Amygdala damage impairs emotional memory for gist but not details of complex stimuli

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Neurobiological studies demonstrate the amygdala's role in emotional memory, and psychological studies suggest a particular pattern: enhanced memory for the gist but not the details of complex stimuli. We hypothesized that these two findings are related. Whereas normal ($n = 52$) and brain-damaged ($n = 22$) controls showed the expected enhancement of gist memory when the encoding context was emotional, persons with unilateral damage to the medial temporal lobe including the amygdala ($n = 16$) did not show this pattern. Furthermore, amygdala volume showed a significant positive correlation with gist memory but not with overall memory. A further study in four subjects with selective medial temporal damage sparing the amygdala, and one with selective damage confined to the amygdala, confirmed the specificity of this effect to the amygdala. The data support a model whereby the amygdala focuses processing resources on gist, possibly accounting for features of traumatic memories and eyewitness testimony in real life.

Studies of normal individuals[1–3] as well as of patients suffering from phobias[4] have documented a pattern of enhanced memory accuracy for gist, but no such enhancement (or perhaps even a suppression) for visual details, when material was encoded during emotional arousal. This pattern has been of interest especially for understanding traumatic, childhood and eyewitness memories, whose accuracy is often contentious[5,6]. The amygdala has been shown to be critical in emotional memory and to enhance memories specifically as a function of emotional arousal[7–13]. It has also been linked to the impaired real-life emotional memories seen in patients with post-traumatic stress disorder[14] or Alzheimer disease[15]. A single-case study[16] reported preliminary data consistent with the idea that the above two sets of findings might be related: that is, that the amygdala specifically enhances emotional memory for gist. However, that study[16] used two different tasks to assess memory for gist and for detail, making the findings equivocal. Thus, although it is unknown whether the amygdala might mediate focusing of emotional memory on gist, the above findings taken together provide strong motivation for such a hypothesis, the primary aim of the present study.

A second aim of our study was to definitively assign effects on memory solely to emotional arousal. Many studies of emotional memory have been unable to fulfill this goal, as different sets of emotional and neutral stimuli were typically used, thus confounding emotional arousal with other properties of the stimulus sets, such as their basic visual properties, complexity or distinctiveness. We therefore presented intrinsically neutral stimuli within a variable emotional context, a manipulation that has been used with success in other studies of emotional memory[17,18]. We presented five intrinsically neutral target pictures that had been embedded in either an emotionally

neutral or an emotionally highly arousing story (**Fig. 1**) to 16 subjects with focal lesions to the medial temporal lobe including the amygdala (see Methods and **Table 1** for details on the subjects). Participants saw the stimuli under one of these two different encoding conditions, and the next day their memory for the five target stimuli was assessed with a fixed set of questions about gist and detail. As everyone saw the same target stimuli and answered the same set of memory questions about those stimuli, we could measure the influence of the emotional context under which the stimuli were encoded independently of other confounds. We found that amygdala damage resulted in a specific impairment in emotional memory for gist, results that were confirmed with further neuroanatomical analyses.

RESULTS
Unilateral amygdala damage
We first compared performances from control subject groups to performances from subjects who had unilateral damage to the medial temporal lobe that included the amygdala. All subject groups gave similar ratings, and showed similar patterns of skin conductance responses, to the embedding stimuli used in the different conditions (**Table 2**), confirming their efficacy in providing an emotional context; all subjects assigned intrinsically neutral valence and arousal ratings to the target stimuli when presented in isolation. We found no differences between genders or between subjects with left or with right amygdala damage by any of the measures reported below, and hence we present data collapsed across these factors.

In order to eliminate the variance owing to overall memory performance for different subjects and obtain clear effects for the measure of interest in the present study, for each subject and for

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Figure 1 Task design. (**a,b**) Subjects were shown the same five target pictures ('Target') embedded in either a neutral (**a**) or a strongly emotional (**b**) context that was provided by standardized emotional pictures[38] together with a narrative telling a story. The sample stimuli shown are the ones used in Experiment 1: a story about parents taking a drive in the countryside for relaxation (**a**) or taking a drive to recover the remains of their children who had died in a plane crash (**b**). Only the first few sample stimuli in the series are shown in the figure, as indicated by the dots to the right.

each target stimulus, we calculated a normalized gist memory score: the accuracy for gist memory divided by the total memory accuracy across all questions for that stimulus (raw memory scores are given in **Supplementary Figure 1** online). This proportional gist memory score showed a clear pattern of memory accuracy: normal and brain-damaged controls obtained the highest gist memory score under the emotional encoding condition, indicating an enhancement of memory for gist (**Fig. 2a,b**). By contrast, subjects with damage to the amygdala showed a highly abnormal pattern of memory that was inverted compared to that of controls: their gist memory under emotional encoding was not enhanced. Instead, subjects with amygdala damage showed a higher gist memory under the neutral encoding condition than under the emotional encoding condition (**Fig. 2c**). A 2 × 3 ANOVA with factors of encoding condition (neutral

or emotional) and subject group (normal control, brain-damaged control, amygdala damage) showed no significant effects of group or emotion, but a significant interaction between the two ($F_{2,63} = 4.26$, $P < 0.02$). Pairwise adjusted post-hoc tests confirmed that the group with amygdala damage showed significantly worse gist memory under the emotional encoding condition than did brain-damaged controls ($P < 0.05$), and significantly better gist memory under the neutral encoding condition than did normal controls ($P < 0.05$).

To establish the reliability of the above effect, we carried out a second experiment using entirely different sets of target stimuli, context stories and memory questions. Here, we restricted ourselves to a comparison of 21 normal controls and 12 subjects with unilateral amygdala damage (all subjects with amygdala damage also participated in Experiment 1, separated by at least 1 year). We found exactly the same patterns as in

Table 1 Characteristics of participants[a]

	Age	Ed	PIQ	VIQ	Benton	BDI	*n*	AVLT trial 5	AVLT delay
Expt. 1									
Neutral									
NC	46	14					7M/8F		
BDC	58.8	13.6	99.3	93.0	44.4	5.1	4M/6F	9.8	8.0
R	39.7	13.3	101.7	97.3	45.7	4.3	3M/1F	11.3	7.3
L	38.5	13.0	113.5	102.5	40.0	2.0	2M/0F	12.5	10.5
Emotion									
NC	45.0	15.0					7M/9F		
BDC	61.0	13.7	100.8	111.2	45.2	6.1	7M/5F	11.4	9.89
R	32.7	15.3	105.3	101.3	45.0	5.0	3M/1F	13.0	9.67
L	35.2	15.2	109.5	98.6	44.2	3.0	4M/2F	11.4	8.80
Hippo	50.0	14.0	91.0	100.0	44.6	7.0	3M/1F	7.8	1.25
S.M.	40.0	12.0	95.0	86.0	44.0	0.0	F	13.0	10.00
Expt. 2									
Neutral									
NC	46.0	15.0					4M/6F		
R	37.0	16.0	100.0	105.0	43.0	4.0	1M/0F	13.0	7.00
L	31.3	14.0	96.5	93.8	43.0	6.0	3M/1F	12.3	9.25
Emotion									
NC	50.0	14.0					4M/7F		
R	37.5	14.0	108.0	100.0	45.0	4.3	2M/3F	11.8	8.50
L	39.5	12.0	96.0	90.5	46.0	10.0	0M/2F	8.5	6.00

[a]Demographics and neuropsychological information (means) are given for each experiment (Experiment 1, top; Experiment 2; bottom) and each subject group (NC, normal control; BDC, brain-damaged control; R, right medial temporal damage; L, left medial temporal damage; Hippo, selective hippocampal damage; S.M., patient S.M., who has selective amygdala damage). Ed, years of education; PIQ/VIQ, performance and verbal IQ from the WAIS-III; Benton, scaled score on the Benton Facial Recognition Task (all in the normal range); BDI, Beck Depression Inventory (none severely depressed); *n*, sample sizes and gender ratios; AVLT, Rey Auditory-Verbal Learning Task, a test of anterograde memory.

our first experiment: whereas normal controls showed superior memory for gist under the emotional encoding condition compared to the neutral encoding condition (**Fig. 3a**), subjects with amygdala damage showed worse gist memory under the emotional encoding condition than the neutral encoding condition (**Fig. 3b**) (significant group × emotion interaction; $F_{2,29} = 8.4$; $P < 0.01$). In both above experiments, normal and brain-damaged controls showed better gist memory than detail memory under the emotionally arousing encoding, corresponding to a proportional gist memory accuracy greater than 0.5 (Experiment 1: normal controls $P < 0.0005$, brain-damaged controls $P < 0.01$; Experiment 2: normal controls $P < 0.02$), whereas subjects with amygdala damage did not ($P > 0.5$ for both experiments; Z-tests).

There were four subjects with unilateral amygdala damage who had participated in Experiment 1 under the neutral encoding condition and in Experiment 2 under the emotional encoding condition, and another four who had participated in Experiment 1 under the emotional encoding condition and in Experiment 2 under the neutral encoding condition. These eight subjects thus permitted an examination of within-subject differences for memory under different encoding conditions, complementing the between-subject analyses we have presented so far. Paired t-tests confirmed that these subjects with amygdala damage did in fact have poorer gist memory when material had been encoded under the emotional context than when it had been encoded under the neutral context ($t(7) = -2.67$; $P < 0.05$, two-tailed) (**Fig. 4**).

Correlations with volume

The above impairments in subjects with unilateral medial temporal lobe damage led us to predict that the volumetric extent of their amygdala damage should correlate with the magnitude of the memory impairment, an issue we examined next. In subjects with unilateral medial temporal lobe damage who were shown the stimuli under the emotional encoding condition, we traced and reconstructed the amygdalae and hippocampi from their magnetic resonance scans (see Methods; $n = 9$ for Experiment 1, $n = 6$ for Experiment 2, all different subjects). We found a significant Spearman correlation between

total amygdala volume and gist memory (**Fig. 5**; $R = 0.6$; $P < 0.02$). In the same subjects, there was no significant correlation of gist memory with hippocampal volume ($R = -0.286$; $P = 0.3$). By contrast, when these correlations with amygdala or hippocampal volume were calculated for global memory performance (the mean absolute performance across all questions for an item), there was no significant correlation with amygdala volume ($R = -0.43$, $P = 0.11$), but there was a correlation showing a trend with hippocampal volume ($R = 0.48$; $P = 0.074$) (**Fig. 5**). These data thus suggest a double dissociation: amygdala, but not hippocampal, volume is correlated with proportional gist memory but not global memory performance, whereas hippocampal, but not amygdala, volume is correlated with global memory performance but not proportional gist memory. This pattern of correlations provides a strong argument for the specific role of the amygdala in emotional memory that is specific to gist, but it is not decisive, because all of the subjects described thus far had damage that encompassed both the amygdala and hippocampus owing to the nature of their lesions (neurosurgical temporal lobectomy).

As a further test of the specificity of the amygdala's role in memory for gist, we calculated the partial correlation of amygdala volume versus gist memory while controlling for hippocampal volume, and it was
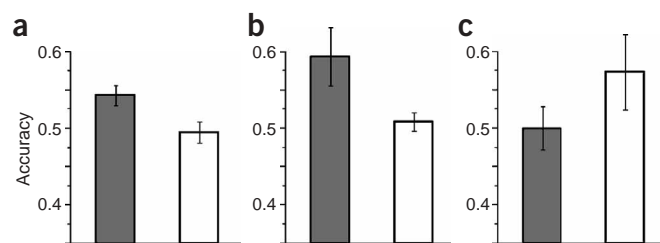
Table 2 Emotional response to the three encoding conditions[a]

	NC		Amygdala		Hippo		S.M.	
	Neutral	Emotional	Neutral	Emotional	Neutral	Emotional	Neutral	Emotional
Expt. 1								
Valence	5.6	1.5	6.2	1.9		1.5		1
Arousal	4.9	8	5	8.2		8.3		7
Unusual	2.7	8.4	2.4	8.8		8.8		8
SCR	0.16	1	0.21	1				
Expt. 2								
Valence	6	1.9	5.9	1.8	4.8		5	
Arousal	4.5	7.9	3.9	7.5	5		5	
Unusual	3.3	7.7	4.7	8.1	3.5		5	
SCR	0.14	1	0.17	1				

[a]Ratings and skin conductance responses (SCR) given by normal controls (NC) subjects with unilateral amygdala damage (Amygdala), selective hippocampal damage (Hippo) and S.M. are shown as means for the embedding stimuli in each of the different encoding conditions. Ratings range from 1 (most unpleasant valence, least arousing, least unusual) to 10. Skin conductance responses (SCR) were measured as the maximal amplitude of response (in microsiemens) within a time window of 0–7 s after stimulus onset. SCR was normalized to the maximal SCR observed for any of the three encoding conditions in one experiment (the emotional encoding condition in all cases, which therefore has a value of 1.0 to which the other values are relative).

Figure 2 Differential modulation of memory for gist by emotion. Gist memory (mean ± s.e.m. score, proportion correct out of total correct) is shown for the emotional (gray bars) and neutral (white bars) encoding conditions. (**a**) Normal controls ($n = 31$). (**b**) Brain-damaged controls ($n = 22$). (**c**) Subjects with unilateral damage to the medial temporal lobe ($n = 16$). Subjects with unilateral temporal lobe damage showed a specific impairment in gist memory under the emotional, but not the neutral, encoding condition.
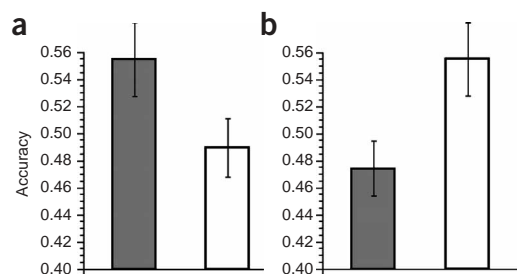

Figure 3 Differential modulation of memory for gist by emotion: replication with Experiment 2. As in **Figure 2**, proportional gist memory (mean ± s.e.m.) is shown for the emotional (gray bars) and neutral (white bars) encoding conditions. (**a**) Normal controls ($n = 21$). (**b**) Subjects with unilateral damage to the medial temporal lobe ($n = 12$). The findings replicated those of Experiment 1 (**Fig. 2**) with an entirely different set of stimuli and questions.

Figure 4 Within-subject gist memory. Data from eight subjects (T1–T8) with unilateral medial temporal lobe damage who participated either in the neutral encoding condition in Experiment 1 and the emotional encoding condition in Experiment 2, or the converse. The majority of subjects showed better proportional gist memory accuracy for the neutral encoding condition (white bars) than for the emotional encoding condition (gray bars).
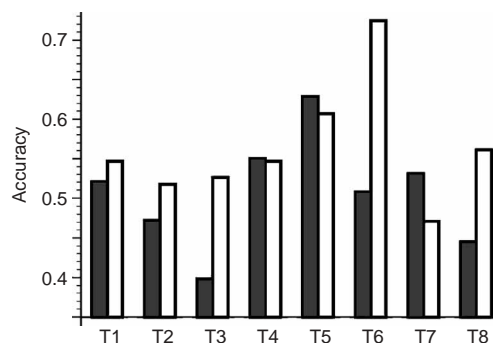
statistically significant using one-tailed testing ($R = 0.48$, $P < 0.05$). Likewise, the partial correlation obtained for hippocampal volume versus global memory, while controlling for amygdala volume, was significant using one-tailed testing ($R = 0.52$, $P < 0.05$). These partial correlations thus confirm the neuroanatomical specificity of the correlation of gist memory with amygdala volume, independent of hippocampal volume.

Selective hippocampal and amygdala damage

To provide further neuroanatomical evidence to corroborate these findings, we carried out an additional study in four patients who had selective bilateral damage to the medial temporal lobe due to cerebral anoxia that included the hippocampus but spared the amygdala, and in one patient who had selective bilateral damage to the amygdala but sparing the hippocampus due to Urbach-Wiethe disease (patient S.M.). The neuroanatomical selectivity of the lesions in these subjects was confirmed by quantification of data from their magnetic resonance scans (**Fig. 6**, **Table 3**) and also corroborated by their neuropsychological profiles (**Tables 1** and **3**; see Methods for additional details). All subjects with bilateral hippocampal damage suffered from a specific anterograde declarative memory impairment; none evidenced any impairment in recognition of fear from facial expressions. Conversely, subject S.M. has no impairment on standard verbal anterograde memory tasks but has a severe and specific impairment in recognizing fear from facial expressions[19]. Whereas S.M. was tested as described above, the amnesia of the subjects with hippocampal damage required shortening the interval between encoding and retrieval so as to preclude floor effects; their memory on the tasks was assessed 1 h after encoding in all cases. The data from these additional subjects (**Fig. 7**) confirmed the above conclusions. Under the emotional encoding condition, the subject with bilateral amygdala damage (S.M.) showed worse proportional gist memory than any of the four subjects with

hippocampal damage (and worse than the normal or brain-damaged controls; see **Fig. 2**). Conversely, under the neutral encoding condition, S.M. showed greatly enhanced gist memory, unlike the two subjects with hippocampal damage who were tested under this condition, but like subjects with unilateral amygdala damage (**Fig. 2**). Whereas all subjects with hippocampal damage showed proportional gist memory under the emotional encoding condition that was as good or better than that of normal controls, S.M. did not.

DISCUSSION

We found that unilateral damage to the medial temporal lobe including the amygdala resulted in a specific impairment in emotional memory: an impairment in memory for the gist of complex stimuli, rather than an overall impairment across all items. This effect correlated with the volumetric extent of amygdala damage, and was also seen in a subject with selective bilateral amygdala damage, supporting the hypothesis that it is attributable to the amygdala alone. In further support of this hypothesis, no such correlation was found with hippocampal volume, nor in patients with selective medial temporal lobe damage that included the hippocampus but spared the amygdala. The data thus argue that the human amygdala enhances memory for complex stimuli encoded under emotionally arousing contexts in a specific fashion: it enhances memory for their gist, but not their details. The finding is in line with the idea that the amygdala focuses processing resources on the most salient information, as Easterbrook had originally proposed[20].

The present findings complement an earlier study[16] that found evidence to suggest that the amygdala is also important for enhancing gist memory for complex scenes that are intrinsically emotional. It thus seems that either intrinsic or contextual emotional arousal can modulate memory for the gist of stimuli. In real life, it is likely that both intrinsic and contextual factors operate together in influencing how we remember emotional events.

Several alternative explanations of these findings are improbable. First, it might be that the effects reported are a result not of the emotional arousal of the story within which the target stimuli were embedded but rather of some other property of the embedding context. Of course, such an effect would still implicate the amygdala in memory modulation, albeit on the basis of a factor other than emotional arousal
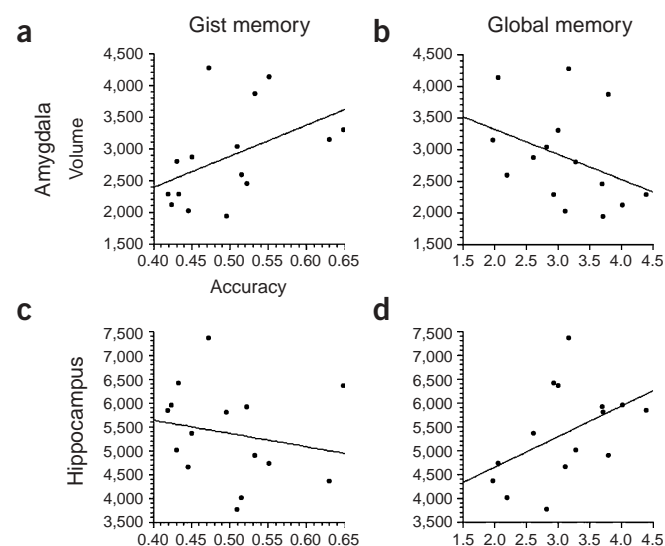

Figure 5 Correlation between memory performance and neuroanatomy. Shown are four correlations between either the proportion of gist memory or global memory performance (the summed score on all questions, not broken down for gist or detail), and amygdala or hippocampal volumes (in mm³). Each data point represents data from one subject with medial temporal lobe damage (total $n = 15$, all from the emotional encoding condition). (**a**) Amygdala volume versus gist memory. (**b**) Amygdala volume versus global memory. (**c**) Hippocampal volume versus gist memory. (**d**) Hippocampal volume versus global memory.
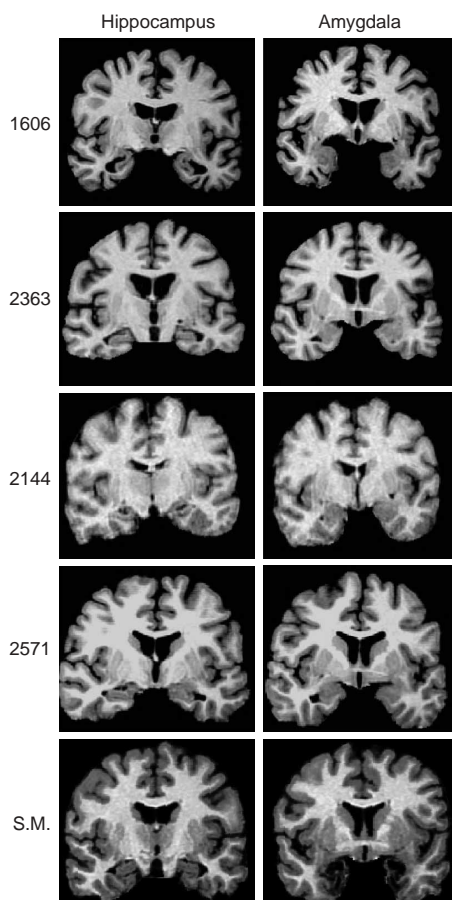
Hippocampus   Amygdala

1606

2363

2144

2571

S.M.

Figure 6 Neuroanatomy of subjects with selective hippocampal or amygdala damage. Coronal magnetic resonance sections are shown at the level of the hippocampus and amygdala for the four subjects with bilateral hippocampal lesions due to anoxia (subject identifier numbers given on the left), demonstrating bilateral atrophy of the hippocampus but not the amygdala, and for subject S.M., showing bilateral damage to amygdala and anterior entorhinal cortex. A quantitative volumetric analysis compared the volumes of the amygdala and the hippocampus in these subjects with the volumes in healthy individuals (given in **Table 3**).

to differences in encoding gist or detail. It may well be that the variance in performance resulting from amygdala lesions in our study introduced such a large effect that it precluded finding such laterality or gender differences. All of our patients had long-standing, and in many cases developmental, lesions of the amygdala. This might result in different patterns of hemispheric lateralization of function than if the lesions had all been acquired in adulthood.

A final interpretive issue concerns the amygdala's role in the encoding, consolidation or retrieval of emotional memory. Although studies in both human and nonhuman animals have confirmed a role in encoding and consolidation [7–9,12], there are also a few studies that point toward a modulation by emotional context at encoding on subsequent retrieval processes [17], including ones associated with activation of the amygdala [29]. The present study leaves open the possibility that the amygdala might have a role during the retrieval that our experiments used to assess differential encoding and consolidation; similarly, the functional imaging studies on retrieval leave open the possibility that the amygdala has a role during the re-encoding that would accompany retrieval.

The rat amygdala can apparently both participate in modulation of hippocampal-dependent memories during encoding and consolidation [12,30] and serve as a site of (non–hippocampal-dependent) emotional memory storage in its own right [31]. Likewise, studies in humans have confirmed that the amygdala modulates other medial temporal lobe structures during encoding [13,32] as well as participating in pavlovian fear conditioning independently of the hippocampus [33]. Furthermore, the amygdala's modulatory influence on other brain structures is itself bidirectional: it influences, and is in turn influenced by, the hippocampus [34]. Thus, we have to acknowledge the amygdala's role in multiple memory processes, and future studies should further explore under which conditions, or for which types of material, a particular memory function comes into play.

alone. However, we consider this unlikely, both because we specifically designed the two different contexts to differ maximally in terms of emotional arousal, and also in view of studies demonstrating that the amygdala modulates memory specifically on the basis of emotional arousal [9,10,13,21] and that any memory facilitation that might result from increased distinctiveness of the stimuli [9,22] or semantic cohesion of the context [23] seems to be independent of the amygdala.

A second possibility resides with perception of the stimuli by the subjects: perhaps subjects with amygdala damage simply did not perceive the stimuli normally, or failed to be emotionally aroused during their encoding. These possibilities are also unlikely given the background neuropsychology and the ratings and skin conductance responses we obtained (**Tables 1** and **2**), documenting intact basic visual perception and normal indices of rated and psychophysiological arousal. Independence of emotional memory from emotion perception [24] and emotion experience [11,25] have also been documented in earlier studies of subjects with amygdala damage.

Although we found no evidence of laterality or gender differences in our study, functional imaging studies have indicated that emotional memory disproportionately recruits the left or the right amygdala in women or in men, respectively [26,27], and a recent pharmacological study [28] has provided suggestive evidence that these differential activations may correspond

Table 3 Background for four subjects with bilateral damage to hippocampus but not amygdala[a]

Subject	Etiology	Amy	Hippo	WMS: GMI	WMS: DRI
1606	Smoke inhalation, cardiac arrest	−1.18	−4	66*	61*
2144	Anoxia due to seizure	−0.22	−3.92	56*	57*
2363	Cardiac arrest	−0.06	−2.64	73*	74*
2571	Cardiac arrest	−0.48	−1.01	Not available	
Mean		−0.485	−2.8925	65	64

[a]The four subjects had each suffered an anoxic episode that left them amnesic. Detailed quantitative volumetric analyses of their total amygdala and hippocampal volumes are given in Z-scores relative to a population of normal subjects whose neuroanatomy has been quantified in a separate study [39]. Raw scores on the Wechsler Memory Scale are given for the General Memory Index (GMI) and the Delayed Recall Index (DRI). In all cases, reductions in hippocampal volume exceeded those for amygdala volume, and in all but one case reductions in hippocampal volume were more than 2 s.d. below the normal mean. Memory scores that are severely defective are indicated by an asterisk.

The neuroanatomical Z-scores were obtained in relation to a normative sample of 43 healthy men and 44 healthy women of similar age to the patients. Amygdala and hippocampus volumes were traced by two independent experimenters in these 87 normal subjects and were used to obtain regression equations of amygdala and hippocampal volume with age, for each gender. The studentized residuals of the volumes from the four anoxic patients from these regressions were used to obtain the data shown in the table.
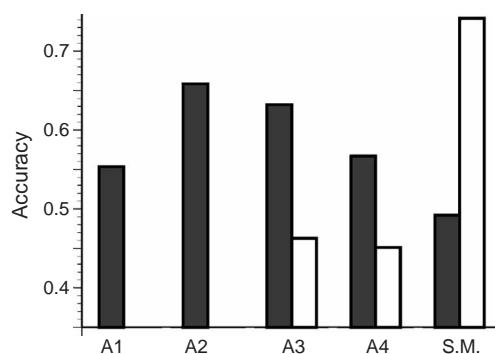
Figure 7 Gist memory in subjects with bilateral hippocampal or bilateral amygdala damage. Data are shown for the four subjects with hippocampal damage but no amygdala damage due to cerebral anoxia (A1–A4) and for subject S.M. with bilateral amygdala damage. Gray bars, emotional encoding condition; white bars, neutral encoding condition. Whereas subjects with hippocampal damage showed increased proportional gist memory under the emotional encoding condition, subject S.M. did not, and instead showed an increased proportional gist memory under the neutral encoding condition.

Our findings here provide strong evidence that the human amygdala helps to focus declarative memory for complex stimuli encoded under emotional contexts through differential effects on memory for gist and for detail. The data suggest that the integrity of the amygdala is responsible for an enhancement of gist memory under conditions of emotional arousal, as amygdala damage results in a disproportionate impairment in gist memory relative to detail memory. Notably, we have found that proportional gist memory under neutral encoding was in fact enhanced after amygdala damage, suggesting that the amygdala can both potentiate and reduce gist memory, depending on the encoding context. Studies in animals indicate that modulation of hippocampal long-term potentiation by the amygdala[35] shows a biphasic pattern: an immediate augmentation followed by a prolonged inhibition[36]. One could speculate that such complex modulation of hippocampal function by the amygdala may be a cellular analog of the differential effects on gist memory we report here.

METHODS

Subjects. A total of 16 subjects with unilateral amygdala damage (Experiment 1, 16 subjects; Experiment 2, 12 subjects) were compared to 22 brain-damaged controls with no amygdala damage (only in Experiment 1) and 52 normal controls (31 in Experiment 1; 21 in Experiment 2). A follow-up experiment tested an additional four subjects with damage to the medial temporal lobe including the hippocampus but sparing the amygdala, as a result of cerebral anoxia (all four in Experiment 1 under emotional encoding, and two of them also in Experiment 2 under neutral encoding), and one subject with damage restricted to the amygdala as a result of Urbach-Wiethe disease (subject S.M., who participated in both Experiments 1 and 2).

All subjects had performance and verbal IQs in the normal range, had normal basic visual perception (Benton Facial Recognition Task raw scores >40) and were not depressed. The four subjects with bilateral hippocampal damage due to cerebral anoxia all had a severe anterograde amnesia. By contrast, none had any impairment in discrimination of faces and or in their ability to recognize emotional facial expressions, indicating intact amygdalae. Demographic and neuropsychological information on all subject groups is given in **Table 1**. All brain-damaged subjects were selected from the Patient Registry of the Department of Neurology at the University of Iowa; their neuroanatomy was obtained from detailed three-dimensional reconstructions of their brains from magnetic resonance images or computed tomography scans (only magnetic resonance images were used for quantitative volumetric analyses)[37]. All subjects with amygdala damage had unilateral neurosurgical temporal lobectomy for the treatment of epilepsy, resulting in variable unilateral damage to the amygdala, hippocampus and adjacent cortices. Furthermore, they all had very infrequent (fewer than one per year) or no seizures, and there was no significant correlation between age of seizure onset and performance on any memory measure in our tasks (R values < 0.15, not significant). Brain-damaged controls had damage resulting from stroke in structures located outside the medial temporal lobe. Normal controls had no history of neurological or psychiatric disease. All subjects had given informed consent to participate in these studies as approved by the Human Subjects Committee of the University of Iowa.

Encoding task. Subjects were shown five intrinsically neutral target images alternately interleaved with standardized neutral or emotional context images[38] (including a context image at the very beginning and the end of the series), for a total of 11 pictures; memory was not assessed for the context stimuli. Each of the 11 stimuli was shown for 20 s on a computer monitor and was accompanied by a simple single-sentence description read by a technician who was blind to the nature of the study. Thus, the series of pictures and read narrative constituted a short story that was presented as a narrated slide show. All images were complex, color photographs of scenes involving social content (**Fig. 1**).

Memory task. Subjects participated in memory tests and subsequently in ratings of the stimuli 24 h after the encoding session (or 1 h after the session for the four subjects with selective bilateral hippocampal damage, to accommodate their severe anterograde amnesia). We asked an invariant set of five written, four-alternative multiple-choice questions about each target stimulus (three about the gist, two about the background visual detail; scores for the background detail questions were multiplied by 3/2 to equate their contribution to that of the gist questions for comparison). The questions were carefully designed to assess memory either about the central, foreground information pertaining to visual information regarding the main gist of the target stimulus, or about background details of the image. Gist and detail were operationalized as described previously[16], as information essential to the meaning of the picture (for example, who the main characters in it were) and as background information that was irrelevant (for example, what the clouds in the sky looked like). Gist and detail questions showed an expected memory difference in our normal controls: under the emotional encoding condition there was a significantly greater enhancement (relative to the neutral encoding condition) for those questions classified as gist, compared with those classified as detail (Experiment 1: $t = 2.2$, $P < 0.05$; Experiment 2: $t = 1.93$, $P < 0.05$). Subjects' answers were scored so as to permit partial credit as they narrowed down their choices: they indicated, for each question, first their top three choices out of the four available (earning them 0.33 points if these contained the correct answer), then their top two choices (earning them 0.5 points if these contained the correct answer), and finally their top choice (earning 1 point if answered correctly), thus yielding for each question possible scores of 0, 0.33, 0.5 or 1.0. This scoring method helped to provide a homogeneous answering strategy for all subjects and provided a more continuous performance score. We also repeated all statistical analyses in the study using a simple binary scoring method (correct or incorrect from the final top choice answer), with similar findings. For the proportional memory scores given in the text, the scores for the three gist questions were summed and divided by the total score on all questions, to obtain a gist memory accuracy score for each stimulus for each subject that was normalized to that subject's overall memory performance for that stimulus. Raw memory scores for both experiments are given in **Supplementary Figure 1**.

Experiments. For organizational purposes, we divide our description into two experiments, all of which followed the methods described above. Experiments 1 and 2 used identical methods but a different set of actual stimuli (both target and embedding pictures, as well as spoken narrative, were different) and a different set of questions about them. Whereas separate sets of normal control subjects participated in the two experiments, the subjects with unilateral amygdala damage, selective hippocampal damage or selective bilateral amygdala damage who participated in Experiment 2 had also all participated in Experiment 1. The second of the two experiments was administered at least 1 year after the first in all subjects who participated in both; both orders were used, and there were no order effects. For the correlational analyses, we

combined data from the two experiments by normalizing each subject's gist or global memory score to the mean global memory score obtained on a particular item by the normal controls.

Anatomical analyses. Quantitative measurements of amygdala and hippocampal volumes were carried out in subjects with medial temporal lobe damage. Each structure was traced in individual magnetic resonance slices by two independent technicians who were blind to the data from the memory tasks. The results from the traces by the two technicians were highly reliable, with correlations of reconstructed volumes for the amygdala and for hippocampus greater than 0.9 in all cases (Cronbach's α for each structure > 0.95). Traces of the amygdala and of the hippocampus were reconstructed through the entire extent of the structure to yield a volumetric measure. We used the reconstructed volume of the entire bilateral amygdala (or hippocampus) in our analyses. We were unable to obtain data for one subject in each of Experiments 1 and 2, as only computed tomography scans were available, which did not provide sufficient spatial resolution for these analyses. Quantitative analyses of the volumes of amygdala and hippocampus in the four subjects with anoxia were obtained similarly and scored in relation to the volumes of matched normal controls (**Table 3**).

Note: Supplementary information is available on the Nature Neuroscience website.

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