Enhancement of Declarative Memory by Emotional Arousal and Visual Memory Function in Alzheimer's Disease

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The specific effects of visual and verbal memory on the ability of emotional arousal to enhance declarative memory were examined by using multiple linear regression analysis on data from a sample of 56 patients with probable Alzheimer's disease (AD). The enhancing effect of emotion on memory was evaluated by an illustrated story paradigm, and the visual and verbal memory by a standard memory test. In AD, memory enhancement by emotion was significantly correlated with visual memory but not with verbal memory, regardless of age, sex, educational attainment, and severity of dementia, suggesting a close association between memory enhancement by emotion and visual memory.

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Everyday experience suggests that emotional events are often more memorable than nonemotional events. Experimental studies have demonstrated that emotional arousal enhances declarative memory in healthy individuals and amnesic patients.[1–4] We also know that memory for emotional events is often accompanied with visual imagery. As noted in studies of "flashbulb memories"[5] and posttraumatic stress disorder (PTSD),[6,7] visual imagery is elicited on recalling emotional events. Flashbulb memories are detailed recollections of the context in which people first heard about important emotional events. These memories are described as having a photographic quality, that is, as being accompanied by a detail-perfect appearance of contextual information about the time and place of the event. Patients with PTSD, after being exposed to a traumatic event, continually reexperience the event in some way, such as through recurrent and intrusive recollections of vivid images of the events. The disorder is characterized by intensification of nonverbal aspects of memory, especially of hypermnemonic visual memory traces related to traumatic events.[6,7] Recent neuroimaging studies of PTSD patients have found a functional alteration in the brain areas involving memory, emotion,

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and visuospatial processing, suggesting that dysfunction not only in memory and emotion but also in visuospatial processing underlies the symptoms of PTSD.[8,9] Although a strong association between visual memory and the effect of emotion in enhancing declarative memory can be hypothesized, no direct evidence has been demonstrated.

In patients with Alzheimer's disease, memory loss is a central and prominent feature. The ability of emotion to enhance declarative memory is also partially lost in Alzheimer's disease, but the loss of this ability is not necessarily proportional to the severity of the disease.[10] We hypothesized that the enhancing effect of emotional arousal on declarative memory would be related to visual memory abilities in patients with Alzheimer's disease across a wide range of dementia severity. This study aimed to examine this hypothesis by correlating performance on an emotional memory task with performance on verbal and visual memory tests in patients with Alzheimer's disease.

METHOD

Subjects

The subjects were 56 patients (42 women and 14 men) who met the National Institute of Neurological and Communicative Disorders and Stroke/Alzheimer's Disease and Related Disorders Association (NINCDS/ADRDA) criteria for probable Alzheimer's disease.[11] They were recruited from among patients who were admitted to our hospital for examination. After the subjects and their relatives were given a complete description of the study, written informed consent was obtained. Four types of patients were excluded from the study: those who had complications of other neurological diseases, psychiatric diseases, or physical illnesses or conditions; those who had any evidence of focal brain lesions on magnetic resonance (MR) imaging or of cerebral arterial occlusive lesions on MR angiography; those who had severe cognitive, attentional, or behavioral disorders that would make memory tests difficult; and those who were on any psychotropic medications that can affect a person's response to negatively emotionally charged contents as well as memory itself. The patients who were included in the study had a mean age of 72 years (SD = 6.8, range, 53–79 years), a mean level of education of 9.7 years (SD = 2.2, range, 6–15 years), and a mean Mini-Mental State Examination[12] score of 23.3 (SD = 2.8, range, 17–28). Dementia, as determined by the Clinical Dementia Rating (CDR),[13] was very mild in six patients, mild in 40 patients, moderate in nine patients, and severe in one patient.

Memory Tests

Evaluation of Effect of Emotional Arousal: The effect of emotional arousal on enhancing declarative memory was determined with the illustrated story paradigm, which has been used in a number of other studies.[3,14–17] Subjects first viewed 11 color images on a 17-inch high-resolution color monitor that were shown in sequence, accompanied by an emotionally uncharged story (the neutral story) narrative. The narrative consisted of one sentence per image and was read by a researcher (H.K.) sitting next to the subject. Together, the images and the narrative told a story. The story consisted of three phases. Phase 1 (images 1–4) depicted a mother taking her son to visit his father at work. In phase 2 (images 5–8), the boy watched a disaster drill in the hospital. In phase 3 (images 9–11), the mother was shown leaving the hospital. The images were presented on the monitor at a rate of one image per 20 seconds, controlled with the Aldus Persuasion program, version 3.0J (Adobe Inc., San Jose, Calif.) on a Power Macintosh 8100/80 (Apple Computer Inc., Cupertino, Calif.). The subjects were told to pay attention to the images and the narrative and to remember the story. Immediately after the story presentation, the subjects were asked to rate the emotional charge of the whole story on a scale of 1 to 4, with 1 indicating "not emotional" and 4 indicating "highly emotional." Five minutes after the end of the presentation of the image, the subjects were given an 11-item recall test.[17] In the recall test, as the images were presented in the original order, subjects were asked to answer one question about the story line for each image. In the recall test, correct, partially correct, and incorrect answers received 2, 1, and 0 points, respectively. Thus, the maximum scores of phases 1, 2, and 3 were 8, 8, and 6, respectively. After an interval of 2 weeks, the experiment was repeated with the same set of images but with an emotionally charged story (the arousing story) narrative instead of the neutral story narrative. The arousing story differed from the neutral story only in phase 2, in which the boy, instead of watching a disaster drill, was badly hurt in an automobile accident, and surgeons struggled to save his life. The arousing and neutral stories are closely matched in content, complexity, and style, and they were confirmed to be matched in comprehensibility;[2] they differed in only the degree of the emotional impact of phase 2.

The trials were repeated in a fixed order after an interval of 2 weeks; with the neutral story first and then the arousing story. The reason we used this fixed-order design rather than a counterbalanced design was to avoid any different influence of the first trial on the second trial between the arousing and the neutral stories. The arousing story is assumed to have a memory-

enhancing effect by emotional arousal in addition to an enhancing effect by repetition. Therefore, the influence of the arousal story presented first might be larger than that of the neutral story presented first, which would more likely affect recall performance 2 weeks later. Because we can assume that the enhancing effect by repetition is constant in all three story phases, the improved recall in phases 1 and 3 is attributable solely to the enhancing effect by repetition, whereas improved recall in phase 2 is attributable to both the enhancing effect by repetition and the effect by emotional arousal. Thus, the effect of emotional charge on declarative memory was represented by the difference of scores between the emotionally contrasted story part (phase 2), and the possible enhancing effect by repetition was canceled out by subtracting the difference of scores in the identical story parts (phases 1 and 3). Mathematically, the effect of emotional arousal on declarative memory was expressed by the emotion-related enhancement effect (EEE) index: EEE = (Ac – Nc) – [(Ai) – (Ni)], where Ac and Ai are a percent recall achievement of the emotionally contrasted story part (phase 2) and of the identical story parts (phases 1 and 3) for the arousing story, and Nc and Ni are those for the neutral story.

Assessment of Verbal and Visual Memory Abilities: Verbal and visual memory abilities were assessed with the Wechsler Memory Scale–Revised (WMS-R).[18] The materials in this test were ordinary and unlikely to be emotionally charged. We used the weighted sum of raw scores on the verbal and visual memory subtests for evaluations.

Statistical Analyses

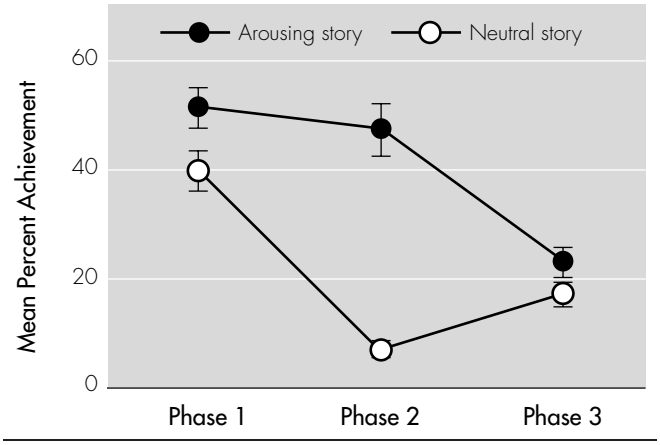
The percent recall achievement across the three phases on the assessment of emotional memory was analyzed by using two-way analysis of variance (ANOVA) for repeated measures with two within factors (story and phase) and post hoc Tukey honestly significant difference (HSD). The specific effects of visual and verbal memories on total recall scores of the neutral and arousing stories and on the EEE index were examined by using multiple linear regression partial correlations with the total recall scores of the neutral and arousing stories or the EEE index as the dependent variable and the WMS-R visual and verbal weighted sum scores as the independent variables. The possible confounding effects of age, sex, educational attainment, and disease severity (as measured by the CDR) were controlled by entering these variables into the model. The t statistic and Pearson's correlation were used where appropriate. All statistical analyses were carried out with STATISTICA software, version 4.1 (StatSoft, Inc., Evanston, Ill.). The statistical significance level was set at $P<0.05$.

RESULTS

The subjects rated the emotional charge of the arousing story (mean = 2.2, SD = 1.3) higher than that of the neutral story (mean = 1.4, SD = 0.9) (t = –4.96, df = 55, $P<0.001$). The results of the recall test for the three phases of the neutral and arousing stories are illustrated in Figure 1. The two-way ANOVA revealed a significant story effect (F = 81.1, df = 1, 55, $P<0.001$), a significant phase effect (F = 50.6, df = 2, 110, $P<0.001$), and a significant story × phase interaction (F = 40.0, df = 2, 110, $P<0.001$). The post hoc test showed that the recall scores in phase 2 were significantly worse for the neutral story than for the arousing story ($P<0.001$). The recall scores in phase 1 were somewhat better for the arousing story than for the neutral story ($P<0.005$), and the recall scores in phase 3 were comparable for the two stories.

The mean scores and ranges of score of the memory tests are listed in Table 1. In the multiple regression model, the total recall score of the neutral story was significantly correlated with the WMS-R visual (β = 0.438, partial r = 0.441, df = 2, 53, P = 0.001) and verbal (β = 0.314, partial r = 0.332, df = 2, 53, P = 0.013) weighted sum scores (Figure 2A,B). The total recall score of the arousing story was also significantly correlated with the WMS-R visual (β = 0.328, partial r = 0.335, df = 2, 53, P = 0.012) and verbal (β = 0.391, partial r = 0.390, df = 2, 53, P = 0.003) weighted sum scores (Figure 2C,D). The EEE index was significantly correlated with the WMS-R visual weighted sum score (β = 0.465, partial r = 0.403, df = 2, 53, P = 0.002) but not with the verbal weighted sum score (β = 0.004, partial r = 0.004, df = 2, 53, P = 0.979) (Figure 2E,F). Even after the possible confounding effects of age, sex, educational

FIGURE 1. Results of recall memory test for three phases of the arousing and neutral stories. Error bars represent standard error of the mean.



attainment, and CDR score were partialed out, all the results remained essentially unchanged (Table 2).

DISCUSSION

Recently, the effect of emotion on memory consolidation and the mechanism underlying the emotional modulation of memory have received greater attention. In this study, we hypothesized that the enhancing effect of emotional arousal on declarative memory would be related to visual memory abilities. We examined this hypothesis by correlating performance on an emotional memory task with performance on verbal and visual memory tests in patients with probable Alzheimer's disease. As hypothesized, our results indicated that the dysfunction in enhancing memory by emotion is related to the visual memory dysfunction in Alzheimer's disease. Verbal memory function was not a predictor of emotional memory function. These results are intriguing, because the only difference between the arousing and neutral settings in the illustrated story paradigm was in verbal stimuli. The visual materials were identical between the arousing and neutral versions. Also, in the recall test, subjects were asked about the verbal materials while the same visual materials were presented again. Thus, our study has provided neuropsychological evidence that the emotional enhancing process strongly depends on the visual memory process. Since the materials in the illustrated story paradigm consisted of both verbal and visual information, significant correlations between the total recall score of each story and both verbal and visual memory functions were, as expected, also observed.

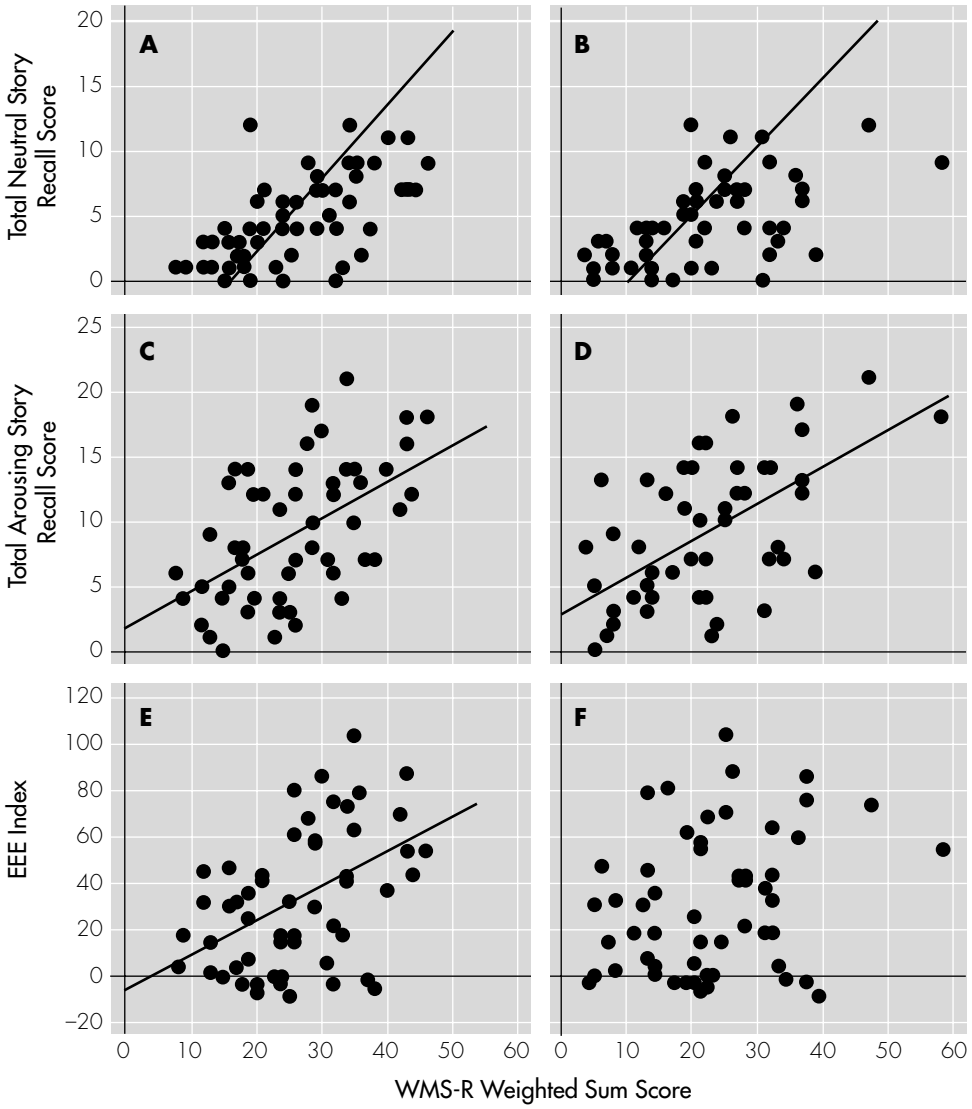
In this study, the effect of emotional arousal on enhancing declarative memory was determined with the illustrated story paradigm we used in a previous study.[17] The results in the present study replicated the findings in our previous studies that patients with Alzheimer's disease were impressed by emotional materials, and that the enhancing effect on declarative memory by emotion is spared, at least to some degree.[10,17] As the story tellings were repeated after 2 weeks in a fixed order (the neutral story before the arousing story), some improvement of the recall performance from the first telling to the second telling was noted for the emotionally neutral phases (phases 1 and 3). This was probably due to an enhancing effect on declarative memory by repetition, which was canceled out in the EEE index. The mean percent recall achievement in phases 1 and 3 were higher than in phase 2 in the neutral version, and the percent recall achievement in phase 1 was higher than that in phase 2 in the arousing version. These relatively high percent recall achievement levels in phases 1 and 3 as compared with those in phase 2 would represent the primacy and recency effects.

It has been suggested that there are special mechanisms for memory for emotional materials.[7,19] Among the neural substrates for the special mechanisms, the amygdala appears to play an important role in the enhancing effect of emotional arousal on memory.[15,16,20,21] The amygdala and the hippocampus are the main loci of Alzheimer's disease. In our previous volumetric study of patients with Alzheimer's disease who had experienced a devastating earthquake, impairment of emotional event memory was related to amygdalar atrophy.[22] In a study of hippocampal and amygdalar volumetry in Alzheimer's disease, we found that amygdalar atrophy specifically predicted visual memory dysfunction.[23] Although the role of the amygdala in declarative memory is controversial,[24,25] studies of patients with amygdalar lesions have also indicated that the amygdala is involved in visual memory function.[26,27] These findings indicate that the amygdala is involved in both visual memory and emotional memory processes and suggest that the visual memory system and the system for memory enhancement by emotion have a common neural network. Further research, including studies with an anatomical approach, is needed.

TABLE 1. Results of memory tests

Measure (possible range)	Mean	SD	Range
Total recall score of the arousing story (0–22)	9.2	5.2	0–21
Total recall score of the neutral story (0–22)	4.7	3.3	0–12
Emotion-related enhancement effect (EEE) index	31.1	29.8	−8.3–103.6
WMS-R visual recall weighted sum score (0–119)	26.0	9.6	8–46
WMS-R verbal recall weighted sum score (0–119)	22.5	11.2	4–58

FIGURE 2. Relations between the results of the illustrated story paradigm and the Wechsler Memory Scale–Revised (WMS-R) weighted sum scores.



A. Relation between total recall score of the neutral story and the WMS-R visual weighted sum score. Pearson's correlation analysis showed a significant correlation between total recall score of the neutral story and the WMS-R visual weighted sum score ($r = 0.61$, df = 54, $P<0.001$).

B. Relation between total recall score of the neutral story and the WMS-R verbal weighted sum score. Pearson's correlation analysis showed a significant correlation between the total recall score of the neutral story and the WMS-R verbal weighted sum score ($r = 0.55$, df = 54, $P<0.001$).

C. Relation between total recall score of the arousing story and the WMS-R visual weighted sum score. Pearson's correlation analysis showed a significant correlation between the total recall score of the arousing story and the WMS-R visual weighted sum score ($r = 0.54$, df = 54, $P<0.001$).

D. Relation between total recall score of the arousing story and the WMS-R verbal weighted sum scores. Pearson's correlation analysis showed a significant correlation between the total recall score of the arousing story and the WMS-R verbal weighted sum score ($r = 0.57$, df = 54, $P<0.001$).

E. Relation between emotion-related enhancing effect (EEE) index and the WMS-R visual weighted sum score. Pearson's correlation analysis showed a significant correlation between the EEE index and the WMS-R visual weighted sum score ($r = 0.47$, df = 54, $P<0.001$).

F. Relation between emotion-related enhancing effect (EEE) index and the WMS-R verbal weighted sum scores. There was no significant correlation between the EEE index and the WMS-R verbal weighted sum score ($r = 0.26$, df = 54, $P = 0.06$).

TABLE 2. Partial correlations of total recall scores and the emotion-related enhancement effect with visual and verbal memory

	WMS-R Visual Memory Score			WMS-R Verbal Memory Score		
	β	Partial Correlation (r)	*P*	β	Partial Correlation (r)	*P*
Total neutral story recall score	0.431	0.406	0	0.303	0.281	0.05
Total arousing story recall score	0.285	0.286	0.04	0.329	0.307	0.03
Emotion-related enhancement effect (EEE)	0.420	0.357	0.01	0.001	0.001	1

Note: The effects of age, sex, education, and dementia severity as confounding factors were partialed out. In multiple linear regression analysis, df = 6, 49.

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