Modulation of prefrontal cortex activation by emotional words in recognition memory

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We employed event-related functional magnetic resonance imaging to examine emotional valence effects on verbal recognition memory. Using a yes/no recognition task, we focussed on prefrontal cortex responses to positive, negative and neutral words. Behavioral data confirmed enhanced processing of emotional items and functional magnetic resonance imaging revealed different subregions in the prefrontal cortex supporting retrieval of emotional words. Activations in the right mid-ventrolateral prefrontal cortex correlated with the correct retrieval conditions for negative words, whereas the right ventromedial and orbitofrontal prefrontal cortex showed enhanced responses to positive words. Additionally, differences between old and new items mainly affected bilateral orbitofrontal regions when processing positive words. The results are discussed in terms of higher monitoring demands owing to familiarity-based recognition bias for emotional words. *NeuroReport* 17:1037–1041 © 2006 Lippincott Williams & Wilkins.

Keywords: emotional valence, functional magnetic resonance imaging, negative words, neuroimaging, neutral, prefrontal cortex, positive, recognition memory

Introduction

Recognition memory is influenced by the affective or emotional valence of the test items. Whereas other imaging studies focus on basic processes underlying episodic retrieval of verbal information [1], the present study was designed to investigate the role of emotional valence for visual word processing in the prefrontal cortex (PFC). In particular, we examined memory performance for positively and negatively valenced words in a yes/no recognition task. Besides the role of medial temporal lobe during episodic memory retrieval [2], PFC is thought to subserve monitoring processes related to familiarity-based judgements at time of retrieval [1]. Orbitofrontal PFC activity is proposed to reflect retrieval success and bilateral mid-dorsolateral PFC was shown to be related to monitoring processes such as evaluation of the retrieved information [3]. If recognition judgements are influenced by the higher familiarity of emotional items [4], one can expect dorsolateral PFC activity to be modulated by emotional valence in the present study. In an event-related potentials (ERPs) study, Windmann and Kutas [5] related an early prefrontal negativity for unstudied negative items judged as 'old' to an automatic bias for emotional material, possibly reflecting more liberal decision criteria for verifying retrieved information. So far, only a few neuroimaging studies attempt to examine the effects of emotional valence on recognition memory for single words, mainly focussing on emotional context effects in sentence processing [6] or pictorial backgrounds [7,8]. According to these studies, orbitofrontal PFC activation was observed for positive emotional contexts, suggesting a role in combination with hippocampus and anterior cingulate gyrus in a network subserving the processing of memories associated with positive affect [8,9]. In contrast, left ventrolateral PFC involvement was found in retrieving items from negative contexts [6,8].

To our knowledge, no other functional magnetic resonance imaging (fMRI) study has examined the contribution of emotional valence to the correct retrieval of items in a standard yes/no recognition task with positive, neutral and negative words. Using an event-related design, we report that the differential effect emotional valence takes on the difference between successful and unsuccessful retrieval of old items. Additionally, we investigated the influence of emotional valence on the so-called 'old/new' effect (the relation between correctly classified old items and correctly rejected new items), previously associated with successful item retrieval mechanisms [5]. Both behavioural and ERP data suggest a modulation of the 'old/new' effect for negative as compared with neutral items. A diminished 'old/new' effect was found for negative items at a late time window on right prefrontal electrodes [4]. On the basis of these results for contextual information, we expected to observe modulated 'old/new' effects for negative items in right PFC in the present study. As this effect is supposed to rely on postretrieval processes, similar neural correlates for positive items should be observed in right PFC.

Methods

Subjects

Twenty right-handed native German-speaking participants (12 females, aged between 20 and 36 years, Ø 25.8) with no history of neurological or psychiatric illness were employed in the study after giving written informed consent in accordance with guidelines set by the local ethics committee.

Procedure

Immediately after solving a lexical decision task in the scanner [9], participants were scanned during two sessions (study and test phases of the recognition memory task), separated by a short (~5 min) verbal filler task (data not reported here). Target ('old') stimuli consisted of the 150 German nouns (50 positive, 50 neutral and 50 negative) that had already been presented during the lexical decision task. Additionally, 150 nouns were selected as 'new' distractors. Targets and distractors were selected from the Berlin Affective Word List [10] and did not differ significantly across emotional valence lists on word frequency (M=20.92/1Mio), word length (5–8 letters), frequency of orthographic neighbours and absolute emotionality ratings (all $P>0.79$, see also [9]). The study phase consisted of a random presentation of the target words centred on a back-projection screen for 1 s, replaced by a fixation cross with a jittered interstimulus interval of 1.2 s ($\pm$0.2 s). Participants were instructed to memorize the presented words without any button press. During the test phase, participants were asked to decide whether a presented word was 'old' or 'new' to them. Every test trial was initiated by the presentation of a fixation cross in the centre of the screen, randomly followed by either one of 150 'old' target words or 150 'new' distractor words displayed for 0.5 s. After this, a fixation cross was displayed until the next appearance of a stimulus (interstimulus interval jittered around 2.8$\pm$0.2 s). Before the next stimulus presentation, participants had to make an old/new judgement by pressing one of two response buttons with either index or middle finger of the right hand. Reaction times and error rates were recorded according to standard recognition memory procedures. Thus, correctly recognized 'old' words were classified as Hits, unrecognized 'old' words as Misses, correctly classified 'new' items as correct rejections (CRs), and new items judged 'old' as false alarms.

Imaging and image processing

fMRI data were acquired from a 3 T Siemens Magnetom Allegra scanner (Siemens, Erlangen, Germany) using a whole head, local gradient coil. A single-shot echoplanar imaging sequence was used incorporating the following parameters: echo time 30 ms, repetition time 2.5 s, 64×64 mosaic images with a field of view of 192 mm, field angle 90°. Echoplanar imaging comprised 38 slices covering the whole brain taken every 3 mm with no interslice gap.

Functional images were slice time corrected, realigned, normalized spatially to the Montreal Neurological Institute template and smoothed with an 8 mm full width at half-maximum Gaussian kernel using statistical parametric map 2 [11]. The first two images of each session were discarded to allow for T1 equilibration effects.

Statistical analysis

At the first level, nine event types were modelled: three events describing each emotional category of correctly judged old items (Hits), three events for the correctly rejected new items (CR), two events comprising Misses and false alarms, and a rest category containing missing responses and response latency outliers. Data were high-pass filtered (1/128 Hz), corrected for intrinsic autocorrelations and convolved with a standard HRF and its temporal derivative. Contrasts of interest for the three valence categories were then entered into a random effects analysis of variance to provide inferences on the population level. Reported results are based on the canonical HRF alone. To reveal emotion-specific effects, conjunction analyses were performed following a procedure described by Dolcos *et al.* [12]. Conjunction analysis is used here to identify several activations jointly significant in a series of subtraction contrasts [13]. For instance, the contribution of positive valence on the 'old/new' effect was defined as the joint activation of two Hits > CR contrasts in which (1) positive items elicited higher activations than negative items and (2) positive items showed higher activations than neutral items [(positive > negative) conj (positive > neutral)]. To ensure that this difference was due to positive activations, this conjunction contrast was then inclusively masked (at $P<0.05$) by the Hits > CR contrast for positive items [12]. A valence-independent contrast was defined as the conjunction of [(positive > neutral) conj (negative neutral)]. Within-PFC regions were identified by thresholding statistical parametric maps with the requirement of six contiguous voxels ($P<0.005$) to control for type I error. In selected regions of interest, percent signal change was computed using Marsbar Toolbox [14]. Stereotactic Montreal Neurological Institute coordinates are translated into standard Talairach space [15] following nonlinear transformations.

Results

Participants took longer to respond correctly to new items than to old items, as revealed by a significant main effect of the old/new manipulation ($P<0.001$) in a repeated-measures analysis of variance. Additionally, hit and false alarm rates showed main effects of emotion ($P=0.031$ and $P<0.001$) owing to both higher hit rates for positive (0.749) and negative (0.749) as compared with neutral items (0.715), and higher false alarm rates for positive (0.232) and negative (0.250) as compared with neutral words (0.159; all pairwise $P<0.025$).

In the present study, we focus on emotion-related modulation of PFC activity (whole brain results can be obtained from the authors by request). Valence-specific effects related to correct retrieval (Hits > Misses contrasts) were only observable in right hemisphere PFC. While retrieval of positive words was associated with right ventromedial PFC, negative items showed an activation cluster in ventral part of the right inferior frontal gyrus. A small region in the caudal dorsolateral PFC was more

Table 1 Brain activation during recognition task

Region of activation	Voxels	*X*	*Y*	*Z*	*Z*-value
(a) Hits > Misses					
Pos > Neg and Neu					
R posterior orbitofrontal cortex (BA 11)	66	2	36	−17	3.35
R medial frontal (BA 25)	36	12	28	−13	3.04
R medial frontal (BA 25)	7	6	21	−16	2.68
Neg > Pos and Neu					
R mid-ventrolateral PFC (BA 13, 47)	13	40	16	12	2.95
Neu > Pos and Neg					
R middle frontal gyrus	6	24	−6	35	2.88
Pos and Neg > Neu					
None					
(b) HITS > ('old/new' effect)					
Pos > Neg and Neu					
L orbitofrontal cortex (BA 11)	14	−32	58	−11	3.20
L medial superior frontal (BA 9)	47	−10	60	26	3.09
R mid-dorsolateral PFC (BA9)	15	34	21	32	2.93
R orbitofrontal cortex (BA10)	8	42	56	−10	2.93
R middle frontal gyrus	26	26	11	31	2.89
R orbitofrontal cortex (BA10)	6	14	34	−12	2.71
Neg > Pos and Neu					
R mid-dorsolateral PFC (BA46)	64	42	30	21	2.97
Neu > Pos and Neg					
R frontal operculum (BA 45/47)	23	46	16	1	3.18
Pos and Neg > Neu					
R superior frontal (BA 9)	10	16	47	42	2.96
R mid-dorsolateral PFC	24	32	23	23	3.01

X, *Y*, *Z*, stereotaxic coordinates in Talairach space [15].
BA, Brodmann's area; L, left; Neg, negative; Neu, neutral; PFC, prefrontal cortex; Pos, positive; R, right.

activated during retrieval of neutral items than during retrieval of emotionally valenced words, whereas no region exceeded significance threshold in a valence-independent contrast (conjunction of positive and negative items compared with neutral ones), suggesting a functional dissociation in retrieval of positive and negative words in the PFC (Table 1).

Similarly, valence-specific 'old/new' effects were mainly observed in right hemisphere PFC, except for positive words for which significant clusters in left hemisphere orbitofrontal regions were identified with greater activation for old as compared with new items (Fig. 1). Both positive and negative words showed 'old/new' effects in right mid-dorsolateral locations [Brodmann's area (BA) 9/46], accompanied by a more caudal activation in the right frontal operculum for neutral words (BA 45/47). Additionally, a valence-independent contrast revealed right medial activation clusters in superior frontal gyrus (Table 1, Fig. 1).

Discussion

The present results provide further evidence for valence-dependent modulation of neural processing in PFC during word recognition. We identified right ventromedial and mid-dorsolateral PFC regions with valence-dependent activations in retrieval when contrasting responses to correctly recognized and unrecognized items. Additionally, emotional valence effects were elicited in right dorsolateral and bilateral orbitofrontal regions, showing a valence-dependent old/new effect. Thus, the present study extends the findings of ERP studies on emotion-based verbal yes/no recognition tasks [4,5] in two directions: first, using fMRI we are able to more precisely specify the frontal regions involved. Second, our

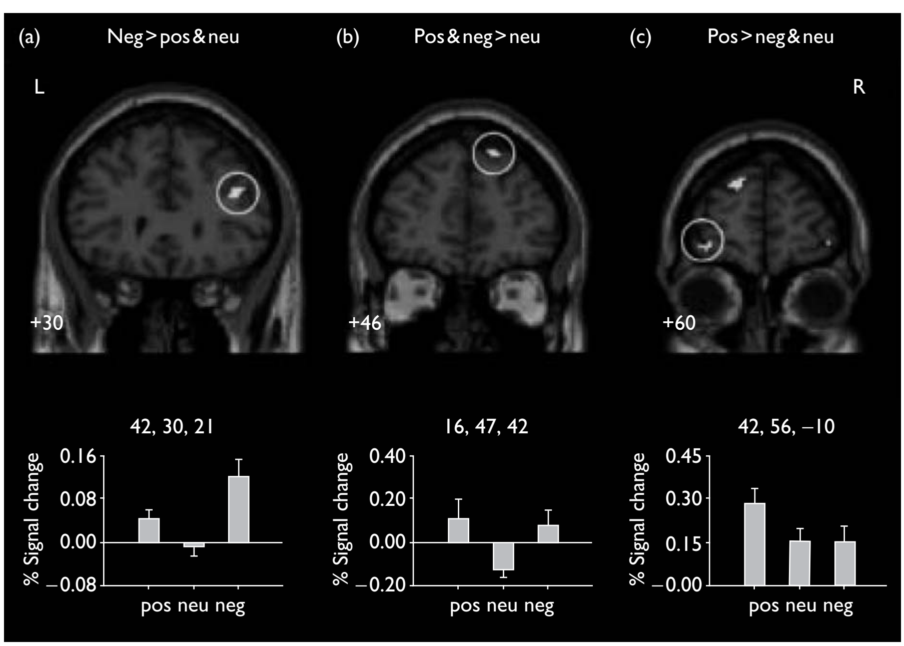

Fig. 1 Prefrontal regions showing above threshold event-related responses for old compared with new responses. (a) Old/new effect was greater for negative words compared with both positive and neutral words in right dorsolateral [Brodmann's area (BA) 46] prefrontal cortex (PFC), (b) greater valence-independent old/new effect in superior (BA 9) PFC, (c) left anterior PFC regions associated with greater old/new effect for positive words compared with negative and neutral words. Upper panel shows statistical parametric maps displayed on single subject anatomical images. Numbers indicate *y*-coordinates in Talairach space [15]. Lower panel, bar graphs show percent signal change and SEMs for the selected old/new contrasts across participants in regions of interest (coordinates in Talairach space). L, left; neg, negative words; neu, neutral words; pos, positive words; R, right.

experiment provides additional information on neural correlates of processing positive words.

Positive and negative words significantly enhanced participants, behavioural performance as compared with neutral ones. This result replicates earlier findings on the emotion-induced recognition bias [5] by extending it to positive words. Recognition bias is thought to rely on automatic processes underlying implicit emotional evaluation. Convincing evidence points to the role of item familiarity in accounting for this effect [4,5,16]. Participants more often respond 'old' to emotionally valenced items (independently of whether they are actually old or not), because these items seem to be more familiar or more detailed [16,17].

A caudal–rostral axis is discussed in recent theories on lateral prefrontal cortex organization [18] with caudal dorsolateral PFC being involved in selection of competing alternatives and rostral parts of the lateral PFC being crucial for monitoring of information in working memory. Rostral right hemisphere PFC activations in the present study for positive and negative Hits might indicate higher post-retrieval monitoring processes [1] or additional monitoring related to semantic retrieval [19], whereas more caudally observed regions for neutral Hits point to higher selection demands in working memory. Thus, emotionally valenced words increased activity in regions known to support episodic retrieval or postretrieval monitoring, which for the present study cannot be related to implicitly learned associations with emotional contexts [8]. Possibly, higher familiarity of emotionally valenced words accounts for increased monitoring processes observed in right dorsolateral PFC [1,6,20]. Ventromedial activation as revealed by correctly retrieved positive items in this study goes in line with recent findings concerning its role in the retrieval of positive contextual information [6,8] or the appraisal of reward [21]. A mid-ventrolateral activation as observed for negative Hits is in accordance with a ventral–dorsal distinction in lateral PFC [18], relating ventral–lateral PFC function to basic explicit mnemonic processes [22].

Successful discrimination between old and new items resulted in bilateral orbitofrontal PFC activations for positive words and anterior dorsolateral regions showing greater responses to the common valence independent contrast. Orbitofrontal cortex is thought to be the highest level on the caudal–rostral axis, supporting more abstract control processes [18], for example, being crucial for abstract planning or monitoring of other monitoring processes. Anterior 'old/new' effects for positive items might therefore reflect increased monitoring requirements owing to familiarity/novelty decisions [18,22]. Possibly, orbitofrontal PFC activation reflects changed expectations regarding the significance of the stimuli [22], accompanied by the role of orbitofrontal cortex in a network supporting the processing of positive information [23]. Only positive words elicited activations in anterior parts of PFC in the present study in accordance with its role in a dopaminergic network [24] supporting positive affect. Retrieval of positive items might be subserved through links to positive affective states or feelings during encoding in the study phase. This could result in greater old/new effects in anterior PFC regions as indices of successful access or processing of associated information. It is questionable whether retrieval success is responsible for this pattern [3]. The behavioural data do not show an additional advantage for positive words as compared with negative words. Again, effects of negative words were only observable in the right dorsolateral PFC.

Interestingly, by discriminating between the neural responses to old and new items, we could replicate a dissociation between dorsal and ventral parts of the medial PFC seen at encoding of pictoral information [12]. While a dorsal region (BA 9) responded more to a valence-independent contrast, only ventral regions showed enhanced activity for positive items. Possibly, valence-independent dorso-medial activations can be related to increased self-monitoring processes induced by emotional words [25]; also see [4].

In summary, we identified distinct prefrontal regions supporting recognition memory for emotionally valenced words. Previous functional imaging studies either did not distinguish between emotional valence categories [1–3] or examined emotion effects on context memory [6–8]. By identifying anterior PFC responses to positive words and right lateral PFC responses to negative words, we could relate lateral activities to familiarity-based monitoring processes at retrieval and anterior PFC activations to a common network for processing positive information.

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