The Effect of Negative and Positive Emotionality on Associative Memory: An fMRI Study

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Abstract

In general, emotion is known to enhance memory processes. However, the effect of emotion on associative memory and the underlying neural mechanisms remains largely unexplored. In this study, we explored brain activation during an associative memory task that involved the encoding and retrieval of word and face pairs. The word and face pairs consisted of either negative or positive words with neutral faces. Significant hippocampal activation was observed during both encoding and retrieval, regardless of whether the word was negative or positive. Negative and positive emotionality differentially affected the hemodynamic responses to encoding and retrieval in the amygdala, with increased responses during encoding negative word and face pairs. Furthermore, activation of the amygdala during encoding of negative word and neutral face pairs was inversely correlated with subsequent memory retrieval. These findings suggest that activation of the amygdala induced by negative emotion during encoding may disrupt associative memory performance.

Introduction

The ability to learn and remember new associations between previously unrelated information is an important aspect of declarative memory. Declarative memory is associative, linking together component parts, such as words and objects, either directly or via spatial, temporal or other relationships. Previous neuroimaging studies have provided crucial information concerning the neural correlates that underlie this process. A variety of associative encoding tasks result in robust hippocampal activation, including the encoding of word pairs [1,2,3,4] and triplets [5,6], object pairs [7], and name-face pairs [8,9,10].

On the other hand, the relationship between memory and emotion is of paramount importance, given that people experience various affective states over the course of daily life. Although a recent review on memory and emotion has demonstrated that emotion may enhance memory processes that occur at all stages, including encoding, storage, and retrieval [11], we previously reported that negative emotionality does not necessarily promote good memory performance and associated hippocampal activation [12]. This discrepancy may be due to procedural differences. The most likely explanation is that the encoding of an association between items may have played a key role. The possible effects of emotionality associated with memory for paired items is unclear, even though the medial temporal lobe (including the hippocampus) showed greater activation for emotional items than for neutral items during both encoding [13] and retrieval [14] in studies of memory for single items. Furthermore, although much functional neuroimaging evidence has linked the memory-enhancing effect of emotion to amygdallic modulation during encoding [13,15,16,17,18,19,20] and retrieval [14], whether similar emotionality effects can be observed on associative memory remains unclear. Indeed, emotion does not necessarily enhance memory. When faced with negative events, people tend to pay attention to central features of such events while ignoring peripheral details [21,22]. As a result, memory of the negative event itself is enhanced, whereas memory of peripheral events is impaired. Furthermore, the difference between memory for gist and memory for detail can be more pronounced for negative than for positive events [23].

In this study, we hypothesized that negative emotion does not necessarily promote good associative memory performance, and that the amygdala has disparate influences on associative memory for positive and negative information. We used fMRI to investigate the effect of emotional (negative or positive) item valence on brain activation during an associative memory task, and examined the relationship between memory performance and brain activation affected by emotion during encoding and retrieval.

Results

Behavioral results

During the fMRI protocol, 15 healthy volunteers performed a novel face-emotional word paired associate task consisted of ‘encoding’, in which subjects were asked to remember pairs of neutral face and emotional (positive or negative) words, and ‘control’ and ‘retrieval’, in which subjects were asked to indicate
the word that was previously paired with that face (Fig. 1; see Methods for details). The mean correct response rates (mean ± SD) during retrieval were 48.9 ± 14.7% for negative word and neutral face pairs and 58.1 ± 13.3% for positive word and neutral face pairs. Accuracy rates across the two emotional conditions differed significantly (paired t-test, $t = -2.208$, $p = 0.044$).

**Group analysis on each contrast**

We performed fMRI group analysis on the four contrasts, subtracting the control condition from each experimental condition, according to a random effect model. All activations satisfying our criteria for significance are shown in Tables 1 and 2. We observed significant activation of the hippocampus during all of the 4 conditions, and significant activation of the left amygdala only during the negative encoding condition.

**Correlation between activations in regions detected by one sample t-tests and associative memory performances**

We conducted a secondary correlation analysis to examine the relationship between brain activation in regions detected by one sample t-tests and associative memory performance. There wasn’t positive correlation between brain activation and associative memory performance in any areas. In contrast, this analysis revealed that left amygdala and hippocampus activation during encoding of negative word and neutral face pairs (contrast estimate of ‘negative encoding – control’) was inversely correlated ($r = -0.527$, $p = 0.045$, and $r = -0.519$, $p = 0.047$, respectively) with successful retrieval (Table 3).

**Differential effects of negative and positive emotion on encoding and retrieval**

A 2x2 ANOVA was performed to examine the differential effects of negative and positive emotion on encoding and retrieval. All activations satisfying our criteria for significance are shown in Table 4. This analysis revealed significant emotion $\times$ task interactions in the left amygdala (Fig. 2A). Post hoc analysis (corrected by Bonferroni) of the averages of contrast estimates of voxels in this cluster revealed that the ‘Encoding of negative word and neutral face pairs’ showed a greater BOLD response compared with the ‘Encoding of positive word and neutral face pairs’ ($F = 7.761$, $p = 0.012$) and the ‘Retrieval of negative word and neutral face pairs’ ($F = 8.335$, $p = 0.015$) in this area (Fig. 2B).

**Correlation analysis between amygdala activation and associative memory performance**

We conducted a secondary correlation analysis to examine the relationship between amygdala activation (mentioned above and shown in Fig. 2A) and the corresponding behavioral performance. This analysis revealed that amygdala activation during encoding of negative word and neutral face pairs (contrast estimate of ‘negative encoding – control’) was positively correlated ($r = 0.599$, $p = 0.018$) (Fig. 3A) with successful retrieval (Fig. 3B). Amygdala activation during retrieval was not significantly correlated with a correct response rate regardless of whether the words were positive ($r = 0.274$, $p = 0.322$) or negative ($r = -0.165$, $p = 0.557$).

**Discussion**

In this study, we explored the effect of emotion on associative memory performance and its underlying neural mechanisms. The hippocampus showed activations during the encoding and retrieval of word and face pairs regardless of whether the words were negative or positive. However, there wasn’t positive correlation between activations in these regions and associative

![Figure 1. Face-Word Association Paradigm.](https://www.plosone.org/figure/Figure%201)
memory performances, and on the contrary, there was significant negative correlations between left hippocampus activation during negative encoding and the rate of successful retrieval. In contrast, left amygdala activation was observed only during encoding with negative emotionality, and there was also significant negative correlations between this amygdala activation and successful retrieval. In addition, a 2×2 ANOVA and subsequent Post-hoc analysis detected the region activated specifically during encoding with negative emotionality in the left amygdala. Furthermore, this amygdala activation was inversely correlated with subsequent memory retrieval with high significance. These results suggest that amygdala activation induced by negative emotionality may disrupt associative memory encoding.

Although research on memory and emotion has demonstrated that emotional (both positive and negative) events are often better remembered than neutral events [13,14], we reported previously that negative emotionality does not enhance memory for associated word pairs [12]. In this study, we demonstrated that paired items with negative emotionality are more poorly remembered than those with positive emotionality. In this discrepancy, the encoding of an association between items may have played a role, as compared to encoding single items. This hypothesis is supported by the results of previous studies [21,22,24] demonstrating that negative emotion enhances memory for gist, but reduces memory for detail. Although the face and emotional word associative memory assessment in the present study are quite different from the gist and event detail assessments used by previous studies, it is possible that the negative word meanings operate as gist, while the relationships between word and face pairs operate as more peripheral, less salient aspect of the encoding task. This emotion-related effect of memory may be

### Table 1. Results of one sample t-test for negative word and neutral face pairs.

| Region            | BA Side | Peak level Z | p   | kE level x | y | z  |
|-------------------|---------|--------------|-----|------------|---|-----|
| Cerebellum        | R       | 5.50         | 0.002 | 25         | 0.002 | 42 | 52 | 30 |
| Inferior Frontal Gyrus | 47 L   | 5.21         | 0.007 | 30         | 0.001 | 42 | 18 | 10 |
| Hippocampus       | R       | 3.97         | 0.008 | 71a        | 0.005 | 28 | 38 | 0  |
| Hippocampus       | L       | 3.37         | 0.050 | 18         | 0.044 | 30 | 22 | 16 |
| Amygdala          | L       | 2.91         | 0.050 | 1h         | 0.046 | 30 | 0  | 22 |

BA, Brodmann area; L, Left; R, Right; Z, Z value of the peak activation within the cluster; Coordinates for the peak voxel are listed as MNI coordinates. p, corrected p value for whole brain or region of interest (* bilateral hippocampus which include 1667 voxels or * bilateral amygdala which include 306 voxels); kE, cluster size (voxels) defined by the same peak-level FWE thresholds and used for the cluster level testing.

doi:10.1371/journal.pone.0024862.t001

### Table 2. Results of one sample t-test for positive word and neutral face pairs.

| Region            | BA Side | Peak level Z | p   | kE level x | y | z  |
|-------------------|---------|--------------|-----|------------|---|-----|
| Cerebellum        | R       | 4.85         | 0.031 | 5          | 0.013 | 42 | 52 | 30 |
| Cerebellum        | L       | 4.72         | 0.048 | 1          | 0.032 | 6  | 50 | 40 |
| Hippocampus       | R       | 4.45         | 0.002 | 103a       | 0.002 | 36 | 36 | 6  |
| Hippocampus       | L       | 4.04         | 0.007 | 4*         | 0.035 | 40 | 16 | 22 |
| Hippocampus       | L       | 3.54         | 0.033 | 13a        | 0.022 | 32 | 22 | 18 |
| Hippocampus       | L       | 3.49         | 0.038 | 1*         | 0.043 | 26 | 40 | 4  |

BA, Brodmann area; L, Left; R, Right; Z, Z value of the peak activation within the cluster; Coordinates for the peak voxel are listed as MNI coordinates. p, corrected p value for whole brain or region of interest (* bilateral hippocampus which include 1667 voxels or * bilateral amygdala which include 306 voxels); kE, cluster size (voxels) defined by the same peak-level FWE thresholds and used for the cluster level testing.

doi:10.1371/journal.pone.0024862.t002
mediated by the amygdala, as suggested by the absence of the effect in individuals with amygdala damage [25]. However, the biological mechanism of such phenomenon has not been examined in detail in human functional neuroimaging studies. The pronounced inverse correlation between amygdala activation induced by negative emotionality and the correct response rate shown in this study provide direct evidence that amygdala activation during encoding is a mediator of this phenomenon.

Although we do not know the neural mechanisms responsible for the disruption of associative memory encoding with negative emotionality by amygdala activation, one possible mechanism is that amygdala activation enhances the attention to the negative word itself and reduces the attention to the association of the items required for task performance. This interpretation is consistent with the idea that the amygdala focuses processing resources on the most salient information, as Easterbrook originally proposed.

| Table 3. Correlation between activations in regions detected by one sample t-tests and associative memory performances. |
|---------------------------------------------------------------|
| **Region (peak coordinate)** | **Correct response rate (negative)** | **Correct response rate (positive)** |
| Encoding (negative) | Hippocampus (28 – 38 0) | $r = 0.446$, $p = 0.096$ |  |
| | Hippocampus (– 30 – 22 – 16) | $r = 0.527$, $p = 0.043^*$ |  |
| | Amygdala (– 30 0 – 22) | $r = 0.519$, $p = 0.047^*$ |  |
| Retrieval (negative) | Hippocampus (– 24 – 30 – 6) | $r = 0.037$, $p = 0.895$ |  |
| Encoding (positive) | Hippocampus (36 – 36 – 6) |  | $r = 0.121$, $p = 0.668$ |
| | Hippocampus (40 – 16 – 22) |  | $r = 0.130$, $p = 0.643$ |
| | Hippocampus (– 32 – 22 – 18) |  | $r = 0.077$, $p = 0.786$ |
| | Hippocampus (– 26 – 40 4) |  | $r = 0.000$, $p = 0.999$ |
| Retrieval (positive) | Hippocampus (– 24 – 30 – 4) |  | $r = 0.140$, $p = 0.618$ |
| | Hippocampus (24 – 26 – 8) |  | $r = 0.079$, $p = 0.780$ |

$r$, correlation coefficient; $p$, p-value; $^*$, $p < 0.05$. 
doi:10.1371/journal.pone.0024862.t003

| Table 4. Results of 2 × 2 ANOVA. |
|----------------------------------|
| **Region** | **BA** | **Side** | **peak level** | **cluster level** | **xyz** |
| **Z** | **p** | **kE** |
| **Main effect of task** |  |
| Encoding > Retrieval |  |
| Angular Gyrus | 39 | L | 6.46 | 0.000 | 312 | −56 | −62 | 38 |
| Parahippocampal Gyrus | 37 | R | 4.94 | 0.007 | 29 | 40 | −38 | −20 |
| Superior Frontal Gyrus | 9 | L | 4.71 | 0.020 | 7 | −20 | 44 | 44 |
| Superior Frontal Gyrus | 6 | L | 4.56 | 0.038 | 2 | −16 | 14 | 60 |
| Middle Temporal Gyrus | 39 | L | 4.53 | 0.042 | 2 | −40 | −66 | 16 |
| Hippocampus | R | 4.86 | 0.000* | 112^* | 38 | −18 | −20 |  |
| Hippocampus | L | 3.56 | 0.024* | 6^* | −32 | −26 | −16 |  |
| **Retrieval > Encoding** |  |
| Inferior Occipital Gyrus | 17 | L | >8 | 0.000 | 13337 | −10 | −92 | −12 |
| Insula | 13 | R | 5.72 | 0.000 | 217 | 32 | 26 | 2 |
| Midbrain | L | 5.63 | 0.000 | 500 | −4 | −20 | −6 |  |
| Inferior Frontal Gyrus | 47 | L | 5.41 | 0.001 | 164 | −30 | 22 | −4 |  |
| Inferior Frontal Gyrus | 9 | L | 5.31 | 0.001 | 53 | −58 | 4 | 30 |  |
| Hippocampus | L | 4.12 | 0.003* | 8^* | −20 | −30 | −4 |  |
| **Main effect of emotion** |  |
| No area |  |
| Interaction Task × Emotion |  |
| Amygdala | L | 3.02 | 0.036^* | 6^* | −24 | −8 | −16 |  |

BA, Brodmann area; L, Left; R, Right; Z, Z value of the peak activation within the cluster; Coordinates for the peak voxel are listed as MNI coordinates. $p$, corrected $p$ value for whole brain or region of interest ("b" bilateral hippocampus which include 1667 voxels or "b" bilateral amygdala which include 306 voxels); $k_E$, cluster size (voxels) defined by the same peak-level FWE thresholds.

doi:10.1371/journal.pone.0024862.t004
In fact, our regression analyses also revealed a significant inverse correlation between the correct response rate and the magnitude of brain activation in the left hippocampus. This means that activation of this region also disrupted rather than contributed to the associative memory processing. Given the fact that amygdala activity has been reported to correlate with subsequent memory for emotional material [15,16,27] and the influence of the amygdala on the efficacy of encoding is believed to be expressed through its effect on the hippocampus, it is plausible that the amygdala may focus processing resources automatically on the negative words and not the association of paired items required for task performance.

In addition to the results mentioned above, amygdala activation during the positive encoding was positively correlated with the task performance of associative memory in this study. Although the mechanism of this inverse effect of amygdala activation on
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Materials and Methods

Ethics Statement

The study was conducted under a protocol that was approved by the Ethics Committee of Hiroshima University. All subjects submitted informed written consent of their participation.

Subjects

Fifteen healthy volunteers (6 men and 9 women), aged 21–27 years (mean age ± SD = 23.6±1.9 years), with no history of neurological or psychiatric illness, participated in the study. All subjects showed a similar level of intelligence as assessed by the Japanese Adult Reading Test (JART) (112.5±5.6).

Experimental task

During the fMRI protocol, subjects performed a novel block-designed face-emotional word paired associate task. We developed this task from a face-name paired associate task [10,28] that included 3 distinct conditions: encoding, distracter (active baseline), and recognition. The task consisted of 18 blocks, each of which was preceded by an instruction slide informing the participant whether the block was encoding, control, or retrieval condition. Of these 18 blocks, 6 were encoding conditions, 6 were control conditions, and 6 were retrieval conditions. Conditions were interleaved and repeated 6 times (Fig. 1). The duration of each condition was 24 seconds and the preceding instruction slide was shown for 4 seconds. This resulted in a total task period of 9 minutes.

During encoding, pairs of a face and an emotional word were presented serially every 3s, and subjects were asked to remember each face-emotional word pair by pressing a button. The active baseline (control) required subjects to press a button when 2 of 3 words disappeared (randomly within a 3s interval). We used the same emotional words during the corresponding control condition, so as to focus on how emotions modulate the associative memory processing and not on emotional responses themselves. During the retrieval condition, each face was shown with 3 emotional words every 3s, and the subjects were asked to indicate, via button press, which word was previously paired with that face. Forty-eight neutral faces paired with 6 emotional words (3 positive and 3 negative) were used during the experiment, because of the difficulty to select 48 appropriate emotional personality trait words. Although this means that the same words were repeatedly presented with different faces, a different face was presented every time and this task did not require the ability to overcome interference. That is, 48 pairs were presented within encoding condition, and no face-word pair was repeated during the experiment. Each retrieval block tested memory for only the pairs that were in the preceding encoding block, but the presentation of faces was not in the same order in the retrieval block as they were presented in the encoding block. Neutral faces were selected from the database of SOFTPIA JAPAN (The database is not available on line to protect the privacy of subjects participates in the database). Three positive words and 3 negative words were selected from Anderson’s list of personality-trait words translated into Japanese, and were rated on emotional valence and familiarity by a different group of participants [29]. Positive words were from the top 20 positive words and negative words were from the bottom 20 negative words of this list. Positive and negative words were matched in familiarity and word length. Each face and word pair was presented only once during the encoding tasks. For the retrieval tasks performed after the encoding tasks, the remaining 2 of the 3 words were used as distracters. The negative and positive conditions were counterbalanced across the subjects. Stimuli were generated using a personal computer with Presentation software (Neurobehavioral Systems, Inc.; San Francisco, CA). Using an angled mirror, participants viewed the stimuli on a back projection screen mounted outside the scanner bore.

Acquisition of MRI data

Imaging data were acquired using a GE 3.0 T scanner (General Electric, Milwaukee, Wisconsin). A time course series of 190
volumes per participant (including pre- and post-task period) was acquired with echo planar imaging sequences (TR = 3000 ms, TE = 27 ms, FA = 90 deg. Matrix size = 64 × 64, FOV = 256 mm, 4 mm slice thickness, 32 slice, no gap). Functional scans lasted 9 minutes 30 seconds. After functional scanning, structural scans were acquired using T1-weighted gradient echo pulse sequences (TR = 7.2 ms, TE = 2.1 ms, FA = 90 deg. Matrix size = 256 × 256, FOV = 256 mm, 1 mm slice thickness, 164 slice).

Analysis
Data were analyzed using the statistical parametric mapping software package, SPM8 (Wellcome Department of Cognitive Neurology, London, UK). The first 5 volumes of the fMRI run (pre-task period) were discarded to ensure a steady-state MR signal, and the remaining 185 volumes were used for the statistical analysis. Each set of functional volumes was realigned to the first volume, spatially normalized to a standard template based upon the Montreal Neurological Institute (MNI) reference brain, and spatially smoothed using an 8-mm FWHM Gaussian kernel.

We modeled four contrasts for each individual, using a general linear model that included each condition (negative encoding, positive encoding, negative retrieval, and positive retrieval) compared to the relevant control conditions. Then, second level analyses were performed according to a random effect model. First, one sample t-tests were performed for each contrast. The statistical threshold of p < 0.05, corrected for whole-brain family wise error (FWE) at a peak level was used, except for a priori hypothesized regions, which were thresholded at p < 0.05, and corrected for small volume (search volume is a priori region of interest mask) FWE at a peak level. These a priori regions of interest included the hippocampus and amygdala, a region implicated in the processing of memory and emotion. The hippocampal and amygdaloid region of the interest mask was created in Montreal Neurological Institute (MNI) space using the WFU Pick Atlas [30]. We used WFU Pick Atlas only for creating the hippocampal and amygdaloid region of interest mask, and all other analyses were conducted by using SPM 8.

Second, Pearson’s correlation analyses were performed using the averages of contrast estimates (negative encoding-control, positive encoding-control, negative retrieval-control, and positive retrieval-control) of voxels within the clusters detected by the one sample t-test, in order to examine whether activations of these regions during each condition were correlated with corresponding memory performances. Third, a 2 × 2ANOVA with factors of task (encoding or retrieval) and emotion (negative or positive) was performed. The statistical threshold for this analysis was also set at p < 0.05, corrected for FWE at a peak level, and small volume correction (SVC) were applied for the hippocampus and amygdala. Finally, Pearson’s correlation analyses were performed using the averages of contrast estimates (negative encoding-control, positive encoding-control, negative retrieval-control, and positive retrieval-control) of voxels within the same amygdaloid cluster detected in the interaction task × emotion interaction shown in Fig. 2, in order to examine whether activations of this region during each condition was correlated with corresponding memory performances.

Acknowledgments
The authors would like to thank the MRI staff at the Hiroshima University Medical Hospital for use of facilities and technical support. Special thanks are due to Y. Akiyama for his contribution to the project. We also thank T. Matsumoto for helpful discussion.

Author Contributions
Conceived and designed the experiments: GO YO YK S. Yoshimura KO ST HY S. Yamawaki. Performed the experiments: GO YK SA YN. Analyzed the data: GO YK. Wrote the paper: GO YO YK KO S. Yoshimura S. Yamawaki.

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