Research Article

The Potentiation of Associative Memory by Emotions: An Event-Related FMRI Study

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Establishing associations between pieces of information is related to the medial temporal lobe (MTL). However, it remains unclear how emotions affect memory for associations and, consequently, MTL activity. Thus, this event-related fMRI study attempted to identify neural correlates of the influence of positive and negative emotions on associative memory. Twenty-five participants were instructed to memorize 90 pairs of standardized pictures during a scanned encoding phase. Each pair was composed of a scene and an unrelated object. Trials were neutral, positive, or negative as a function of the emotional valence of the scene. At the behavioral level, participants exhibited better memory retrieval for both emotional conditions relative to neutral trials. Within the right MTL, a functional dissociation was observed, with entorhinal activation elicited by emotional associations, posterior parahippocampal activation elicited by neutral associations, and hippocampal activation elicited by both emotional and neutral associations. In addition, emotional associations induced greater activation than neutral trials in the right amygdala. This fMRI study shows that emotions are associated with the performance improvement of associative memory, by enhancing activity in the right amygdala and the right entorhinal cortex. It also provides evidence for a rostrocaudal specialization within the MTL regarding the emotional valence of associations.

1. Introduction

Episodic memory refers to the capacity to recollect individual events [1], which include perceptive dimensions of physical objects as well as the time and the place in which they occurred. All this disparate information has to be bound to create a unique coherent representation in memory [2]. This ability to bind and integrate disparate elements is an essential feature of episodic memory and has been referred to as associative memory [3].

It is now generally accepted that the medial temporal lobe (MTL) is involved in processing episodic events, but the exact nature of the contribution of its different parts is still a matter of debate. The MTL is composed of the amygdala, the hippocampus, and surrounding cortices (i.e., the perirhinal, the entorhinal, and the parahippocampal cortices). In nonhuman primates, the perirhinal and parahippocampal cortices, and to a lesser extent the entorhinal cortex, receive projections from unimodal and polymodal sensory cortices. In turn, MTL cortices, and mainly the entorhinal cortex, provide inputs to the hippocampus [4–7]. Guided by these neuroanatomical considerations, it has been proposed that the MTL mediates different associative networks [5]. One hypothesis is that the hippocampus is required in the processing of associations between multiple stimuli, such as words [8–12], objects [13, 14], faces, and names [15–17]. Given their connections with sensory cortices, perirhinal and parahippocampal cortices are implicated in the processing of objects and scenes, respectively [16, 18–26].

Most of studies on associative memory were conducted using neutral materials, limiting their ecological validity, as people encounter multiple emotional stimuli and experience

various affective states in their live. To overcome this limitation, emotion must be taken into account [12]. Emotion generally increases the likelihood that single information is remembered, and this effect reflects in part the influence of the amygdala on encoding and consolidation processes occurring in the hippocampus and MTL cortices [27–29].

Most neuroimaging studies that have investigated the effects of emotion on memory were limited to item memory [30]. Remembering discrete items is an important aspect of memory; however, remembering items associated with others or items placed in a context is another important aspect that also needs to be considered, since it better reflects what is experienced by individuals [30, 31]. Indeed, it is rare that people encounter information presented in isolation in everyday life. The effects of emotion on memory for discrete stimuli have been demonstrated in numerous studies [30]. Nonetheless, the effects of emotion on an individual's capacity to associate information remain unclear, since results of studies are contradictory [32]. Some studies report enhanced remembering, whereas others report impaired performance, and some report no effect of emotion [30].

In the current study, we used fMRI to investigate the neural correlates of the effects of emotion on associative memory. In light of previous work, we systematically examined MTL activations, as well as the interactions between amygdala activity and both hippocampal and MTL cortical activity.

2. Material and Methods

2.1. Subjects. Twenty-five participants (16 males; 18–29 years) were recruited by means of advertisements placed in local newspapers. All were right-handed as established by the Edinburgh Inventory (91.44 ± 7.78%). The participants were examined with the Non-Patient Edition of the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I/NP) to rule out current or past Axis I psychiatric disorder.

The ethics board of the Montreal Neurological Institute (MNI) approved the study. Each participant signed an informed consent form prior to the experiment and received financial compensation for their participation.

2.2. Procedure. Prior to scanning, participants were provided with a detailed description of the task and instructions. Participants were instructed to memorize pairs of images. They were explicitly asked to memorize both images and also their pairing. Then, a short practice session was administered in order to familiarize participants with the experimental task.

The experimental task was adapted from that initially developed by Touryan et al. [33]. A graphical representation of the procedure is presented in Figure 1. During the scanned encoding session, participants had to memorize 90 pairs of standardized images. Each trial began with the presentation of a fixation cross (3000 ms), followed by a pair of pictures (3000 ms). These parameters were in line with our previous fMRI studies using emotional stimuli [34–36]. Each pair was composed of a picture depicting a complex scene (e.g.,
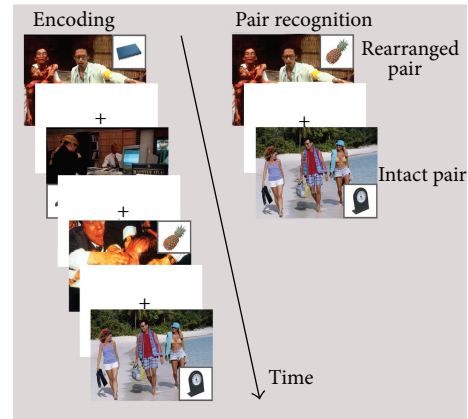

Figure 1: Illustration of the behavioral task. The left part represents a segment of the encoding session, with pairs composed of a scene and an unrelated common object presented in one of the four corners. The right part represents the pair recognition test during which intact and rearranged pairs were presented.

smiling people walking on the beach, a robbery in the subway) and a common object (e.g., a screwdriver). The scenes were selected from various sources (for more details, see [34]). Of these scenes, 30 were negatively valenced , 30 were positively valenced, and 30 were neutral. To minimize the potential confounding effect of arousal level differences between positive and negative pictures, we excluded pictures known to trigger high arousal (based on previous pictures rating from the IAPS), such as pictures presenting erotic scenes or mutilated bodies. The objects were selected from the BOSS standardized database [37] and were conceptually unrelated to the pictures with which they were presented. Each object was placed in a white box delimited by gray borders to dissociate the object from the scene. The corner designated for object location was equally distributed among the four corners, across valence. The order of stimulus presentation during the encoding phase was pseudorandom, with no more than three consecutive positive, negative, or neutral pictures. On each encoding trial, subjects had to indicate with a fiberoptic response pad whether the object was located on the left or on the right side, regardless of whether it was located at the top or the bottom of the screen. This task, in combination with associative-encoding instructions, ensured that subjects focused on both stimuli during their presentation. In other words, associative encoding is intentional.

Approximately 10 minutes after completing the encoding session, participants were required to make a pair recognition judgment. No functional scanning was conducted during the associative recognition test. Participants were presented with 90 consecutive trials (45 intact pairs and 45 rearranged pairs) and were instructed to indicate whether pairs were intact (objects and scenes presented in the same pairing as in the encoding session) or rearranged (pictures previously studied but presented in a new pairing). For rearranged pairs, the object was located in the same corner as during encoding to control for potential source memory effects. Additionally,

a given object, if presented at encoding with a negative scene, was rearranged with another negative scene at recognition and not with a positive or neutral scene. The use of rearranged pairs as lures is designed to avoid judgment based on the familiarity of items. Thus, accurately rejecting rearranged pairs requires explicit knowledge of stimuli as well as their association.

Approximately 30 minutes after completing the recognition session, a cued recall test and a valence rating task were administrated outside the scanner. We included a cued recall test to determine how an emotional stimulus (i.e., the scene) influences the between-stimuli binding of a neutral stimulus (i.e., the object). We also included a valence rating task since we were interested in confirming that the participants considered the emotional pictures as emotional and the neutral pictures as neutral. In both the cued recall test and the valence rating task, the central scenes were presented again but without any objects. In the cued recall test, participants were asked to (i) recall from memory the object that was presented with the scene during encoding; and (ii) indicate in which corner it was presented, even if they could not recall the objects themselves. During the valence rating task, participants were asked to rate the emotional valence of each visual scene using a 9-point Likert scale ranging from 1 (extremely negative) to 9 (extremely positive), with 5 indicating a neutral valence. The order of these two tasks was fixed, with the cued-recall test first and the valence task second.

2.3. FMRI Scanning Protocol.

Scanning was carried out on a whole-body 1.5T Siemens Sonata System, using gradient-echo EPI sequences. The head was stabilized with a moldable vacuum cushion to minimize head movements. First a localizer scan was acquired followed by the functional run consisting of 214 T_{2*}-weighted images acquired with a blood oxygenation level-dependent contrast (TR = 2540 ms; TE = 50 ms; Flip angle = 90°; 30 interleaved slices; voxel size 4 × 4 × 4 mm). Functional scans were acquired parallel to the anterior-posterior commissural plane. After completing the functional run, a 3D-T_1 MDEFT sequence was used for the acquisition of anatomical images (voxel size 1 × 1 × 1 mm).

2.4. Data Analysis

2.4.1. Behavioral Analyses. Behavioral performance was analyzed using Statistica 6.0 (Statsoft). In order to estimate pair recognition accuracy separately from response bias, a primary recognition index was examined using the Two-High Threshold Theory [38]. The Pr index (hits-false alarms) provides an unbiased estimate of recognition accuracy and reflects the participant's ability to discriminate between intact and rearranged pairs. Recall performance was scored by the proportion of correct responses. A response was considered correct when the object and its location were correctly recalled.

In all behavioral analyses, the alpha level was set at 0.05.

2.4.2. Neuroimaging Analyses. Functional images acquired during memory encoding were pretreated with SPM5 (http://www.fil.ion.ucl.ac.uk/spm/software/spm5/). The T_{2*} images were first realigned to the 29th image in their respective run and normalized to the Echo Planar Imaging (EPI) template. Images were then spatially smoothed with an 8-mm full width half maximum (FWHM) isotropic Gaussian kernel. Prior to individual analyses, the movement correction logs were examined to ensure that none of the participants presented movements greater the 5 mm or 5°.

To assess the effects of emotion on associative memory, four event types were modeled: positive, negative, and neutral associations and the fixation cross (baseline). Positive and negative trials were pooled into a single condition named "emotional" condition, as analyses revealed no significant differences between positive and negative valence conditions for either behavioral performance ($t_{24} = 0.63$; $P = 0.78$) for the recognition test and ($t_{24} = 0.12$; $P = 0.13$) for the recall test or brain activations ([Positive-Negative]) analysis threshold at $P < 0.001$ uncorrected. Functional images were analyzed in two steps. In a first-level analysis, a general linear model was created for [Emotional-baseline], [Neutral-baseline], [Emotional-Neutral], and [Neutral-Emotional] contrasts, for each subject. In a second-level analysis, [Emotional-Neutral] and [Neutral-Emotional] contrasts were pooled for main effects into one-sample t-tests of within-group effects (random effect analysis). Main effects were assessed at the whole-brain level. Activations were considered significant with a voxel extent threshold of 10 or more voxels, with $P < 0.001$ (uncorrected for multiple comparisons). [Emotional-baseline] and [Neutral-baseline] contrasts were used to conduct a conjunction analysis ($P < 0.001$ uncorrected) [Emotional ∩ Neutral] in order to determine cerebral areas activated by both emotional and neutral associations. Lastly, restricted analyses focusing on the MTL were conducted using a small-volume correction implemented in SPM5. To that end, masks were obtained using the Automated Anatomical Labeling (AAL) atlas [39], included as a subset of regions of interest into the PickAtlas toolbox [40]. Masks comprised bilateral hippocampi, parahippocampal gyri, and amygdala. The threshold for these restricted analyses was lowered based on a priorihypotheses of the involvement of the hippocampus and its surrounding cortices in associative memory and the amygdala in emotion. Accordingly, analyses were thresholded at $P < 0.005$ (uncorrected), with a voxel extent threshold of >10 voxels.

3. Results

3.1. Behavioral Analyses

3.1.1. Recognition and Recall Tests. Data are summarized in Table 1. The analysis of the Pr index showed that participants were significantly more accurate in recognizing emotional associations than neutral associations ($t_{24} = -2.20$; $P = 0.04$). Similarly, the analysis of recall performance showed that participants better recalled the object and its location when it was associated with emotional scenes than with neutral scenes ($t_{24} = -2.45$; $P = 0.02$).

TABLE 1: Mean (and SEM) proportions of hits (H), false alarms (FA), Pr index, and recall score as a function of emotional associations and neutral associations conditions.

	Recognition			Recall
	H	FA	Pr	
Emotional associations	0.80 (0.03)	0.15 (0.04)	0.63 (0.04)	0.33 (0.04)
Neutral associations	0.79 (0.04)	0.20 (0.03)	0.57* (0.06)	0.28** (0.04)

*P value significant at 0.04 (for the emotional versus neutral associations comparison).
**P value significant at 0.02 (for the emotional versus neutral associations comparison).

3.1.2. Emotional Valence. T-tests showed that the ratings of positive (mean: 7.02; SEM: 0.15) and negative (mean: 2.90; SEM: 0.13) pictures significantly differed from 5 ($t_{24} = 13.05$; $P < 0.001$ and $t_{24} = -16.05$; $P < 0.001$ for positive and negative pictures, resp.) but that the ratings of neutral pictures (mean: 5.09; SEM: 0.09) did not differ from 5 ($t_{24} = 1.77$; $P = 0.10$). The ratings of positive pictures significantly differed from the rating of negative pictures ($t_{24} = 15.54$; $P < 0.001$). Together, these results confirmed that participants considered the positive and negative pictures as positive and negative, respectively, and the neutral pictures as neutral. As a result, they validate the appropriateness of stimuli for an emotional task.

3.2. Functional Neuroimaging Analyses. Two participants were excluded from fMRI analyses as they failed to reach criterion for performance during the encoding phase (<75% correct responses for the object-location judgment). The 23 remaining participants achieved above 96% correct responses (mean: 99%; SEM: 0.22), a performance level clearly indicative of full attention during stimulus presentation.

Whole brain analyses revealed that emotional associations activated predominately posterior regions, relative to neutral associations. Activations were observed in occipital (inferior and middle gyri), cuneus, parietal (postcentral, supramarginal gyri, and precuneus), temporal (middle, superior and fusiform gyri, entorhinal cortex), frontal (precentral superior frontal gyri, cingulate), and subcortical (substantia nigra and reticular formation) areas. Conversely, neutral associations elicited greater activations than emotional associations, predominately in anterior regions, including the cingulate (posterior and anterior gyri), temporal (superior and parahippocampal gyri), and frontal (middle and inferior gyri) areas. The conjunction analysis revealed that both emotional and neutral associations induced activations in the left premotor cortex and in the left anterior cingulate cortex, as well as in the right caudate nucleus, fusiform gyrus, culmen, and the hippocampus. Details about all these activations are reported in Table 2.

Restricted analyses focusing on the MTL showed that emotional associations induced greater activations in the right entorhinal cortex (26/−12/−32; $Z = 3.65$; 40 voxels) and the right amygdala (30/4/−26; $Z = 2.86$; 11 voxels). Conversely, greater activations were observed in the posterior part of the right parahippocampal gyrus (24/−42/−6; $Z = 3.63$; 50 voxels) for neutral associations relative to emotional associations (levels of activation were estimated in these

three clusters to ensure that entorhinal and amygdala activations were due to greater activity for emotional associations and that parahippocampal activation was due to greater activity for neutral associations. To that end, the peak of the entorhinal and amygdala clusters for the [emotional-baseline] contrast and the parahippocampal cluster for the [neutral-baseline] contrast were determined as the center of a 5 mm diameter sphere. Activation levels were then estimated. Paired t-tests showed significantly greater levels of activation for emotional than neutral associations in entorhinal ($t_{22} = 3.43$; $P = 0.002$) and the amygdala ($t_{22} = 2.76$; $P = 0.01$) clusters. Conversely, significantly greater levels of activations were observed for neutral than emotional associations in the parahippocampal cluster ($t_{22} = 3.22$; $P = 0.004$)). Finally, activations were observed in the hippocampus (32/−28/−12; $Z = 2.62$; 10 voxels) for both emotional and neutral associations. Activations are illustrated in Figure 2. Here we considered that the cluster is located in the right entorhinal cortex. However, it should be mentioned that it remains difficult to straightforwardly determine whether the anterior parahippocampal activations arise from entorhinal or perirhinal cortex.

The mean activation level in each of these four clusters was then evaluated. Using the amygdala modulatory hypothesis as a model to explore MTL interregional covariation in activity [41, 42], correlations between amygdala activation and the other three MTL clusters were evaluated. The mean activity of each cluster for each participant was assessed for the [Emotional-Neutral] contrast and then correlations based on individual differences were calculated. The data of two participants were removed, as their individual activation levels in the entorhinal and in the parahippocampal clusters were more than 2 S.D. lower than the mean activation levels in these clusters. After removing these two outliers, correlation analyses showed that amygdala activity significantly covaried with entorhinal activity ($r = 0.51$; $P = 0.02$) and posterior parahippocampal activity ($r = -0.60$; $P = 0.008$) but not with hippocampal activity ($r = -0.25$; $P = 0.25$).

4. Discussion

This event-related fMRI study yielded three main results. First, participants had better memory performance for emotional than for neutral associations. This enhancement was observed for both recognition and recall test modalities. Second, rostrocaudal dissociation within the medial temporal lobe was observed as a function of the emotional valence of associations: greater activations were found in the

TABLE 2: Activations elicited by encoding when contrasting the emotional and neutral conditions.

Cerebral domain	BA	Z score	Stereotaxic coordinates			Cluster size (voxels)
			x	y	z	
Emotional > neutral						
Middle occipital gyrus (R)	19	4.54	48	−76	0	231
Postcentral gyrus (L)	3	4.51	−52	−26	58	73
Cuneus (R)	18/19	4.30	12	−88	14	150
Inferior occipital gyrus (L)	18	3.96	−38	−86	−18	25
Fusiform gyrus (R)	37	3.94	36	−52	−22	66
Posterior cingulate gyrus (L)	31	3.86	−14	−42	42	42
Inferior occipital gyrus (R)	17	3.85	28	−96	−6	43
Middle temporal gyrus (L)	19	3.81	−52	−72	14	75
Culmen		3.76	16	−66	−12	26
Superior frontal gyrus (R)	8	3.71	24	40	52	35
Entorhinal cortex (R)	28	3.65	26	−12	−32	15
Precuneus (L)	19	3.63	−2	−78	38	53
Inferior occipital gyrus (L)	18	3.62	−28	−98	−10	24
Posterior cingulate gyrus (R)	30	3.56	4	−48	18	84
Supramarginal gyrus (L)	40	3.55	−50	−46	32	19
Substantia nigra		3.55	12	−12	−8	12
Superior temporal gyrus (R)	22	3.50	54	−60	14	16
Pons (reticular formation)		3.49	−2	−28	−36	13
Precentral gyrus (L)	6	3.47	−52	6	38	27
Precuneus (R)	7	3.46	12	−58	30	41
Fusiform gyrus (R)	19	3.37	32	−78	−12	12
Pulvinar		3.32	−10	−30	12	13
Neutral > emotional						
Parahippocampal gyrus (R)	36	4.28	16	−36	−16	24
Middle frontal gyrus (R)	46	4.19	32	44	16	17
Superior temporal gyrus (R)	22	3.96	50	−6	−4	22
Inferior frontal gyrus (L)	46	3.73	−34	34	12	21
Parahippocampal gyrus (R)	36	3.63	24	−42	−6	12
Posterior cingulate gyrus (R)	23	3.48	22	−32	28	13
Anterior cingulate gyrus (R)	33	3.41	10	12	22	15
Emotional ∩ neutral						
Caudate nucleus (R)		4.26	22	20	18	65
Fusiform gyrus (R)	37	3.86	34	−56	−10	168
Anterior cingulate gyrus (L)	24	3.44	−20	−2	34	33
Precentral gyrus (L)	6	3.44	−48	−8	22	41
Precentral gyrus (L)	4	3.05	−22	−18	50	10
Culmen		2.85	30	−40	−28	12
Hippocampus (R)	36	2.62	32	−28	−12	10

L: left, R: right, and BA: Brodmann area.

entorhinal cortex for emotional associations while greater activations were found in the posterior parahippocampal gyrus for neutral associations. In addition, amygdala activity had an opposite effect on entorhinal and parahippocampal activity. Third, emotional and neutral associations shared common cerebral areas, comprising the hippocampus and other regions belonging to an attentional network.

As previously mentioned, the behavioral effects of emotion on associative memory are mixed [32]. The attention-narrowing hypothesis and priority-binding theory illustrate the discrepancy observed in the literature. According to the attention-narrowing hypothesis [43], emotions have an impact on memory by selectively modulating attention. Itsuggests that an arousing stimulus would narrow the focus of attention, which directs the attention to this same specific stimulus and therefore more details of this item are retrieved [44]. Indeed, the amount of attention available for surrounding information is decreased, leading to a lack of attentional resources for remembering the association between the concomitant information. Accordingly, associations comprising emotional stimuli are more poorly remembered relative to associations composed of neutral stimuli. Alternately, the priority-binding theory stated by MacKay and colleagues [45, 46] suggests that arousing stimuli evoke emotional
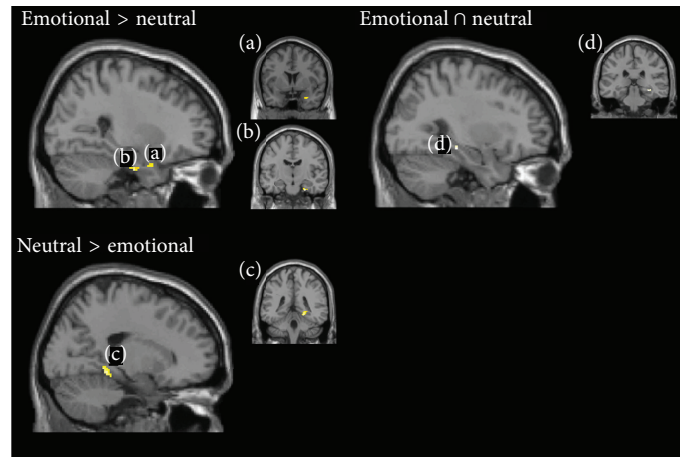
FIGURE 2: Illustration of activations revealed by ROI analyses. Emotional associations induced greater activations than neutral associations in (a) the right amygdala ($x = 30$; $y = 4$; $z = -26$) and (b) the right entorhinal cortex ($x = 26$; $y = -12$; $z = -32$). Conversely, neutral associations induced greater activations in the posterior part of (c) the right parahippocampal gyrus ($x = 24$; $y = -42$; $z = -6$). Emotional and neutral associations both induced activations in (d) the right hippocampus ($x = 32$; $y = -28$; $z = -12$).

reactions that give priority to the binding mechanisms, strengthening the association between emotional stimuli and associated nonemotional stimuli. As a result, associations between emotional information and neutral information are better remembered than associations between solely neutral information.

In our study, participants were more accurate in recognizing emotional associations than neutral associations. Similarly, participants better recalled objects and their location when these were associated with emotional scenes than neutral scenes. These results converge with many previous findings [45–48] and are also consistent with the priority-binding theory [46]. However, our results are in sharp contrast with other studies [12, 33] reporting lower performance for emotional (i.e., negative associations) relative to neutral associations. At the current stage, various factors may explain these discrepancies, such as the fact that results of memory performance may be a function of parametric differences. For instance, the nature of the stimuli (words, pictures, and object), the presentation modality (visual versus auditory) or their duration of presentation (3 s versus 6 s), the length of the delay between study and test (whether the task is administered as a working memory or long-term memory task), the way associative recognition is assessed (intact/rearranged pair recognition test versus cued associative test), and encoding instructions (intentional versus incidental associative encoding) vary among all studies and are important to consider because they alter the manner in which the information is held and how it is retained [49]. Furthermore, the way in which the emotion is induced and manipulated, the valence, and arousal levels of stimuli may also strongly influence the way the information is retained [49]. Further studies are required to examine the contribution of each of these factors. The use of emotional images, for example, compared to words, may potentially induce a greater effect of emotions on associative memory, as they are more elaborated and

might have the ability to evoke stronger emotions. Also, participants were explicitly instructed to encode both items and their association, whereas in other studies, such as that of Touryan et al. [33], they had to remember as much about each stimulus as possible. It has been established that instructions determine encoding and/or retrieval strategies [50, 51].

Within the right MTL, we observed a functional specialization along the longitudinal axis: encoding emotional associations led to enhanced activations in the entorhinal cortex, whereas encoding neutral associations led to enhanced activations in the posterior parahippocampal cortex. Such rostrocaudal dissociation has already been demonstrated with IAPS pictures [27] and words [52]. Our study confirms the role of MTL cortices in the processing of scenes but also examines their respective role. It may thus be hypothesized that the entorhinal cortex is implicated in the processing of emotional scenes, while the posterior parahippocampal cortex is implicated in the processing of neutral scenes. This dissociation may result from amygdala influence, as revealed by the correlation analyses. More precisely, amygdala activity positively covaried with entorhinal activity but negatively covaried with posterior parahippocampal activity. This modulation effect fits well with anatomical connections, given that amygdala shares strong connections with these MTL cortices [53–57].

Previous hypotheses with respect to rostrocaudal dissociation of medial temporal function have been proposed. For instance, a meta-analysis of experimentally induced changes in blood flow ("activation") in positron emission tomography (PET) studies of memory revealed such functionally dissociation between rostral and caudal regions of the hippocampal formation [54]. The authors observed that rostral regions were strongly activated during encoding tasks, while caudal regions were highly activated during retrieval tasks. Lepage and colleagues refer to this general pattern as the HIPER (hippocampal encoding/retrieval) model [54]. Our results are not compatible with this model, given that we observed activations in the right medial temporal lobe only (Lepage

and colleagues pooled activations in both hemispheres) and that clusters were more rostral and caudal when compared to Lepage's report. Our results may also be consistent with another model proposing that the anterior part of the MTL is associated with semantic information and the posterior part with perceptual information [58]. With respect to this model, it has been suggested that greater activity in the entorhinal cortex reflects enhanced semantic and relational processing for emotional stimuli, whereas greater activity in the posterior parahippocampal cortex reflects enhanced perceptual processing of neutral stimuli [27]. However, there is currently no demonstration validating this hypothesis and future research is needed to clarify the specific mechanism involved in processing emotional/semantic and neutral/perceptual information.

In parallel with the functional specialization of MTL cortices, the conjunction analysis revealed that the right hippocampus was activated by both emotional and neutral associations, regardless of amygdala activity. This result is consistent with the proposal that the hippocampus binds distinct elements of an event into an integrated representation [59–62]. Guided by neuroanatomical knowledge reviewed in the Introduction, our results support the view of different associative networks within the MTL. A first associative network comprises MTL cortices. Given that they share strong connections with unimodal and polymodal sensory cortices, MTL cortices may bind multiple sensory information, composing IAPS scenes into an integrated representation [16, 20, 23–26]. This may explain why we observed the same pattern of activations in MTL cortices as Dolcos et al. [27], as both studies used IAPS scenes. Another associative network is composed of the hippocampus, which receives convergent inputs from MTL cortices, and may thus mediate encoding processes associating scenes and concomitant objects.

In addition to the hippocampal activation, greater activations were also induced by both emotional and neutral associations in various areas subserving attentional processing. For instance, common activations were found in the premotor cortex, the posterior part of the fusiform gyrus, and the dorsal part of the anterior cingulate gyrus. This pattern of activations has been consistently found in tasks demanding spatial attention [63–65]. Finally, activations in the caudate nucleus may be related to ocular movements essential to focusing spatial attention [66, 67]. Spatial attention is needed to establish associations between multiple stimuli and to maintain these associations in memory [68–70].

One limitation of this study is that interactions between amygdala activity and hippocampal and MTL cortices activity rely on correlation analyses, which do not indicate the direction of these interactions. Further analyses examining effective connectivity should be performed to overcome this limitation. Another limitation of this study is the lack of a condition assessing the processing of individual stimuli. At the current level, it remains difficult to straightforwardly conclude that the results were driven by associative processes per se, rather than by emotions. Lastly, the subsequent memory effect, which represents the difference during encoding between brain activity for items that are subsequently remembered and brain activity for items that are subsequently forgotten [27], could not be evaluated. This limits the understanding of neural mechanisms that predict encoding success depending on the emotional valence of associations. A comparison between successfully and unsuccessfully encoded associations was not possible because of an insufficient number of "miss" trials by most participants. Future studies would benefit from a modified design that might induce a greater number of misses by participants. For instance, the delay between encoding and recognition sessions might be increased, as well as the number of studied associations. All of these parameters would be expected to increase the number of forgotten associations, thus allowing the estimation of the subsequent memory effect. Future studies may also benefit from scanning both the encoding and recognition sessions, in order to investigate effects of emotion on retrieval processes.

With respect to previously published data, our results confirm that the hippocampus, in concert with attentional network regions, participates in the encoding of associations in memory. Our results also extend past findings by demonstrating that emotions are associated with the performance improvement of associative memory. This potentiation may result from enhanced activity in the right entorhinal cortex by the right amygdala. Future research may consider functional connections among these cerebral structures to elucidate the neural mechanisms assuming their respective functions.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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