amygdala, which are a common characteristic of early AD [22, 23].

Surprisingly little is known about emotional effects on working memory, and few studies have assessed whether emotional content affects processes supporting working memory function.

Empirical findings on working memory for emotional stimuli come primarily from healthy participants [6, 24–26], although research with specific populations has also been conducted.

When comparing the effects of age on emotional working memory, researchers found that older adults exhibited superior performance on positive compared to negative emotional stimuli, whereas younger adults exhibited the opposite pattern [24]. In a study exploring working memory for emotional stimuli in patients with mild cognitive impairment, patients remembered negative targets significantly better than neutral and positive targets, in contrast to the results found in healthy older adults [27].

Given the relative preservation of emotional processing and emotional memory effects in healthy aging, we predicted that healthy older adults would show intact performance on an emotional working memory task. In contrast, in AD patients it is not known if the emotional memory effect is intact, and results are inconsistent concerning the influence of emotional valence (positive vs. negative) on emotional memory. Compared to the number of studies exploring the emotion effect in working memory, there have been few investigations of emotional working memory in patients with dementia. We were therefore interested in investigating whether the performance of AD patients on an emotional memory task would differ from elderly healthy adults in terms of the ability to maintain and manipulate emotional information.

To examine this question, we designed the present study to assess whether patients with AD showed a preserved ability to maintain and manipulate information with emotional content over short periods of time, as was necessary to guide task-relevant behavior. In other words, we specifically focused on the extent to which emotion effects facilitated working memory performance within the clinical AD population.

To answer these questions, we examined participants' performance on versions of two working memory tasks incorporating emotional stimuli: the delayed matching to sample/delayed non-matching to sample task (DMST/DNMST) and the spatial-delayed recognition span task (SRST; unique/varied).

Table 1. Sample characteristics of AD and EC groups

	AD patients (n = 22)	EC (n = 40)
Age, years	78.27 ± 6.70*	71.10 ± 6.72
Range	65–88	60–84
Females/males	15/7	23/17
Education, years	6.73 ± 4.00*	13.25 ± 5.57
Range	2–15	2–22
Duration of illness, years	3.73 ± 1.77	–
CDR score	1.25 ± 0.57*	0.01 ± 0.79
Instrumental ADL	19.00 ± 7.15*	0.18 ± 0.78
IQCODE score	3.90 ± 0.58*	2.57 ± 0.96
NPI total score	17.36 ± 11.8*	4.90 ± 6.53
CDS total score	10.14 ± 6.81*	5.28 ± 4.50

ADL = Activities of Daily Living; CDR = Clinical Dementia Rating; CDS = Cornell Depression Scale in Dementia; NPI = Neuropsychiatric Inventory. Values are means ± SD. * p < 0.001 vs. EC (Student's t test).

Methods

Participants

The study included 22 patients (15 women) with a diagnosis of AD and 40 healthy elderly adults [elderly controls (EC): 24 women]. Mean age was 74 years (AD patients: 78.27 ± 6.70 years; EC: 71.10 ± 6.72 years), school education was 10 years on average (AD patients: 6.73 ± 4.00; EC: 13.25 ± 5.57). Groups differed significantly with respect to these variables (table 1) in that AD patients were older and had less formal education than EC.

All AD patients met the criteria of AD described in the *Diagnostic and Statistical Manual of Mental Disorders* (ed. 4) by the American Psychiatric Association in 1994 and by the National Institute of Neurological and Communicative Diseases and Stroke/Alzheimer's Disease and Related Disorders Association. Participants were recruited from the Geriatric Medical Center, University Hospital of Brasilia, Brasilia, Brazil, and were examined by a social worker, a neuropsychologist, and a geriatrician. A clinical diagnosis of AD was determined for each patient at an interdisciplinary team meeting. The severity of AD ranged from mild to moderate (scores 1 or 2) according to the Clinical Dementia Rating Scale [28]. All patients exhibited a 1- to 4-year history of progressive cognitive impairment predominantly affecting memory, which was confirmed by their caregiver using the IQCODE (Informant Questionnaire on Cognitive Decline in the Elderly) [29], but showed normal consciousness and lived with their families.

Written, informed consent in accordance with the ethical guidelines for research with human subjects (196/96 CNS/MS resolution) was obtained from all participants and their caregivers (where appropriate). The study was approved by the Human Subject Committee of the Faculty of Medicine, University of Brasilia.

All participants had normal or corrected-to-normal vision and hearing. The Neuropsychiatric Inventory was applied for all subjects [30]. If any evidence of behavior disturbance or significant depression was noted after the interview, the subject was excluded. However, it is important to note that the AD group showed higher scores on the Cornell Depression Scale in Dementia [31] compared to older adults. Characteristics of the participants are shown in table 1.

Neuropsychological Assessment

The neuropsychological evaluation was performed on each individual in both groups by the same investigator (C.S.). All participants were evaluated using the neuropsychological and emotional tests during three sessions on separate days, and the tests were always applied in the same order.

As part of the initial assessment, standardized neuropsychological tests were used to assess different cognitive functions.

Global Cognition Score

We used a Brazilian version of the Mini-Mental State Examination (MMSE) [32] and the Mattis Dementia Rating Scale (DRS) [33].

Memory

The Digit Span Forward (DRS) [33] and Corsi's Block-Tapping Test [34] assessed short-term memory (verbal and visual memory, respectively). The Rey Auditory Verbal Learning Test [35] was used as a measure of episodic recall. The 15-item version of the Boston Naming Test (Consortium to Establish a Registry for Alzheimer's Disease) [36] and Rey-Osterrieth Complex Figure Recall [37] were used to test semantic and nonverbal recall, respectively.

Executive and Attention Functions

Executive function and attention measures were assessed using the following tests: the Clock Drawing Test (to command) [38], Trail Making Tests A and B [37], Wisconsin Card Sort Test-modified version [39], the Weigl Test [40], and the 5-Point Test [37]. These tests evaluated planning, set shifting, selective attention, speed of visuomotor coordination, and divided attention.

Verbal Fluency

Word Fluency Test (FAS) [37] and category (animals) [37] assessed production.

Visuoconstructive Abilities

The Clock Drawing Test (copy) [38] and Rey-Osterrieth Complex Figure Copy [37] assessed constructive praxis.

Emotional Working Memory Tasks

Two tests of working memory were administered for emotional stimuli over the course of approximately 2 h. The DMST/DNMST paradigm employed in this study was assumed to have two components: one related to the memory for the object presented before the choice trial (recognition memory) and the other related to the memory for the rule allowing problem solving.

On the other hand, the good performance on SRST depends on multiple factors, with domain-specific skills, for example, facilitating storage and a domain-general capability allowing for cognitive control and executive attention.

Emotional Picture Stimuli

To evaluate emotional working memory, we used a normed set of picture stimuli: the International Affective System (IAPS) [41], which includes a wide range of emotional content such as natural landscapes, buildings, scenes of love or affection, children, and mutilated individuals. A set of negative, neutral, and positive pictures was selected for use on working memory tests. The high- and medium-arousal pictures selected included an equal number of negatively and positively valenced pictures; the low-arousal pictures were neutral in valence.

As in other studies, we did not use sexual or erotic images because previous investigation in our population showed difference in valence (positive or negative) according to gender [22]. Additionally, we used a group of geometrical figures in both tests.

Delayed Matching and Non-Matching to Sample Task Condition

Concerning the working memory measure, the picture stimuli were presented as part of computerized DMST/DNMST with trial-unique stimuli and short-delay interval. This test assesses the emotional memory of the individual and is capable of affecting the frontal lobe (working memory) and the medial temporal lobe (emotional memory) simultaneously.

The stimuli were 36 (neutral, positive, and negative) pictures from IAPS and 12 geometrical figures, amounting to a total of 48 pictures.

During both the DMST/DNMST conditions, participants were tested individually and given oral instructions about the experimental procedures.

The procedure was as follows: each trial began with the presentation of the first sample stimulus for 5 s in the middle of the computer screen. After a 3-second delay, two choice picture stimuli were presented for a maximum of 20 s or until the subject responded. One of the two pictures was the previous stimulus, and the other was a novel picture.

The DMST required that participants choose the familiar stimulus. In contrast, the DNMST required that participants choose the novel stimulus from the pair of stimuli after viewing the target. The order of the two tasks was always kept the same (first DMST then DNMST).

The subject indicated which of the two choice pictures was a correct match by touching the screen and consequently they received an auditory feedback on their performance. Each correct response was accompanied by a high tone, and a low tone signaled an incorrect response.

This process was then repeated across 48 trials. The pictures were randomly selected. Both accuracy and latency of performance were measured, but only accuracy data will be discussed here. Scores were based on 1 point for each correct response; thus, participants could obtain a total of 48 points for each condition (DMST or DNMST).

In summary, with the help of this emotional working memory test, we analyzed whether AD patients perform a working memory task better using emotional stimuli than neutral ones and whether these patients preserve the ability to learn an implicit rule.

To investigate the preservation of the ability to learn an implicit rule, accuracy on each task (DMST/ DNMST) was analyzed based on the number of correct responses exceeding the chance performance rate of 50% (24 trials).

Considering the valence of the sample stimulus (neutral vs. emotional), we investigated whether AD patients and EC differed in performance across the tasks (DMST/DNMST) and whether performance was affected by stimulus category (neutral, positive, negative, and geometrical).

Finally, we investigated whether AD patients showed better performance when the test pair of stimuli belonged to the same category (neutral, positive, negative, and geometrical). For this analysis, the pairs of stimuli were classified as congruent condition (CC) when both stimuli were in the same category (for example, two neutral pictures appearing simultaneously) and incongruent condition (IC) when the pair presented different categories (for example, a neutral and a positive picture). Thus, overall each subject was presented with 24 CC and 24 IC trials, totaling 48 trials for each task (DMST/DNMST).

Spatial-Delayed Recognition Span Task (Unique and Varied)

The picture stimuli were presented as part of a computerized working memory spatial span task with emotional and neutral stimuli and short-delay interval. Due to the need of

holding spatial locations ‘online’, the subprocess image maintenance constitutes an important component of this visuospatial working memory paradigm. Additionally, we used a span task to determinate the number of images which participants are able to store on the recognition task.

During both task conditions, unique and varied, participants were tested individually and given oral instructions about the experimental procedures.

Each trial began with the presentation of a picture on a gray screen for 5 s. During the exposure time, the participant touches the picture. After a 3-second delay, a new picture appears along with the previous one. The participant is to choose the new picture. This procedure continues through a set of 8 pictures. Subjects are required to remember the locations of the pictures and the pictures during the two conditions. For the unique condition, the 8 pictures that constitute the set were the same, and for the varied condition the pictures exhibit different emotion types on the same trial.

We counterbalanced the order of the two task conditions (unique/varied) within each group. Within each group, half of the participants performed 16 trials of the unique task first and then 16 trials of the varied task second with the reverse order for the other half of participants. One point was given for each correct response in the attempt (trial made by 8 pictures). Participants could obtain a maximum of 128 points for each task. Both accuracy and latency of performance were measured, but only accuracy data will be discussed here.

In this task, we used pictures from IAPS and geometrical figures. For the unique task, we selected a total of 16 pictures: 4 for each category (neutral, positive, and negative) and 4 geometrical figures. For the varied task, 16 trials were grouped: 4 trials for each category (neutral, positive, negative, and geometrical), i.e. there were 32 pictures for each category.

The exposure time of working memory tasks was chosen according to a previous study on working memory in older adults [24].

Using the SRST, we investigated whether AD patients and EC had the same performance pattern with emotional or neutral stimuli and if the performance pattern of each group was similar using unique or varied emotional stimuli.

Additionally, we analyzed whether AD patients and EC remember a larger number of pictures when they have emotional valence. For this analysis, we considered the number of total correct responses of each category (neutral, positive, negative, and geometrical) only for the unique task.

Equipment

All participants were tested individually in a room with normal interior lighting. All experiments were carried out on a PC and a 15-inch touch-sensitive computer screen.

Statistical Methods

In order to evaluate the neuropsychological data, t tests for independent samples were performed for each test.

For DMST and DNMST, we hypothesized that several factors could modulate the performance of the older adults, so independent 3-way analyses were performed to test each of these factors. The first two factors in each analysis were group (EC/AD) and task (DMST/DNMST); the other factor was valence (neutral and emotional), category (neutral, positive, negative, and geometrical) and condition (congruent and incongruent), respectively.

For SRST, we performed a mixed design analysis of variance (ANOVA), considering 2 main factors: group (EC/AD) and task (unique/varied). Further, for unique task, we performed a mixed design ANOVA, considering 3 main factors: group (EC/AD), task (unique/varied), and category (neutral, positive, negative, and geometrical).

Table 2. Test performance of AD patients (n = 22) and EC (n = 40)

Test	AD patients	EC	Significance
<i>Global cognition score</i>			
MMSE, n/30	17.95 ± 4.19	27.03 ± 6.42	t = 0.95, d.f. (60), p < 0.001
DRS, n/144	112.82 ± 8.59	136.15 ± 22.37	t = 0.69, d.f. (60), p < 0.001
<i>Short-term memory</i>			
Digit Span Forward (DRS)	5.05 ± 1.36	6.60 ± 1.49	t = 0.03, d.f. (60), p < 0.001
Corsi's Block-Tapping Test Forward	4.59 ± 2.13	5.00 ± 3.35	nonsignificant
<i>Episodic recall</i>			
Rey Auditory Verbal Learning Test			
Trial 5	4.00 ± 2.60	11.20 ± 2.02	t = 0.08, d.f. (60), p < 0.001
Delayed recall	0.91 ± 2.11	8.35 ± 2.49	t = 0.83, d.f. (60), p < 0.001
Recognition	−9.67 ± 13.91	10.54 ± 3.56	t = 0.54, d.f. (58), p < 0.001
List B	1.68 ± 1.24	4.03 ± 1.42	t = 0.46, d.f. (60), p < 0.001
LOT	6.27 ± 5.65	16.43 ± 6.28	t = 0.29, d.f. (60), p < 0.001
<i>Semantic recall</i>			
Boston Naming Test, n/15	12.59 ± 2.15	14.50 ± 2.40	t = 0.09, d.f. (60), p = 0.003
<i>Nonverbal recall</i>			
Rey-Osterrieth Complex Figure Recall	3.55 ± 3.22	16.51 ± 6.99	t = 0.55, d.f. (55), p < 0.001
<i>Working memory</i>			
Digit Span Backward (DRS)	2.64 ± 1.36	4.28 ± 1.39	t = 0.45, d.f. (60), p < 0.001
Corsi's Block-Tapping Test Backward	2.68 ± 1.61	3.85 ± 2.53	t = 0.21, d.f. (60), p = 0.056
<i>Executive and attention functions</i>			
Clock Drawing Test (part 1)	4.59 ± 2.88	8.60 ± 2.64	t = 0.52, d.f. (60), p < 0.001
Trail Making Test A (time)	51.22 ± 66.03	52.22 ± 28.56	nonsignificant
Trail Making Test B (time)	not complete	128.05 ± 64.77	no statistical values
Wisconsin Card Sort Test			
Categories	1.59 ± 1.56	3.73 ± 2.11	t = 0.52, d.f. (60), p < 0.001
Perseverations, %	61.02 ± 27.80	34.57 ± 22.27	t = 0.09, d.f. (60), p < 0.001
Total errors	27.32 ± 13.14	16.58 ± 10.66	t = 0.49, d.f. (60), p < 0.001
Weigl Test, n/5	3.00 ± 1.38	4.58 ± 0.95	t = 0.75, d.f. (60), p < 0.001
5-Point Test			
Total unique	5.32 ± 4.32	16.80 ± 10.57	t = 0.01, d.f. (60), p < 0.001
Perseverations, %	3.00 ± 3.81	2.15 ± 2.93	nonsignificant
Total perseverations, %	80.38 ± 141.15	11.86 ± 16.67	t = 0.26, d.f. (60), p = 0.034
<i>Verbal fluency</i>			
Letters (FAS)	16.50 ± 9.95	35.55 ± 13.78	t = 0.70, d.f. (60), p < 0.001
Categories (animals)	5.59 ± 2.68	17.18 ± 5.42	t = 0.24, d.f. (60), p < 0.001
<i>Visuoconstructive abilities</i>			
Clock Drawing Test (part 2)	7.45 ± 2.48	9.28 ± 2.21	t = 0.86, d.f. (60), p < 0.001
Rey-Osterrieth Complex Figure Copy	20.26 ± 11.66	32.57 ± 5.93	t = 0.51, d.f. (56), p < 0.001

Means ± SD. Trial 5 = 5th attempt at list A recall; Delayed recall = 7th attempt at list A recall; Recognition = recognition of list A; list B = list of interference; LOT = learning over trials; t = T score; d.f. = degrees of freedom. Higher test scores indicate better performances, except for the Trail Making Tests A and B, where high scores indicate poor performance.

Mauchly's sphericity tests were performed for all the repeated measures, and degrees of freedom were corrected using the Greenhouse-Geisser method; however, the original degree-of-freedom values are presented. Significance level was set at p < 0.05 (two tailed) for all tests.

Results

Neuropsychological Assessment

Neuropsychological results are listed in table 2 and revealed a significant main difference among EC and AD patients which showed statistical significance on most tests except Corsi's Block-Tapping Test Forward [$t(60) = 0.607$] and Trail Making Test A [$t(60) = 0.934$]. In general, t tests showed that AD patients performed significantly worse than EC.

Delayed Matching and Non-Matching to Sample Task Condition

Would AD Patients Perform a Working Memory Task Better Using Emotional Stimuli instead of Neutral Ones?

ANOVA (mixed design) comparing AD patients and EC revealed a significant main effect of group [AD, EC; $F(1, 59) = 35.150$, $p < 0.001$], a significant main effect of the tasks [DMST, DNMST; $F(1, 59) = 11.294$, $p < 0.001$], but not a significant effect of valence [neutral, emotional; $F(1, 59) = 1.911$, $p = 0.172$; fig. 1].

ANOVA indicated no significant task $\times$ group [$F(1, 59) = 1.225$, $p = 0.273$]; task $\times$ valence [$F(1, 59) = 0.417$, $p = 0.521$] or group $\times$ valence [$F(1, 59) = 0.001$, $p = 0.973$] interactions. Post hoc t tests indicated that healthy adults performed consistently higher than AD patients on the tasks ($p < 0.001$). However, EC exhibited between 95 and 100% of correct responses; thus this is evidently a ceiling effect.

On the other hand, the groups had a similar performance pattern on the tasks, higher scores on DMST (AD: 14.66 ± 0.872 ; EC: 22.11 ± 0.632) compared with DNMST (AD: 12.33 ± 1.458 ; EC: 17.48 ± 1.057), independent of the valence of the stimuli.

Do These Subjects Preserve the Ability to Learn an Implicit Rule? Would Emotional Stimuli Enhance the Learning Rule?

Regarding the preservation of the ability to learn an implicit rule, the correct responses for each task (DMST/DNMST) were analyzed with a 1-sample t test. Our results indicated that AD patients were not able to perform above chance on DNMST in contrast to EC (12.33 ± 1.458 ; fig. 1).

Considering the Valence of the Sample Stimulus (Neutral/Emotional), Would AD Patients Have a Similar Performance for Both Tasks (DMST/DNMST)?

Although both groups presented different performance on the tasks [$F(1,59) = 11.29$, $p < 0.001$], regarding the valence of the sample stimulus, ANOVA revealed no significant main effect [$F(1, 59) = 1.911$, $p = 0.172$] or significant interaction [valence $\times$ group: $F(1, 59) = 0.001$, $p = 0.973$; fig. 1], i.e. results indicated a similar pattern of performance with higher scores on DMST compared with DNMST, independently of the valence of the sample stimulus (neutral/emotional).

Would AD Patients Show a Better Performance on the Tasks (DMST/DNMST) when the Sample Stimuli Belong to a Specific Category (Neutral, Positive, Negative, and Geometrical)?

Performance of AD patients and EC on DMST/DNMST was not significantly different [$F(1, 59) = 2.401$, $p = 0.127$]. A mixed-design ANOVA indicated no significant main effect of category [$F(3, 177) = 2.455$, $p = 0.074$], and there was not an interaction [$F(3, 177) = 0.235$, $p = 0.846$] between group $\times$ category factors. Therefore, when the groups were pooled, ANOVA revealed a significant interaction [$F(3, 177) = 4.703$, $p = 0.008$] between task $\times$ category factors (fig. 2). Each task was analyzed separately, and results for DMST showed significant a category effect [$F(3, 180) = 2.917$, $p = 0.046$]. A post hoc test indicated a high-

Fig. 1. Scores (mean $\pm$ SEM) regarding the total amount of correct responses on DMST/DNMST for AD patients and EC. * $p < 0.001$, EC vs. AD patients; ** $p < 0.001$, DMST vs. DNMST. ^aAD patients were not able to perform above chance level on DNMST, which is in contrast to EC (12.33 ± 1.458).

Fig. 2. Scores (mean $\pm$ SEM) regarding the total amount of correct responses on DMST/DNMST considering the categories of the sample stimulus. * $p < 0.041$, positive vs. negative (DMST); ** $p < 0.008$, negative vs. positive (DNMST).

er number of correct responses for positive sample stimuli than negative ones ($p = 0.018$). Results for DNMST indicated a significant category effect [$F(3, 180) = 5.898$, $p = 0.002$]. A post hoc analysis indicated a higher number of negative than positive sample stimuli ($p = 0.009$).

Would AD Patients Show a Better Performance when the Test Pair of Stimuli Belongs to the Same Category (Neutral, Positive, Negative, and Geometrical)?

A mixed-design ANOVA indicated a significant main effect of group [AD, EC; $F(1, 59) = 36.425$, $p < 0.001$], task [DMST, DNMST; $F(1, 59) = 13.580$, $p < 0.001$] but not of condition [congruent, incongruent; $F(1, 59) = 2.233$, $p = 0.140$].

When we analyzed the interactions between factors, results showed a significant $F(1, 59) = 14.561$, $p < 0.001$ interaction between task $\times$ condition but not between task $\times$ group [$F(1, 59) = 0.894$, $p = 0.348$], or group $\times$ condition [$F(1, 59) = 2.233$, $p = 0.140$]. Thus, the groups were pooled and t test indicated a significant difference for condition in both tasks: DMST CC/IC [$t(60) = 0.035$], DNMST CC/IC [$t(60) = 0.005$], i.e. that there were higher numbers of correct responses on DMST for CC (CC: 83.060 ± 22.71 ; IC: 80.919 ± 22.37) and for IC on DNMST (CC: 62.568 ± 31.97 ; IC: 66.439 ± 29.05).

Fig. 3. Scores (mean $\pm$ SEM) regarding the total amount of correct responses on SRST for AD patients and EC. * $p < 0.001$, EC vs. AD patients; ** $p < 0.001$, varied vs. unique.

Fig. 4. Scores (mean $\pm$ SEM) regarding the total amount of correct responses on unique SRST considering the categories of the sample stimulus for AD patients and EC. * $p < 0.001$, EC vs. AD.

Spatial-Delayed Recognition Span Task (Unique and Varied)

Would AD Patients and EC Have the Same Performance Pattern in a SRST with Emotional Stimuli? Is the Performance Pattern of Each Group Similar Using Unique or Varied Emotional Stimuli?

Mixed-design ANOVA revealed a major significant effect of group [AD, EC; $F(1, 60) = 46.655$, $p < 0.001$] and task [unique, varied; $F(1, 60) = 14.919$, $p < 0.001$]. Moreover, ANOVA indicated no significant [interaction between task $\times$ group factors ($F(1, 60) = 0.374$, $p < 0.543$)] (fig. 3). Post hoc analysis showed that EC performed consistently higher than AD patients in both tasks (unique/varied; $p < 0.001$), although the pattern of performance was the same, the scores on varied task were higher (AD: 65.864 ± 5.586 ; EC: 104.975 ± 4.143) than on unique task (AD: 54.727 ± 4.672 ; EC: 89.650 ± 3.465).

Would AD Patients Remember a Larger Number of Pictures when They Have Emotional Valence?

ANOVA indicated a significant main effect of group [AD, EC; $F(1, 60) = 56.738$, $p < 0.001$] and category [geometrical, neutral, positive, negative; $F(3, 180) = 84.432$, $p < 0.001$]. Moreover, ANOVA indicated a significant [interaction between

category $\times$ group factors (fig. 4). Post hoc analysis showed better performance for EC than AD patients ($p < 0.001$).

When compared for each group (AD/EC), the numbers of total correct responses of each category (neutral, positive, negative, and geometrical) were higher for negative pictures than positive ($p < 0.001$), geometrical ($p < 0.001$), and neutral ($p < 0.001$) pictures. There were higher numbers of total correct responses in positive and geometric pictures than neutral ($p < 0.001$) ones.

Discussion

The first goal of the present study was to examine whether AD patients preserve the ability to maintain and manipulate information with emotional content over short periods of time necessary to guide their behavior. This investigation indicated that this ability to maintain and manipulate information is diminished in AD patients compared with healthy EC. Patients with AD were impaired on almost all neuropsychological tests, which assessed executive functions and working memory, e.g. computerized tasks (DMST/DNMST and SRST). We return to this finding below.

The second goal was to find out whether AD patients and healthy older adult controls perform a working memory task better using emotional stimuli instead of neutral ones. We hypothesized that working memory for emotional material would be relatively well preserved in EC, considering prior researches showing better memory for emotional versus non-emotional information [24, 27]. In general, neither AD patients nor healthy EC showed emotional enhancement for their memory on DMST/DNMST tasks. However, both groups performed better on negative than positive or neutral stimuli on SRST.

Analysis of performance between the DMST and DNMST showed that healthy EC had lower correct responses on the DNMST compared to the DMST, with a prominent ceiling effect evident on DMST. These results are in accordance with previous studies that demonstrated that the DNMST is harder than DMST in older adults [42], i.e. DNMST involves an additional processing stage to DMST, necessitating inhibiting responses to familiar stimuli [42, 43].

Several studies suggest that age-related declines in the efficiency of controlled attention may contribute to the poor performance of older adults in different cognitive domains, such as selective attention and working memory. Consequently, it would seem that with advancing age working memory processes become increasingly susceptible to disruption by task-irrelevant information [10, 44]. Furthermore, the theoretical mechanisms posited to underlie this age-related increase in interference include general slowing and impaired inhibitory mechanisms [44, 45].

Considering the neuroanatomical view, successful performance in DNMST depends on the involvement of the prefrontal cortex, particularly ventral and medial regions [43]. Additionally, it is well documented that the prefrontal cortex is one of the brain regions most sensitive to negative effects of aging. Studies suggest alterations in such prefrontal functions as working memory, complex problem solving, concept formation, and inhibition of response [46].

Regarding AD patients, results indicated that they were not able to learn the implicit rule of the DNMST in contrast to EC. Evidence of this incomplete rule learning is reflected by the low level of overall performance, as indexed by the initial discriminability of the working memory procedure. Therefore, their difficulty stems from aspects of the task that change from trial to trial, and successful encoding requires selective attention to the stimuli to be remembered on a given trial. According to this hypothesis, deficits in attention are mani-

fested in relatively greater error scores [47]. Additionally, performance at chance level might have resulted because AD patients had difficulty in maintaining the items over the delay period.

The results of the present study suggest that the attentional component would explain the difficulty in DNMST by healthy EC and with even greater intensity by AD patients. Thus, these results are consistent with current evidence suggesting that AD patients are more prone to the effects of interference from distractors due to impaired inhibitory mechanisms [44, 45, 48]. In other words, considering that the neuropathology of AD spreads beyond medial temporal lobe structures to the association cortices of the temporal, frontal, and the parietal lobes, a number of higher-order cognitive abilities are affected [10].

With respect to several other DMST/DNMST effects, we found a high number of correct responses for positive sample stimuli on DMST and for negative sample stimuli on DNMST. Considering that negative stimuli capture more attention than positive stimuli, one might expect to find better performance on DNMST for negative stimuli. Moreover, it is important to consider that healthy EC and AD patients both showed this effect, suggesting the benefit of emotion on their performance in this account.

Additionally, we found that, on both tasks, performance was similar independent of the category of the sample and stimulus. However, this effect was more marked for AD patients, who exhibited better performance when the comparison stimulus had different valence, facilitating discrimination of the stimuli and recognition of the correct response.

Regarding SRST (unique/varied), results indicated that AD patients perform worse than healthy EC on the varied and unique tasks, suggesting that in this case patients have either not memorized the information or forgotten it. However, although healthy EC performed consistently higher than AD patients in both tasks, results showed the same performance pattern: higher scores on varied versus unique tasks, indicating the possibility of storage when the stimuli were different within each trial. These results suggest that patients with AD present short-term memory deficits. Therefore, they have greater difficulty in holding >1 element at a time available in working memory, specifically when they are shown the same stimuli in a trial (unique task).

Considering the emotional valence effects on the unique task in our study, AD patients and healthy EC remembered a larger number of negative pictures than positive or neutral ones. Previous studies have demonstrated that negative arousing content can enhance the likelihood that various aspects of an event are remembered, i.e. there is an attentional effect of emotion that may be related to the enhanced memory [9].

The memory enhancement in both AD patients and healthy EC for negative information is consistent with findings that different brain structures may modulate the effect of negative versus positive stimuli on memory. Evidence to support this hypothesis has come from both animal and human studies demonstrating interactions between emotion-processing regions (particularly the amygdala) and the hippocampus [9]. In contrast to healthy older adults, the amygdala is involved in the course of early AD [22, 23]. However, it would seem that these changes in the limbic system do not appear to affect the ability to detect emotion given the benefit of emotion on working memory observed.

So far, there is no evidence of studies assessing working memory for emotional information in these patients, and research assessing declarative memory has reported conflicting findings. While some researchers claim that AD patients lack the same enhancement of memory for emotional information demonstrated by healthy older adults [20, 21, 49], other studies suggest relatively intact enhancement of declarative memory for negative material [14, 15, 17, 19].

Conclusions

From this work, several conclusions can be drawn: (1) These findings are consistent with previous studies showing that healthy EC and AD patients are particularly sensitive to tasks involving the maintenance of relevant information. (2) AD patients do not benefit from emotional content of stimuli using the DMST/DNMST paradigm even at mild-to-moderate stages of the disease, which is in contrast to SRST. (3) Consistent with previous work, age-related deficits in working memory during healthy aging can be attributed to a small impairment in attentional function and deficits in inhibitory processes exhibited by a decline in performance, while AD patients show a more dramatic impairment.

Further studies in large study cohorts are necessary to confirm this hypothesis and to compare the performance in emotional content in working memory among the different stages of the AD process.

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