Modulation of PFC activation by emotional words in recognition memory

CHAPTER 6

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Abstract

We employed event-related functional magnetic resonance imaging (fMRI) to examine emotional valence effects on verbal recognition memory. Using a yes/no recognition task we focussed on prefrontal cortex (PFC) responses to positive, negative and neutral words. Behavioral data confirmed enhanced processing of emotional items and fMRI revealed different subregions in PFC supporting retrieval of emotional words. Activations in right mid-ventrolateral PFC correlated with the correct retrieval conditions for negative words, while right ventromedial and orbitofrontal PFC 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 due to familiarity-based recognition bias for emotional words.

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Introduction

Recognition memory is influenced by the affective or emotional valence of the test items. While different imaging studies focussed on basic processes underlying episodic retrieval of verbal information (Henson, Rugg, Shallice and Dolan, 2000), the present study was designed to investigate the role of emotional valence for visual word processing in the prefrontal cortex. 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 (MTL) during episodic memory retrieval (Rugg, Otten, and Henson, 2002), prefrontal cortex (PFC) is discussed to subserve monitoring processes related to familiarity based judgements at time of retrieval (Henson et al., 2000). 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 (Rugg, Henson, and Robb, 2003). If recognition judgements are influenced by the higher familiarity of emotional items (Maratos et al., 2000), one can expect dorsolateral PFC activity to be modulated by emotional valence in the present study. In an event related potentials (ERP) study Windmann and Kutas (2001) 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 few neuroimaging studies attempted to examine the effects of emotional valence on recognition memory for single words, mainly focussing on emotional context effects in sentence processing (Maratos et al., 2001) or pictoral backgrounds (Erk et al., 2005; Smith et al., 2004). 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 (Erk et al., 2005; Kuchinke et al., 2005). In contrast, left ventrolateral PFC involvement was found in retrieving items from negative contexts (Erk et al., 2005; Maratos et al., 2001).

To our knowledge no other fMRI study has yet examined the contribution of emotional valence to correctly retrieved items in a standard yes/no recognition task with positive, neutral and negative words. Using an event-related design we report 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 (Windmann and Kutas, 2001). Both, behavioural and ERP data suggest a modulation of the ‘old/new’ effect for negative as compared to neutral items. Only a diminished ‘old/new’ effect was found for negative items at a late time window on right prefrontal electrodes (Maratos et al., 2000). 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. Because this effect is supposed to rely on post-retrieval processes, similar neural correlates for positive items should be observed in right PFC.

Methods

Subjects

Twenty right-handed native German speaking participants (12 female, aged between 20-36 years, Ø 25,8) with no history of neurological or psychiatric illness were employed in the study after having given written informed consent in accordance with guidelines set by the local ethics committee.

Procedure

Immediately after solving a lexical decision task in the scanner (Kuchinke et al., 2005), participants were scanned during two sessions (study and test phase 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 (Võ et al., in press) and did not differ significantly across emotional valence lists on word frequency (M = 20.92 /1Mio), word length (5-8 letters), frequency of orthographic neighbors, and absolute emotionality ratings (all $p>0.79$, see also Kuchinke et al., 2005, chapter 2). 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 (ISI) of 1.2 s (± 0.2 s). Subjects were instructed to memorize the presented words without any button press. During the test phase, subjects 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. Following, a fixation cross was displayed until the next appearance of a stimulus (ISI jittered around 2.8 s ±0.2 s). Before the next stimulus presentation subjects 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 (FAs).

Imaging and image processing

Functional MRI data were acquired from a 3T SIEMENS Magnetom Allegra scanner (SIEMENS Erlangen, Germany) using a whole head, local gradient coil. A single shot EPI sequence was used incorporating the following parameters: TE 30 ms, TR 2.5 s, 64x64 mosaic images with a FOV of 192 mm, FA 90°. EPI comprised 38 slices covering the whole brain taken every 3mm with no interslice gap.

Functional images were slice time corrected, realigned, normalized spatially to the Montreal Neurological Institute (MNI) template and smoothed with an 8mm FWHM gaussian kernel using SPM2 (Welcome Dept. London, http://www.fil.ion.ucl.ac.uk/spm/). 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 FAs, 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 ANOVA 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. (2004). Conjunction analysis is used here to identify several activations jointly significant in a series of subtraction contrasts (Friston, Penny, and Glaser, 2003). For instance, the contribution of *positive valence* on the ‘old/new’ effect was defined as the joint activation of two HITS>CR contrasts where (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 (Dolcos et al., 2004). A valence independent contrast was defined as the conjunction of [(positive>neutral) conj (negative neutral)]. Within PFC regions were identified by thresholding SPMs 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 (http://marsbar.sourceforge.net/). Stereotactic MNI coordinates are translated into standard Talairach space (Talairach and Tournoux, 1988) following non-linear transformations.

Table 6.1
Brain activation during recognition task

Region of Activation	Voxels	X	Y	Z	Z-value
a) HITS>MISSES					
Pos>Neg&Neu					
R posterior orbitofrontal cortex (BA 11)	66	2	36	-17	3.35
R medial frontal (BA25)	36	12	28	-13	3.04
R medial frontal (BA25)	7	6	21	-16	2.68
Neg>Pos&Neu					
R mid-ventrolateral PFC (BA13,47)	13	40	16	12	2.95
Neu>Pos&Neg					
R middle frontal gyrus	6	24	-6	35	2.88
Pos&Neg>Neu					
None					
b) HITS>CRs (‘old/new’ effect)					
Pos>Neg&Neu					
L orbitofrontal cortex (BA11)	14	-32	58	-11	3.20
L medial superior frontal (BA9)	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&Neu					
R mid-dorsolateral PFC(BA46)	64	42	30	21	2.97
Neu>Pos&Neg					
R frontal operculum (BA 45/ 47)	23	46	16	1	3.18
Pos&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; L = left, R = right; Pos = positive, Neg = negative, Neu = neutral; BA = Brodmann Area, PFC = prefrontal cortex

Results

Subjects took longer to correctly respond to new items than to old item, as revealed by a significant main effect of the old/new manipulation (P<0.001) in a repeated measures ANOVA. Additionally, hit and false alarm rates showed main effects of emotion (P=0.031, and P<0.001) due 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 pair wise 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

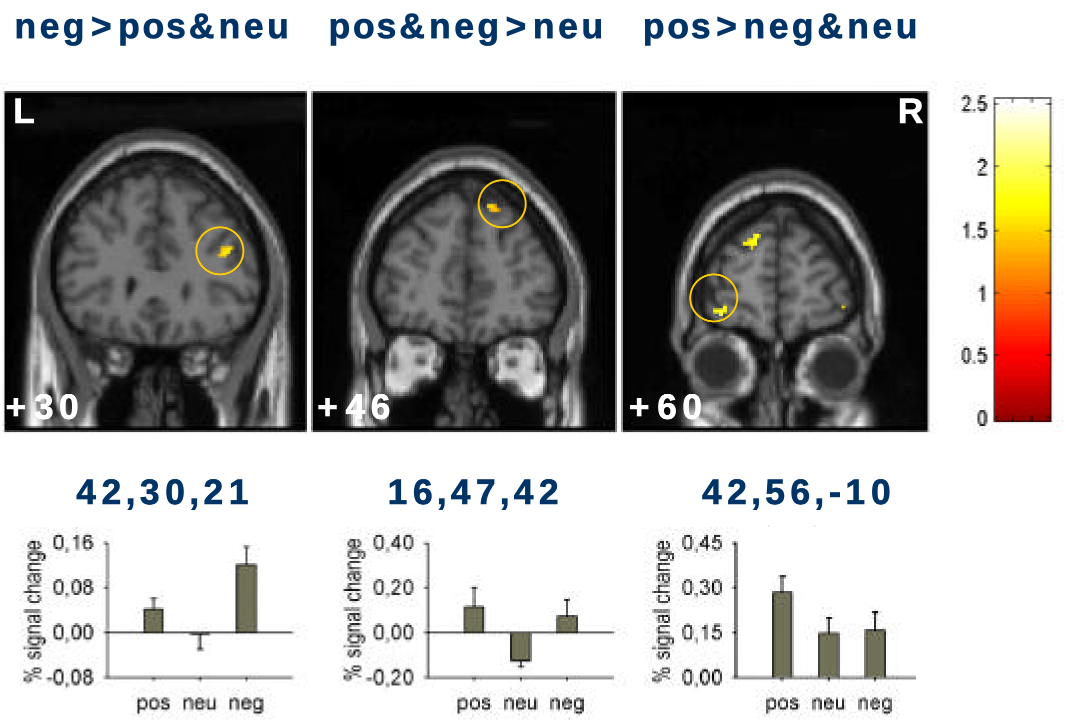

Figure 6.1 Prefrontal regions showing above threshold event-related responses for old compared to new responses. (a) old/new effect was greater for negative words compared with both positive and neutral words in right dorsolateral (BA 46) PFC (b) greater valence-independent old/new effect in superior (BA 9) PFC (c) left anterior PFC regions associated with greater old/new effect for positive words compared to negative and neutral words. Upper panel shows SPMs 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 subjects in regions of interest (coordinates in Talairach space). L = left, R = right; pos = positive words, neu = neutral words, neg = negative words.

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 caudal dorsolateral PFC was more 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 to neutral ones), suggesting a functional dissociation in retrieval of positive and negative words in the PFC (Table 6.1a).

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 (see Figure 6.1). Both, positive and negative words showed ‘old/new’ effects in right mid-dorsolateral locations (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 6.1b, Figure 6.1).

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 (Maratos et al., 2000; Windmann and Kutas, 2001) in two directions: First, using fMRI we are able to more precisely specify the frontal regions involved. Second, our experiment provides additional information on neural correlates of processing positive words.

Positive and negative words significantly enhanced subject’s behavioural performance as compared to neutral ones. This result replicates earlier findings on the emotion induced recognition bias (Windmann and Kutas, 2001) 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 (Kensinger and Corkin, 2003; Maratos et al., 2000; Windmann and Kutas, 2001). Subjects 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 (Kensinger and Corkin, 2003; Ochsner, 2000).

A caudal-rostral axis is discussed in recent theories on lateral prefrontal cortex organization (Petrides, 2005) 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 (Henson et al., 2000) or additional monitoring related to semantic retrieval (Wagner, Pare-Blagoev, Clark, and Poldrack, 2001), 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 post retrieval monitoring, which for the present study can not 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 (Henson, Rugg, Shallice, Josephs, and Dolan, 1999; Henson et al., 2000, Maratos et al., 2001). 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 (Erk et al., 2005; Maratos et al., 2001) or the appraisal of reward (Rolls, 2000). A mid-ventrolateral activation as observed for negative HITS is in accordance with a ventral-dorsal distinction in lateral PFC (Petrides, 2005), relating ventral lateral PFC function to basic explicit mnemonic processes (Petrides, Alivisatos, and Frey, 2002).

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 discussed to be the highest level on the caudal-rostral axis supporting more abstract control processes (Petrides, 2005), e.g. being crucial for abstract planning or monitoring of other monitoring processes. Anterior ‘old/new’ effects for positive items might therefore reflect increased monitoring requirements due to familiarity/novelty decisions (Petrides et al., 2002; Wagner et al., 2001). Possibly, orbitofrontal PFC activation reflects changed expectations regarding the significance of the stimuli (Petrides et al., 2002), accompanied by the role of orbitofrontal cortex in a network supporting the processing of positive information (Damasio, 1996). Only positive words elicited activations in anterior parts of PFC in the present study in accordance with its role in a dopaminergic network (Ashby et al., 1999) 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 (Rugg et al., 2003). The behavioural data do not show an additional advantage for positive words as compared to negative words. Again, effects of negative words were only observable in 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 (Dolcos et al., 2004). 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 (Lane, Reimann, Bradley, Lang, Ahern, and Davidson, 1997; also see Maratos et al., 2000).

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 (Henson et al., 2000; Rugg et al., 2002, 2003) or examined emotion effects on context memory (Erk et al., 2005; Maratos et al., 2001; Smith et al., 2004). 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.