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An fMRI Study of the Activation of the Hippocampus by Emotional Memory

Matthew Bellace,[1] J. Michael Williams,[1] Feroze B. Mohamed,[2] and Scott H. Faro[2]

AQ2 [1]*Department of Psychology, Drexel University, Philadelphia, Pennsylvania, USA*
[2]*Department of Radiology, Functional Brain Imaging Laboratory, Temple University School of Medicine, Philadelphia, Pennsylvania, USA*

ABSTRACT

The current study examined the role of the hippocampus in emotional memory encoding using functional magnetic resonance imaging (fMRI). The present study examined the activation patterns of 12 healthy participants who were associated with memory for words and pictures with moderately high emotional tone. Results revealed significant activation in the temporal and frontal lobes for emotional and neutral stimuli. There was greater activation in the left hippocampus for emotional words and the right hippocampus for emotional pictures. However, a separate analysis of gender suggested that the emotional responses of the women accounted for the activation of the hippocampus; men did not have a pattern of hippocampus activation consistent with the type of stimuli. These findings have important implications for the design of a clinical memory assessment using fMRI.

AQ3 **KEYWORDS:**

The central hypothesis of this study was that consistent activation of the hippocampus will occur when the subjects are given stimuli to remember that have significant emotional tone. Although numerous studies have demonstrated a clear role for the hippocampus in memory, it is also an important part of the limbic system and has significant association with the amygdala, a structure implicated as an emotion-mediating structure in numerous studies [1, 2]. The hippocampus represents a major interface between the sensory systems in the cerebral cortex and the emotion-mediating limbic system within the medial temporal lobe [3]. As a result, it may only become sufficiently active to produce reliable functional magnetic resonance imaging (fMRI) AQ4 BOLD responses when the stimuli are associated with emotion and mood states. It may be the case that the hippocampal system encodes the emotional tone of sensory experiences so that they may be remembered and later recalled in an association with an emotional valence.

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AQ5 Address correspondence to J. Michael Williams, PhD, Department of Psychology, Drexel University, 3141 Chestnut Street, Philadelphia, PA 19104, USA. E-mail: jw37@drexel.edu

There is a practical aspect to this investigation in addition to testing hypotheses regarding emotion and the hippocampus. The development of fMRI as a clinical examination of cognition and memory requires the invention and testing of methods that systematically activate specific parts of the brain that mediate specific cognitive functions. For example, temporal lobe epilepsy is associated with specific pathology of the hippocampus, and this structure may be removed to reduce the seizures [4, 5]. The fMRI method has the potential for identifying the functional status of each hippocampus. This would be very helpful in deciding whether a hippocampus can be removed without causing significant memory disorder. However, the fMRI protocol must be tested for valid and reliable activation of the structure. Discovering the set of stimuli that consistently activate the hippocampus is the first necessary step in establishing the validity of the clinical examination [6].

Recent studies of gender and emotion using functional neuroimaging suggest that men and women have different patterns of activation associated with emotional stimuli. Although a consensus has not yet emerged, the findings suggest that women have stronger emotional reactions to positive and negative stimuli, greater overall brain activation, and more activation of the limbic system [7, 8]. Since the present study examined similar emotional stimuli in a memory paradigm, we hypothesize there will be similar patterns present among men and women in response to the stimuli. The hippocampus and other parts of the limbic system of men and women should be more active when exposed to emotional stimuli, but women should have more limbic system areas involved, or more consistent activation when compared to men.

Numerous studies of patients receiving unilateral hippocampal resections for the treatment of seizure disorder and patients who sustained naturally occurring unilateral lesions of the hippocampus indicate that memory processes are lateralized according to content. Left-sided lesions interfere with verbal memory processes, whereas right-sided lesions interfere with visual-spatial memory processes [9–11]. As a result, the current study presented healthy volunteers with verbal and visual emotional information in an attempt to test whether this would result in greater activation of the hippocampus. We examined the effects of emotional and neutral stimuli, both verbal and visual, on the hippocampus and related memory structures in healthy participants. We hypothesized that words with emotional content would activate the left hippocampus more than neutral words, whereas pictures with emotional content would activate the hippocampus, bilaterally, greater than neutral images.

MATERIALS AND METHODS

Research Participants

Participants included 12 adult volunteers, seven women and five men, with no history of neurological illness or memory disorder. All participants were right-handed, native English speakers who ranged in age from 26 to 37 years. They were community volunteers recruited through local media advertisement. All subjects gave informed consent consistent with the requirements of the institutional review board.

Inclusion/Exclusion Criteria

All participants who responded to the advertisements were given a self-report handedness examination. Only right-handed individuals were included. A semistructured interview was used to screen participants for personal and familial medical history and symptoms, including neurological, psychiatric, and substance abuse. None of the participants reported past or present symptoms of a major psychiatric disorder or neurological disorder, such as a head injury with loss of consciousness for greater than 5 min. None of the participants were taking psychotrophic, cardiovascular, or other medications that might influence brain function or cerebral blood flow.

Procedure

The participants wore headphones connected to a Macintosh laptop computer. The computer contained programs written by the authors for playing the sound samples and displaying images. Images were presented through goggles containing a video display.

During scanning, participants were presented with 80 items, 40 neutral and emotional words, and 40 neutral and emotional pictures. The item sets were presented three times, at the rate of one item every 2 s during the active phase of the scanning. The words were selected from over 1,000 standardized words from the Affective Norms for English Words [12]. The emotional words included “abuse,” “cruel,” and “terrible,” and the neutral words included, “bus,” “book,” and “table.” Normative ratings for all stimuli were available on a 9-point scale for the dimensions of emotional valence (1, most unpleasant, to 9, most pleasant) and arousal (1, calm/dull, to 9, most arousing or intense). The emotional words were selected on the basis of their normative ratings of valence and arousal, which ranged from 1.0 to 3.0 for valence and 5.5 to 9.0 for arousal. The pictures were selected from over 750 images in the Affective Norms for the International Affective Picture Series [13]. The emotional pictures included scenes of people crying, natural disasters, and threatening animals, and the neutral pictures included pictures of people shopping, a cow grazing, and landscapes. The emotional pictures were selected on the basis of their normative ratings of valence and arousal, which ranged from 1.5 to 4.5 for valence and 5.5 to 7.5 for arousal.

Stimuli were chosen associated with negative emotions of fear and anxiety because a previous study examining the activation patterns associated with pleasant and unpleasant emotional encoding found that unpleasant emotional pictures were distinguished from pleasant pictures because they activated the left parahippocampal gyrus and hippocampus, whereas pleasant emotional pictures activated the medial prefrontal cortex, thalamus, hypothalamus, and midbrain but not the hippocampus [14].

Prior to the scanning, a separate group of 30 volunteers rated the emotional words and pictures on scales for the dimensions of emotional valence (1, most unpleasant, and 9, most pleasant) and arousal (1, calm/dull, and 9, most arousing or intense). There were no significant differences between the normative and volunteer ratings for valence and arousal for all types of word and picture stimuli. Arousal and valence ratings were correlated at moderate high levels ($r = -0.81$).

The images used for fMRI contrasts were acquired using a 1.5 Tesla Siemens Vision whole body scanner capable of high-speed echo planar imaging (EPI). Participants were placed in the supine position in the scanner. Their heads were restrained using cushions to reduce motion artifacts. Whole brain scans were conducted with 26 contiguous no-gap 5-mm axial oblique image planes to cover the cerebrum. Slice planes were positioned and aligned parallel to an imaginary line passing through the anterior–posterior commissures (AC-PC line). The orientation relative to the AC-PC line was selected to assist a spatial transformation of the volumes into a standard anatomical space.

Anatomical references were acquired with high-resolution T1-weighted images. The imaging parameters of the spin echo sequence used to acquire the images were as follows: TR = 500 ms, TE = 14 ms, matrix size = 256 pixels, FOV = 22 × 22 cm, flip angle 90°, slice thickness = 5 mm, NEX = 1, and in-plane resolution = 0.86 × 0.86 mm. The T2* weighted images for fMRI contrasts were collected with an EPI free induction decay (EPI-FID) single-shot pulse sequence. The positions of the images were identical to those of the anatomical reference images. EPI-FID image parameters were as follows: TR = 4000 ms, TE = 54 ms, matrix size = 128 pixels, FOV = 22 × 22 cm, flip angle = 90°, slice thickness = 5 mm, NEX = 1, bandwidth = 1470 Hz/pixel, and in-plane resolution = 1.72 × 1.72 mm.

Participants were placed in the scanner and instructed to remain as still as possible. The participants were then instructed to keep their eyes open during the picture presentation and their eyes closed during the word presentation. Participants were asked to remember each of the 20 words. For verbal encoding, participants listened to items at a rate of one item every 2 s with a 10-s intertrial interval. For visual encoding, participants were given a similar paradigm and asked to remember each of the 20 pictures. There were 20 each of emotional words, neutral words, emotional pictures, and neutral pictures. Items were presented three times during the active phase of the scanning. The participants were also told that they would be tested for their memory after the scanning. Approximately 10-min after the scan, participants completed a recognition memory test in which they were asked to identify all of the words presented in the scanner (targets) and 20 new words (distracters). The testing served to motivate the subjects to pay attention while they were in the scanner, and it also constituted a memory performance measure.

The general design for all four series was a conventional on–off boxcar design [15]. The sequence consisted of 20 s of rest followed by 20 s of the activation condition. Scans of the whole brain were acquired every 4 s. The activation sequence alternated six times and resulted in a set of 60 whole brain volumes.

fMRI Data Analyses

Functional images were analyzed using statistical parametrical map (SPM) [16]. Region of interest (ROI) analyses were conducted using the WFU Pick Atlas [17]. This software allowed for the generation of ROI masks based on the Talairach database [18]. A slice timing correction was performed to compensate for delays associated with acquisition time differences between slices during the sequential imaging. In the second step, a three-dimensional automated image registration routine (six-parameter ridged body, sinc interpolation, second-order adjustment for movement) was applied to the volumes to realign them with the first volume of the series used as a spatial reference. All functional and anatomical volumes were then transformed into a standard anatomical space [18] using the T2 EPI template and the SPM normalization procedure [19]. This procedure used a sinc interpolation algorithm to account for brain size and position with a 12 parameter affine transformation, followed by a series of nonlinear basic function transformations and nonlinear basic functions for the *x*, *y*, and z directions, respectively, with 12 nonlinear iterations to correct for morphological differences between the template and the given brain volume. Next, all volumes underwent spatial smoothing by convolution with a Gaussian kernel of 3.44 × 3.44 × 10 mm^3 full width half maximum, two times the voxel size, to increase the signal-to-noise ratio and account for residual intersession differences [20].

To determine the spatial extent of the recruited neurons and subsequently calculate the BOLD signal, SPM general linear model procedures were used to identify the voxels associated with the auditory and visual stimulation. This was achieved by administering a series of voxel-based *t* tests and creating SPMs, a visual representation of the statistically significant BOLD contrast responses. Then the quantitative analyses of changes in the activation extent, and the magnetic resonance signal was carried out using a set of these maps produced for each participant's trial. The criteria chosen for all images in the cluster analyses were at least $p < .05$; the ROI analysis of the hippocampus attained the $p < .01$ criterion. These were corrected for family-wise error. The initial analyses of the whole brain were also set to include clusters with a minimum extent of five voxels. The ROI analyses also included the examination of single voxels.

The initial analysis of emotional versus neutral words and pictures was an indirect comparison. The data from the active condition, words or pictures, were compared to a rest condition. The rest condition for pictures consisted of a blank, white screen with a fixation point.

The rest condition for words consisted of the subject lying quietly in the scanner with eyes closed. The direct comparison of emotional versus neutral stimuli used the same data, but the active condition consisted of emotional stimuli directly compared to the neutral stimuli. Removing the initial rest condition files, replacing them with neutral condition files and reanalyzing the data, allowed us to perform the direct comparison. In total, there were 30 volumes of rest condition data replaced by 30 volumes of neutral condition data. The data were realigned, normalized and smoothed, and analyzed according to the procedure described above.

RESULTS

Behavioral Results

A one-way analysis of variance was conducted to evaluate the relationship between stimulus type, emotionality, and gender on recall of information. The analysis indicated a significant main effect for stimulus type. Picture recall was superior to words, $F\ (1, 48) = 7.17$, $p < .05$. In addition, there was a main effect for emotionality. Emotional item recall was superior to neutral item recall, $F\ (1, 4) = 7.31$, $p < .05$. There was a significant interaction between emotionality and stimulus type, $F\ (1, 4) = 9.09$, $p < .05$. Pictures were recalled significantly better than words [$t\ (1, 46) = 7.59$, $p < .05$], and emotional words were recalled significantly better than nonemotional words [$t\ (1, 48) = 3.13$, $p < .05$]. There were no gender differences in memory recall [$t\ (1, 46) = 0.75$, $p < .05$]. Overall, participants remembered emotional items (87%) significantly better than nonemotional items (77%). Emotional pictures (96%) and neutral pictures (97%) were significantly better recalled than emotional words (79%) and neutral words (60%).

Group BOLD Responses

In the direct comparison of emotional versus neutral pictures, significant activation was seen in the frontal, temporal, parietal, and occipital lobes. Extensive occipital lobe activations were found in the two picture conditions. Frontal lobe activation was found in the left middle frontal gyrus, inferior frontal gyrus, corpus callosum, and subcortical white matter. Parietal lobe activation was found in the left cingulated gyrus, superior parietal lobe, and left and right precuneus. A specific ROI analysis revealed activation of the right hippocampus.

In a direct comparison of emotional versus neutral words, significant BOLD contrasts were observed in fewer areas than those associated with pictures. Frontal lobe activation was seen in the left cingulate gyrus, right cingulate gyrus, left and right anterior cingulate gyrus, left and right medial frontal gyrus, left inferior frontal gyrus, and subcortical white matter. Parietal lobe activation was seen in the left inferior parietal lobe. Temporal lobe activation was seen in the left insula. Specific ROI analysis of the hippocampus revealed activation in the left hippocampus, parahippocampal gyrus, amygdala, and uncus.

Gender-Specific Analyses

The gender analyses showed significant activation across several brain regions for pictures and words (Figure 1). The ROI analysis of the hippocampus in women was consistent with the ROI analysis of the men and women combined (Table 1). In the initial analysis, women showed activation in the right hippocampus during encoding emotional pictures, but the activation did not attain the probability threshold ($p < .05$). When the direct comparison was performed using neutral stimuli as the rest condition, there was significant activation ($p < .01$) for women in the right hippocampus for emotional pictures, as well as significant activation ($p < .01$) in the left hippocampus for emotional words. There was also significant activation ($p < .01$) in the left amygdala for women when comparing emotional versus neutral words. There were no significant activations of the

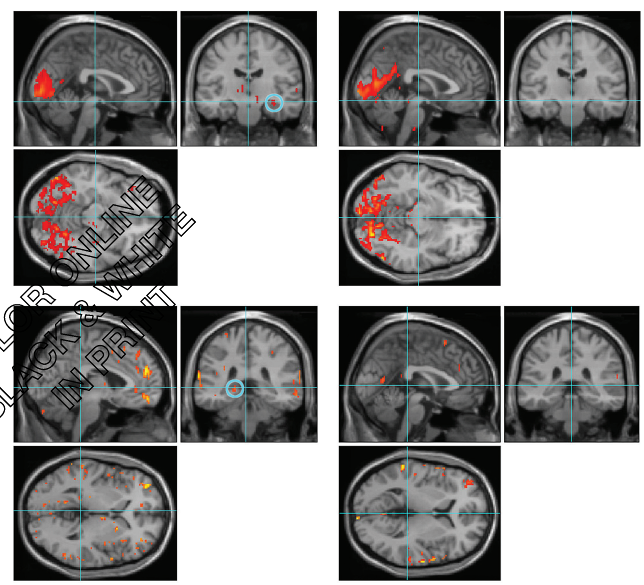

FIGURE 1. Activation patterns of men and women associated with emotional words and pictures. The responses to picture stimuli are at the top and words are below; women are depicted on the left and men on the right. The circled areas in the coronal sections indicate activations of the hippocampus. Women had activation of the left hippocampus for emotional words and activation of the right hippocampus for emotional pictures. The hippocampi were not active in either condition among the men.

TABLE 1. Gender analyses contrasting neutral versus emotional stimuli for specific regions of the hippocampus and amygdala

Structure	*p* value	Coordinates	*T*-score
Women—Pictures			
R hippocampus	.01	32, −18, −14	2.51
L hippocampus	NS		
R amygdala	NS		
L amygdala	NS		
Women—Words			
R hippocampus	NS		
L hippocampus	.01	−26, −38, −4	5.49
L hippocampus	.01	−28, −38, 0	2.88
R amygdale	NS		
L amygdala	.01	−20, −8, −18	4.67
L amygdala, BA 34	.01	−18, −8, −16	4.58
L amygdala	.01	−26, −6, 20	3.69
L amygdala	.01	−22, −6, −22	3.67
L amygdala	.01	−18, −6, −20	3.56
Men—Pictures & Words			
R hippocampus	NS		
L hippocampus	NS		
R amygdala	NS		
L amygdala	NS		

NS: Not significant.

hippocampi for the men in the picture or word conditions (Figure 1).

DISCUSSION

The present study used functional MRI to examine the differences in hippocampal activation during the memory encoding of emotional versus neutral information. Several brain areas, including the frontal, parietal, and temporal lobes, showed activity during these tasks. When each condition was examined using conventional rest conditions, there was no significant hippocampal activation for pictures or words. When emotional versus neutral pictures were directly compared, the right hippocampus showed greater activation for emotional pictures. There was significantly more left hippocampus and parahippocampal gyrus activation for emotional words. In addition, the study found activation in the left amygdala for emotional words. The gender analysis showed a similar pattern of activation for females but not for males.

Prior studies suggested that pictures, both emotional and nonemotional, produced bilateral activation of the hippocampus [21–26]. We not only hypothesized similar findings, but also that emotional pictures would produce greater and more consistent hippocampal activation compared to neutral pictures. The direct comparison revealed greater activation in the right hippocampus for emotional pictures. This finding supported the notion that the hippocampus plays a role in emotional memory processing. These results also support a lateralized pattern that is consistent with many lesion studies of brain function and memory [4, 27]. This study supports the hypothesis that verbal memory is mediated by the left hippocampus, and visual-spatial memory is mediated by the right hippocampus. Many previous studies of patients with brain lesions, including epilepsy surgery patients, provided inconsistent support for this hypothesis [4]. The uncertainties in the lateralized pattern of deficit among epilepsy patients and the rarity of other patients with clear acquired lesions in the area of the left or right hippocampus contributed to this uncertainty [28].

A lateralized activation pattern was only revealed when emotional and neutral stimuli were directly compared. This may have been the result of activation caused by the rest condition. Between each stimuli presentation, participants in the picture memory condition were shown a blank, white screen and asked simply to keep their eyes open and prepare for the next image. When the data were initially analyzed, each active condition was compared to the blank screen rest condition. A recent study suggested that these types of rest periods, especially when the activation is a memory paradigm, result in activation of the medial temporal lobe, including the hippocampus and parahippocampal cortex [29]. It may be impossible for subjects inhibit rehearsing stimuli during the rest period of a memory task. Thus, our rest task may have produced hippocampal activation, offsetting the activity produced by the emotional images. This would also explain why the neutral images did not produce hippocampal activation. When we replaced the data from the rest condition data with data collected with the active phase of the neutral pictures condition, we found significant hippocampal activation.

On the basis of the previous research, we hypothesized that women would have greater bilateral hippocampal activation than men to emotional words and pictures [25]. Using the direct comparison analysis, women demonstrated significant activation in the right hippocampus for emotional pictures and the left hippocampus for emotional words. Men did not demonstrate significant hippocampal activation in either condition. Since the present sample sizes of men and women were small, it is important to consider that the gender differences cannot be reasonably generalized without replication of this study with larger samples.

One explanation for the gender differences in encoding affective experiences is the cognitive-style hypothesis. This hypothesis states that there are gender differences in the amount of detail encoded for emotional experiences, which serves to improve memory recall. Thus, women have better memory for emotional information because they experience life events with more emotional intensity [25, 30].

Additional Activation During Encoding

Emotional pictures and words also showed activation in the middle and inferior frontal gyrus. Activation in this area is consistent with anatomical evidence suggesting the middle and inferior frontal gyri include afferents containing sensory information conveyed to the hippocampus [31], and that the pathway is important for emotional responses. The right middle frontal gyrus has been shown to be active during emotion-related events [14, 32]. Prohovnik and colleagues [32] used emotional AQ8 faces from the IAPS to evoke emotional responses and asked participants to indicate at the onset of an emotional reaction. Significant activation was detected in the middle frontal gyrus and hippocampus using this paradigm.

Emotional picture encoding also revealed extensive activation of the precuneus. This parietal lobe structure has been shown to be involved in memory-related imagery and is believed to play a key role in the neural substrate of visual imagery in memory recall [33]. Participants in the current study were most likely utilizing this process to retain the visual information.

Analyses of emotional words showed activation in the medial frontal gyrus and superior temporal gyrus, both areas reportedly involved in verbal processing [32, 34, 35]. Jancke et al. [34] used fMRI to identify cortical regions involved in emotional dichotic listening. The superior temporal region was activated when the participants focused on words with emotional tone.

IMPLICATIONS FOR A CLINICAL fMRI EXAMINATION

The study has implications for the development of a standardized fMRI clinical memory examination. First, the results are encouraging in suggesting that lateralized hippocampal activation is possible. The activations associated with verbal memory in the left hippocampus and visual-spatial memories in the right hippocampus suggest that fMRI can be used to ascertain which hippocampus is dysfunctional in disorders such as temporal lobe epilepsy and other illnesses associated with memory disorder [4, 36, 37]. The results also suggest that the stimuli used in the fMRI protocol can serve as a memory performance measure in similar fashion to the memory tests administered in the neuropsychological evaluation.

The gender differences demonstrated in this study represent an interesting finding in the study of gender but represent a major practical problem for the clinical assessment of memory using fMRI. At this point in time, this is the only study of protocols designed to assess memory and hippocampal function that has examined gender differences. Since numerous studies of gender and memory have not found a difference between men and women in memory ability, a gender difference in emotional responses probably did not occur to previous investigators as a factor to examine in their studies.

The most likely solution to this problem will come from developing independent sets of items that produce a sufficient emotional response for men and women. These must be calibrated to elicit hippocampal activation without being so provocative that they cause extreme reactions in the subjects.

The stimulus types also differ in their emotional tone and should be calibrated better for these differences. Although the visual depiction of something emotional, such as a murder, may generate an emotional response, hearing the word “murder” recited over headphones stimulates a much lower emotional reaction. In addition, the emotional tone of language is conveyed by the speech intonation and not only by language content. Hearing the word “murder” properly inflected and emphasized likely generates a stronger emotional response than hearing the word in a calm tone. The standardized words are specified to be presented in a neutral, calm tone. Future studies should examine this factor in increasing the emotional tone of the verbal stimuli.

Another stimulus set that has not been examined in this context is emotionally provocative environmental sounds. Sounds of glass breaking, screams, animals growling, and similar sounds should produce a nonverbal emotional response that is difficult to inhibit. If the subjects are encouraged to name the sound, it may also work as a verbal stimulus and activate the left hippocampus. A recent study of environmental sounds using fMRI revealed that environmental sounds activated the areas of the left temporal lobe associated with semantic knowledge [38]. This may solve the problem of lower emotional valiance associated with words alone.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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REFERENCES

1. Murray E. The amygdala, reward and emotion. Trends Cogn Sci. 2007;11:489–97. AQ10
2. Phelps EA. Human emotion and memory: interactions of the amygdala and hippocampal complex. Curr Opin Neurobiol. 2004;14:198–202.
3. Traub R, Miles R. Neural networks of the hippocampus. New York: Cambridge University Press; 1991.
4. Lee T, Yip J, Jones-Gotman M. Memory deficits after resection from left or right anterior temporal lobe in humans: a meta-analytic review. Epilepsia. 2004;43:283–91.
5. Detre J, Maccotta L, King D, et al. Functional MRI lateralization of memory in temporal lobe epilepsy. Neurology. 1998;50:926–32. AQ11

6. Powell H, Koepp M, Richardson M, Symms M, Thompson P, Duncan J. The application of functional MRI of memory in temporal lobe epilepsy: a clinical review. Epilepsia. 2004;45:855–63.
7. Lang P, Bradley M, Fitzsimmons J, Cuthbert B, Scott J, Moulder B, Nangia V. Emotional arousal and activation of the visual cortex: an fMRI analysis. Psychophysiology. 1998;30:261–73.
8. Koch K, Pauly K, Kellerman T, Seiferth N, Reske M, Backes V, Stoker T, Shah N, Amunts K, Kircher T, Schneider F, Habel U. Gender differences in the cognitive control of emotion: an fMRI study. Neuropsychologia. 2007;45:2744–54.
9. Milner B. Visual recognition and recall after right temporal-lobe excision in man. Neuropsychologia. 1968;6:191–209.
10. Milner B. Disorders of learning and memory after temporal lobe lesions in man. Clin Neurosurg. 1972;19:421–66.
11. Golby AJ, Poldrack RA, Brewer JB, Spencer D, Desmond JE, Aron AP. Material-specific lateralization in the medial temporal lobe and prefrontal cortex during memory encoding. Brain. 2001;124:1841–54.
12. Bradley M, Lang P. Affective norms for English words: ANEW. Gainesville: NIMH Center for the Study of Emotion and Attention, University of Florida; 1999.
13. Lang P, Greenwald M, Bradley M, Hamm A. Looking at pictures: affective, facial, visceral, and behavioral reactions. Psychophysiology. 1993;25:199–210.
14. Lane R, Reiman E, Bradley M, Lang P, Ahern G, Davidson R, Schwartz G. Neuroanatomical correlates of pleasant and unpleasant emotion. Neuropsychologia. 1997;35(11):1437–44.
15. Huettel S, Song A, McCarthy G. Functional magnetic resonance imaging. Sunderland, MA: Sinauer; 2004.
16. Friston K, Ashburner J, Kiebel S, Nichols T, Penny W. Statistical parameter mapping. New York: Academic Press; 2007.
17. Maldjian J, Laurienti P, Kraft R, Burdette J. An automated method for neuroanatomic and cytoarchitechtonic atlas-based interrogation of fMRI data sets. Neuroimage. 1993;19(3):1233–9.
18. Talairach J, Tournoux P. Co-planar stereotaxic atlas of the human brain: 3-dimensional proportional system: an approach to cerebral imaging. New York: Thieme; 1988.
19. Ashburner J, Friston K. Nonlinear spatial normalization using basis functions. Hum Brain Mapp. 1999;7(4):254–66.
20. Mohamed F, Pinus A, Faro S, Patel D, Tracy J. BOLD fMRI of the visual cortex: quantitative responses measured with a graded stimulus at 1.5 Tesla. J Magn Reson Imaging. 2002;16:128–36.
21. Stern C, Corkin S, Gonzalez G, Guimares A, Baker J, Jennings P, Carr C, Sugiura R, Vedantham V, Rosen B. The hippocampal formation participates in novel picture encoding: evidence from functional magnetic resonance imaging. Proc Natl Acad Sci. 1996;93:8660–5.
22. Gabrieli J, Brewer J, Desmond J, et al. Separate neural basis of two fundamental memory processes in the human medial temporal lobe. Science. 1997;276(5310):264–6.
23. Kesinger E, Corkin S. Memory enhancement for emotional words: are emotional words more vividly remembered than neutral words? Mem Cognit. 2003;31:1169–80.
24. Richardson M, Strange B, Dolan R. Encoding of emotional memories depends on amygdala and hippocampus and their interactions. Nat Neurosci. 2004;7(3):278–85.
25. Canli T, Desmond J, Zhao Z, Gabrieli J. Sex differences in the neural basis of emotional memories. Proc Natl Acad Sci. 99 2002;16(10789–94).
26. Wright C, Martis B, Shin L, Fischer H, Rauch S. Enhanced amygdala responses to emotional versus neutral schematic facial expressions. Neuroreport. 2002;13(6):785–90.
27. Ojemann G, Dodrill C. Verbal memory deficits after left temporal lobectomy for epilepsy. Mechanism and intraoperative prediction. J Neurosurg. 1985;62(1):101–7.
28. Katz A, Awad I, Kong A, Chelune G. Extent of resection in temporal lobectomy for epilepsy, II: memory changes and neurologic complications. Epilepsia. 1989;30:763–71.
29. Stark C, Squire L. When zero is not zero: the problem of ambiguous baseline conditions in fMRI. Hippocampus. 2001;10:329–37.
30. Seidlitz L, Diener E. Sex differences in the recall of affective experiences. J Pers Soc Psychol. 1998;74(1):262–71. **AQ12**
31. Hanaway J, Woolsey T, Gado M, Roberts M. The brain atlas: a visual guide to the human central nervous system. Bethesda, MD: Fitzgerald Science Press; 1998.
32. Prohovnik I, Skudlarski P, Fulbright R, Gore J, Wexler B. Functional MRI changes before and after onset of reported emotions. Psychiatry Res. 2004;132(3):239–50.
33. Fletcher P, Frith C, Baker S, et al. The mind's eye–precuneus activation in memory-related imagery. Neuroimage 1995;2:195–200.
34. Jancke L, Buchanan T, Lutz K, Shah N. Focused and nonfocused attention in verbal and emotional dichotic listening: an fMRI study. Brain Lang. 2001;78:349–63. **AQ13**
35. Ochsner K, Knierim K, Ludlow D, Hanelin J, Ramachandran T, Glover G, Mackey S. Reflecting upon feelings: an fMRI study of neural systems supporting the attribution of emotion to self and others. J Cogn Neurosci. 2004;16: 1746–76.
36. Pouratian N, Bookheimer SY. Clinical challenges of fMRl. In: Faro S, Mohamed F, editors. Functional MRI: basic principles and clinical applications. New York: Springer-Verlag; 2006. p. 99–126.
37. McDonald BC, Saykin AJ, Williams JM, Bassam AA. fMRI Wada test: prospects for presurgical mapping of language and memory. In: Faro S, Mohamed F, editors. Functional MRI: basic principles and clinical applications. New York: Springer-Verlag; 2006. p. 278–314.
38. Lewis J, Wightman F, Brefczynski J, Phinney R, Binder J, DeYoe E. Human brain regions involved in recognizing environmental sounds. Cereb Cortex. 2004;14(9):1008–21.