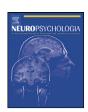
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# Emotional self-reference: Brain structures involved in the processing of words describing one's own emotions $^{\!\!\!\!/}$

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#### ABSTRACT

The present functional magnetic resonance imaging study investigated the role of emotion-related (e.g., amygdala) and self-related brain structures (MPFC in particular) in the processing of emotional words varying in stimulus reference. Healthy subjects (N=22) were presented with emotional (pleasant or unpleasant) or neutral words in three different conditions: (1) self (e.g., my fear), (2) other (e.g., his fear) and (3) no reference (e.g., the fear). Processing of unpleasant words was associated with increased amygdala and also insula activation across all conditions. Pleasant stimuli were specifically associated with increased activation of amygdala and insula when related to the self (vs. other and no reference). Activity in the MPFC (vMPFC in particular) and anterior cingulate cortex (ACC) was preferentially increased during processing of self-related emotional words (vs. other and no reference). These results demonstrate that amygdala activation in response to emotional stimuli is modulated by stimulus reference and that brain structures implicated in emotional and self-related processing might be important for the subjective experience of one's own emotions.

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#### 1. Introduction

Emotion and the self are two fascinating research topics. Ever since William James, researchers have sought answers to the questions what constitutes emotions and the self and how both phenomena might interact. Although no clear theoretical consensus has yet been reached, contemporary empirical research converges on the view that both, emotion and the self, are neurally grounded phenomena (Damasio, 1994, 1999), and associated with activity changes in specific brain regions. Regarding emotions, neuroimaging studies have been successful in tracing the brain circuitry underlying the processing of emotional stimuli. One robust finding of this research is that processing of emotional stimuli leads to enhanced activity in the amygdala. This could be demonstrated for different stimulus materials, including high arousing pictures. faces (Zald, 2003, for reviews) as well as more symbolic stimuli such as emotionally arousing words (e.g., Cunningham, Raye, & Johnson, 2004; Hamann & Mao, 2002; Herbert et al., 2009; Tabert, Borod, & Tang, 2001). Although the amygdala responds rapidly to emotional information this does not mean that the subjects themselves actually experience fear or any emotion at all when looking at a

photograph of a fearful face, or while reading an emotionally challenging word. In general emotions can be characterized as adaptive response patterns of an organism, associated with changes in the body and the brain, that are elicited instantaneously in the presence of emotionally significant external or internal events that promote or challenge the organisms survival and well-being (Russell, 2003; Scherer, 2005). These response patterns and concomitant changes in the body and the brain need not be consciously aware to the subject (Craig, 2008; Damasio, 1994, 1999). Feelings might result from emotions, however in contrast to emotions, feelings refer to the subjective and conscious experience of emotions (e.g., Barret, Mesquita, Ochsner, & Gross, 2007; Damasio, 1994, 1999).

Lesion studies suggest that the amygdala is involved in more basic emotional processing, but not necessarily in conscious emotion processing and the generation of feelings (e.g., Adolphs, Tranel, Damasio, & Damasio, 1994; Anderson & Phelps, 2002; for reviews see Adolphs, 2002). The amygdala is an emotion detection structure (Damasio, 1994, 1999; LeDoux, 1996; Öhman & Mineka, 2001). It ensures reflexive responding to stimuli that challenge or protect individual survival and well-being. Activation of the amygdala might therefore also change, and/or increase in intensity during processing of personally relevant emotional stimuli (Adolphs, Tranel, & Damasio, 1998; Cristinzio, N'Diaye, Seeck, Vuilleumier, & Sander, 2011; N'Diaye, Sander, & Vuilleumier, 2010; Modinos, Ormel, & Aleman, 2009; Rameson, Satpute, & Lieberman, 2010; Yoshimura et al., 2009). This would be in line with the suggestion that the amygdala responds to a broad range of stimuli of emo-

<sup>†</sup> The complete list of the words used in this study (original and translation) is available from the authors upon request.

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tional significance and of subjective emotional relevance (Sander, Grandjean, & Scherer, 2005).

Regarding the self, several neuroimaging studies demonstrate specific brain regions to be more active when individuals engage in self-referential processing tasks like judging stimuli (e.g., trait adjectives) in terms of their personal relatedness or selfdescriptiveness (Craik et al., 1999; Kelley et al., 2002; Zysset, Huber, Samson, Ferstl, & von Cramon, 2003; for review see Northoff et al., 2006). Subcomponents of this so called cortical midline structures (CMS) comprise, in particular, the medial prefrontal cortex (MPFC), and, amongst others, the posterior cingulate cortex (PCC) and the inferior parietal cortex (e.g., the precuneus) (for reviews on CMS see Northoff & Bermpohl, 2004). Several studies report changes in activity in regions of the CMS during active emotional modulation tasks. Most of these studies used tasks, in which participants were explicitly instructed to evaluate the emotional stimuli for their self-descriptiveness, their personal relevance (e.g., like me vs. not like me), or from a first relative to a third person perspective (e.g., Fossati et al., 2003; Gusnard, Akbudak, Shulman, & Raichle, 2001; Moran, MaCrae, Heatherton, Wyland, & Kelley, 2006; for an overview see Lee & Siegle, 2009). Other tasks employed in these studies used active emotion regulation conditions during which participants actively regulated their responses to emotional stimuli by reappraising their meaning with regard to the implications for themselves (e.g., Ochsner, Bunge, Gross, & Gabrieli, 2002; Ochsner, Knierim, Ludlow, Hanelin, Ramachandran, & Glover, 2004; Ochsner, Ray, Cooper, Robertson, Chopra, & Gabrieli, 2004).

One emerging point of evidence from these studies is that reflection upon the own emotional state enhances activity in the medial prefrontal cortex (MPFC). The MPFC is interconnected with dorsal prefrontal cortex, the anterior cingulate cortex (ACC) and the insular cortex and receives in- and output from limbic emotion structures such as the amygdala (Fuster, 2008), thus providing a converging zone for the integration of information about interoceptive sensations, cognitive and emotional states. Notably the ventral MPFC (vMPFC) is more engaged in the evaluation of own emotions compared to, for instance, the emotions of others or a control condition (e.g., passive viewing). The dorsal MPFC (dMPFC), in contrast, appears to be related to self-referential processing in general (Schmitz & Johnson, 2007). Models based on meta-analytical data regarding emotion and the self (Northoff & Bermpohl, 2004; Schmitz & Johnson, 2007) suggest two different medial prefrontal sub-systems: The first system primarily comprises the vMPFC, the anterior cingulate (ACC), amygdala and insula. This sub-system is hypothesized to be responsible for the online evaluation of incoming emotional information as self-relevant. The second sub-system, including the dMPFC, precuneus and posterior cingulate cortex, is supposed to enable a more detailed stimulus analysis based on selfreflection either in conjunction with or independent of the former sub-system. Up to now, it remains unclear if changes in activity in one or both of these MPFC systems can be stimulated by selfrelated emotional stimuli in the absence of presented self-reflective processing instructions.

Research on embodied cognition (e.g., Barrett & Lindquist, 2008; Barrett, Lindquist, & Gendron, 2007), as well as traditional semantic network models of emotion and cognition (Bower, 1981; Lang, 1979) suggest that processing of emotional content encompasses links to all aspects of its perceptual properties, its usage and emotional connotations. Thus, the word *fear*, for example, not only represents the concept of fear, but includes links to the word's purpose, operations and physiological consequences, possibly reinstating feelings of pleasure/displeasure and arousal even in the absence of a concrete emotion eliciting external event. This has also been highlighted by emotion models stating the relevance of the representation of actual and reactivated bodily experiences (Craig, 2002, 2009; Damasio, 1994, 1999). Reading verbal expres-

sions describing own emotions might thus automatically arouse and activate the amygdala, and additionally direct the reader's attention towards the monitoring of internal, mental and bodily states and the evaluation of emotional experience from current and past experience.

Previous research suggest that both the vMPFC, the insula and the ACC are key structures associated with subjective awareness of inner bodily states (interoception) and the representation and regulation of subjective emotional experience (Barret, Mesquita, et al., 2007; Craig, 2002, 2009; Lane, 2000; Paulus & Frank, 2003; Zysset et al., 2003). Accordingly, one would expect activity in the amygdala, insula but also the MPFC (vMPFC in particular) and the ACC to be more active during processing of words related the own emotion compared to a control condition of passive viewing of emotion words that contain no particular reference or are related to another person.

Building upon and extending previous research the present study aimed, for the first time, to directly investigate this hypothesis by measuring brain activity underlying the processing of one's own emotions without confounding effects related to a specific task at hand. To this end, healthy participants underwent functional imaging while they read silently a series of verbal expressions that described either own emotions, the emotions of another person or contained no self-other reference at all.

#### 2. Materials and methods

#### 2.1. Participants

Twenty-two healthy, right-handed native speakers of German (eight males, fourteen females; mean age: 23.5 years, SD=2.7) without history of drug abuse, chronic bodily or neurological and psychiatric diseases, or medication for any of these participated in the fMRI experiment. All participants scored normally on self-report measures of mood (M=3.3; SD=2.5) (BDI, Hautzinger, Bailer, Worall, & Keller, 1194), and also state (M=35.7; SD=5.3) and trait anxiety (M=36.3; SD=5.8) (STAI, Laux, Glanzmann, Schaffner, & Spielberger, 1981). Handedness was determined with the Edinburgh Handedness Inventory (Oldfield, 1971). All subjects had normal or corrected to normal vision. Participants gave written informed consent prior to participation, and the study was approved by the Local Institutional Review Board. Subjects were paid 15€ in return for participation.

#### 2.2. Stimulus material

The stimulus set consisted of emotional and neutral words. Emotional words consisted of 45 pleasant, 45 unpleasant and 45 neutral nouns. Nouns were taken from a corpus of words previously collected by our own research group (Kissler, Assadollahi, & Herbert, 2006), and were rated on the Self-Assessment Manikin Scales (SAM, Bradley & Lang, 1994) for emotional arousal, valence and a SAM like 9-point scale for concreteness by an independent sample of adult native German speakers, who had comparable backgrounds and ages to the participants of the current study. According to these ratings pleasant and unpleasant nouns did not differ significantly in emotional arousal ( $M_{pleasant} = 4.55$ , SE = 0.13;  $M_{\text{unpleasant}} = 4.75$ , SE = 0.10; p = 0.23). Neutral nouns were rated as significantly less arousing ( $M_{\text{neutral}} = 2.37$ , SE = 0.11; p < 0.001) and lower in emotional valence compared to emotional nouns ( $M_{pleasant} = 7.18$ , SE = 0.1;  $M_{unpleasant} = 2.51$ , SE = 0.07;  $M_{\text{neutral}} = 5.18$ , SE = 0.06; p < 0.001). Stimuli did not differ significantly in concreteness ( $M_{\text{pleasant}} = 4.29$ , SE = 0.14;  $M_{\text{unpleasant}} = 4.49$ , SE = 0.13;  $M_{\text{neutral}} = 4.56$ , SE = 0.23; p = 4.1). All nouns comprised on average seven characters ( $M_{pleasant} = 6.8$ , SE = 0.29;  $M_{\text{unpleasant}} = 7.2$ , SE = 0.3;  $M_{\text{neutral}} = 7.1$ , SE = 0.27; p = 0.46) and according to the CELEX database (Baayen, Piepenbrock, & Gulikers, 1995) were frequently used in German  $(M_{\text{pleasant}} = 173.45, SE = 26.5; M_{\text{unpleasant}} = 110.1, SD = 18.2; M_{\text{neutral}} = 159.1, SD = 24.9;$ 

One third of the nouns of each emotional valence category was paired with the possessive pronoun *my* indicative of participants' own emotions ("self-condition"), the possessive pronoun *his* indicative of the emotional state of another person ("other-condition") or a definite article, *the*, devoid of any self-other-reference ("control-condition"). Linguistically, pronouns are agents or markers of possession indicating whom a respective object or content represented by a noun belongs to. Articles by itself convey little semantic meaning and no particular reference. Therefore, pronouns and articles appear especially suitable for the investigation of spontaneous processing effects attributable to stimulus-driven changes in self-referential processing. Assignment of the unpleasant, pleasant and neutral nouns to the three stimulus conditions (self, other, control) was randomized across participants. Three lists of words (A, B, and C) were generated such that across the three lists, emotional and neutral nouns did not differ in word length, word frequency or

concreteness, but unpleasant and pleasant words were more arousing than neutral words. In one third of the participants, list A was presented in the self condition, list B in the other condition and list C in the no reference condition and vice versa. Thus, across participants each word had the possibility to be either self- or other-related or to be paired with an article to avoid any confounding list effects attributable to a priori selection of words to a specific condition (self, other, article).

#### 2.3. Experimental design

Words were presented event-related, in one functional imaging session. Stimuli (pronoun–noun and article–noun pairs) were presented randomly for 1000 ms and followed by an inter-stimulus interval during which a fixation cross was shown for 7.5–9 s, corresponding to 2.5–3 TR. Words were written in black letters on a white background (Times font, 40 points) and projected directly onto the eyes of the participants using MR compatible glasses. Experimental runs were generated and controlled by "Presentation" software (Neurobehavioral Systems, Inc.).

#### 2.4. Procedure

Upon arrival at the laboratory participants were made familiar with the imaging procedure, the technique was explained to them in detail, they were questioned about their health and filled in the self-report questionnaires on mood and state and trait anxiety. Participants were given detailed instruction concerning the task before scanning. They were told that during functional imaging a series of words will be presented to them that could describe either the own emotions, the emotion of an unknown third person or simply an emotional state of no particular reference. They were asked to read the words silently. To ensure that participants followed the instructions, they were told to repeat the words silently as soon as they appeared on the screen and keep their eyes open and fixate the cross in the middle of the screen during the intertrial-interval. After the completion of the scanning procedure, participants were asked to write down as many of the presented words as they could remember in a surprise free recall test and rate the words for perceived valence and arousal on the SAM. Finally, participants were debriefed in detail about the purpose of the present experiment.

#### 2.5. Physiological data collection and reduction

#### 2.5.1. Image acquisition

Functional and anatomical images were acquired on a 1.5 T-whole body scanner (Siemens Avanto, Erlangen, Germany). T1-weighted, high-resolution (1 mm  $\times$  1 mm  $\times$  1.5 mm voxel size) structural brain images were obtained for each subject using a magnetization prepared rapid acquisition gradient echo (MPRAGE) sequence (160 slices, no gap, TR=1870 ms, TE=3.74 ms,  $\alpha$ =15°, FOV=256 mm  $\times$  256 mm). Functional images were acquired using a T2-weighted multislice echo-planar imaging (EPI) sequence (28 axial slices acquired in descending direction, 4-mm thickness, 1-mm gap, TR=3 s, TE=39 ms,  $\alpha$ =90°, FOV=192 mm  $\times$  192 mm, 64  $\times$  64 matrix, 3 mm  $\times$  3 mm  $\times$  4 mm voxel size), during one functional run that lasted about 23 min.

## 2.5.2. Image analysis

Imaging data were analyzed with Statistical Parametric Mapping software (SPM5, Wellcome Department of Imaging Neuroscience, London, UK). The first eight EPI images were discarded from analysis excluding images preceding T1 saturation. Preprocessing of functional images consisted of slice time correction, 3D motion correction, and normalization to MNI space (Montreal Neurological Institute, resampled voxel-size 3 mm  $\times$  3 mm  $\times$  3 mm). Data were smoothed spatially with an isotropic Gaussian Filter of 4 mm full width at half maximum (FWHM) to remove high-frequency artefacts. Low-frequency signal drifts were filtered using a cutoff period of 128 s.

Statistical analysis was based on the general linear model (GLM, Friston et al., 1995). Hemodynamic responses during stimulus presentation were modelled using a stick function (time-locked to stimulus onset) convolved with the canonical hemodynamic response function (hrf) of the SPM5 software package. Stick functions were time-locked to the onset of the stimuli and separate regressors were used to model each condition. To account for signal changes due to head movements during scanning, six regressors representing estimated head movements were added as covariates of no interest into the statistical model (Friston, Williams, Howard, Frackowiak, & Turner, 1996). Effects of "emotion" and "reference" were examined by comparing activity in the left and right amygdala, the left and right insula (anterior and posterior insular cortex), the ACC, and the ventral and dorsal MPFC across the  $3\times3$  stimulus presentation conditions. Therefore, individual contrast images (see below) were calculated and entered into a second-level analysis using one-sample t-tests. Contrasts were as follows:

(1) Effects of emotion, unreferenced (controls): unpleasant<sub>no reference</sub> vs. neutral<sub>no reference</sub> pleasant<sub>no reference</sub> vs. neutral<sub>no reference</sub>

(2) Effects of self-reference on emotion processing:

 $\begin{array}{l} unpleasant_{self} \ vs. \ unpleasant_{no \ reference} \ or \ vs. \ unpleasant_{other} \\ pleasant_{self} \ vs. \ pleasant_{no \ reference} \ or \ vs. \ pleasant_{other} \\ unpleasant_{self} \ vs. \ neutral_{self} \\ pleasant_{self} \ vs. \ neutral_{self} \end{array}$ 

- (3) Effects of other-reference on emotion processing:
   unpleasant<sub>other</sub> vs. unpleasant<sub>no reference</sub>
   pleasant<sub>other</sub> vs. pleasant<sub>no reference</sub>
   unpleasant<sub>other</sub> vs. neutral<sub>other</sub>
   pleasant<sub>other</sub> vs. neutral<sub>other</sub>
- (4) Effects of reference (neutral words): neutral<sub>self</sub> vs. neutral<sub>other</sub> or vs neutral<sub>no reference</sub>

Activity in brain regions of interest (ROIs) was determined by means of anatomical masks (left/right insula, amygdala ACC, vMPFC and dMPFC, respectively). Anatomical masks for ROI analyses were generated on the basis of a priori anatomical criteria as defined in the automatic anatomic labeling atlas (AAL) integrated in SPM5 (Tzourio-Mazover et al., 2002).

#### 3. Results

#### 3.1. Imaging data

## 3.1.1. Effects of emotion, unreferenced

Activity in the left amygdala as well as the right insula was significantly enhanced during reading of unpleasant compared to neutral nouns that contained no self-other reference (Table 1a). For pleasant nouns, there was no difference in amygdala or insula activity compared to neutral nouns. Also, there was a significant increase in activity in occipital, parietal as well as temporal brain regions during reading of emotional (unpleasant and unpleasant) compared to neutral nouns (Table 1b).

## 3.1.2. Effects of self-reference on emotion processing

Activity in the amygdala and the insula was significantly enhanced during processing of self-related pleasant nouns relative to the processing of self-related neutral nouns, of unreferenced pleasant nouns and of other-related pleasant nouns. Amygdala and insula activation was also enhanced during processing of self-related unpleasant nouns compared to the processing of self-related neutral nouns, but for self-related unpleasant nouns activity patterns in the amygdala and the insula did not differ significantly from other-related unpleasant nouns or unpleasant nouns that contained no particular reference (Tables 2a–4a, and Figs. 1 and 2). Overall, effects were more pronounced in the left amygdala. Insula activity included both the right and the left insula.

In addition, a significant increase in activity in the MPFC and the ACC was observed. Activity in each of these brain regions was significantly greater during processing of self-related unpleasant and pleasant nouns relative to the processing of self-related neutral nouns (Table 2a) and compared to the processing of other-related or unreferenced emotional nouns (Tables 3a–4a). Activation of the ACC included peak voxels in the left ACC (Brodmann area 32). Activation of the MPFC comprised activity in the left superior medial prefrontal cortex and particularly in more ventral regions of the left (vMPFC, Brodmann area 10, Fig. 3).

Additional brain regions showing larger activity during processing of self-related emotional nouns than during processing of other-related or unreferenced emotional nouns are listed in Tables 2b–4b and comprised mainly posterior regions of the brain like the middle and posterior cingulate cortex (PCC), the precuneus, and also peak voxels in subcortical and frontal regions like the hippocampus and the inferior frontal gyrus (IFG). Activation of these regions (PCC, precuneus and hippocampus) was somewhat greater for self-related pleasant than self-related unpleasant nouns.

## 3.1.3. Effects of other-reference on emotion processing

During processing of other-related words, activity in the left amygdala and the right insula was also significantly enhanced

**Tables 1a–5a** Suprathreshold voxels (x, y, z in MNI space) in the brain regions of interest for the relevant contrasts of interest (T > 2.83, p < 0.005, uncorrected).

Brain region	Hemisphere	$xyz$ {mm}	T-value	Cluster
(1a)				
Unpleasant vs. neutral (no reference)				
Amygdala	Left	-18 - 3 - 15	3.24	14
Insula	Right	33 –69	3.47	31
Pleasant vs. neutral (no reference)				
reasant vs. neutral (no reference)	Ν	o suprathreshold voxels		
(2a)				
Unpleasant vs. neutral (self)				
Amygdala	Left	-300-21	4.00	33
runygaala	Right	270-27	3.57	16
Insula	Left	-39 - 66	5.85	300
	Right	36 –27 18	6.19	302
ACC	Left	-1548-6	5.89	86
MPFC				
dMPFC	Left	-9483	3.19	15
vMPFC	Left	-1245-6	5.54	65
VIVIFIC	Right	030-15	3.16	14
Pleasant vs. neutral (self)				
Amygdala	Left	-18 - 6 - 18	4.03	36
runyguaia	Right	270 - 12	3.40	13
Incula	Left	-36 - 150	5.51	152
Insula	Right	33 –21 6	5.73	208
ACC	Left	-1542-6	5.09	61
ACC	Right	0429	3.10	11
MPFC				
dMPFC	Left	-9486	3.61	25
vMPFC	Left	-1248-6	4.47	60
(3a)				
Unpleasant (self) vs. unpleasant (no reference)				
Amygdala	Left/right	n.s.		
Insula	Left/right	n.s.		
	Left	-32118	4.39	97
ACC	Right	0429	3.33	35
MPFC				
dMPFC	Left	-6546	3.01	12
vMPFC	Left	-1251-6	4.81	67
Pleasant (self) vs. pleasant (no reference)				
Amygdala	Left	-300-18	3.83	20
Timygaara	Left	-36 -15 -3	5.05	136
Insula	Right	33 –21 6	4.25	40
ACC	Left	-9 42 6	3.58	89
MPFC	zere	5 12 5	3.50	00
dMPFC	Left	-12456	3.69	28
vMPFC	Left	-348-9	4.31	55
· <del>-</del>		3.0	113 1	55
(4a)				
Unpleasant (self) vs. unpleasant (other)				
Amygdala	Left/right	n.s.		
Insula	Left/right	n.s		
ACC	Left	-1548-6	5.17	71
MPFC				
dMPFC	Left	-9543	3.00	9
vMPFC	Left	-1248-6	4.17	54
Pleasant (self) vs. pleasant (other)				
Amygdala	Left	-27 - 3 - 15	3.07	10
Milyguala	Left	-39 -15 -3	3.95	22
Insula	Right	-39-13-3 33-216	4.28	33
ACC	Left	-15 45 -6	5.09	61
	LCIL	-1343-0	5.09	10
MPFC dMPFC	Loft	12 45 6	2 55	າາ
dMPFC vMPFC	Left Left	-12 45 6 -12 45 -6	3.55 4.07	23 51
VIVIFIC	LCIL	-1243-0	4.0/	51
(5a)				
Unpleasant vs. neutral (other)				
Amygdala	Left	-30 - 3 - 18	3.33	15
Insula	Right	3627 - 3	2.99	10
Pleasant vs. neutral (other)		o suprathreshold voxels		

Tables 2b-4b
Suprathreshold voxels (x, y, z in MNI) obtained from whole brain analyses for the relevant contrasts of interest. T-values are reported at p < 0.005, uncorrected (T > 2.83).

Brain region	Hemisphere	xyz {mm}	<i>T</i> -value	Cluster
(1b)				
Unpleasant vs. neutral (no reference) Temporal				
Middle temporal	Left	-39-18-12	3.97	391
gyrus	Right	48 –42 24	3.83	132
Fusiform gyrus	Left	-36-3-30	3.36	57
Parietal				
Superior parietal gyrus Occipital	Left	-15 -75 45	3.46	170
Superior occipital gyrus	Left	-9-8448	3.34	133
Middle occipital gyrus	Left	-42 -63 33	3.52	72
Caudatus/pallidum	Left	-909	3.78	59
Thalamus	Left	-21 -27 0	3.14	27
Pleasant vs. neutral (no reference)				
Temporal	x 6	62 40.0	2.50	150
Middle temporal gyrus	Left	-63 -48 9	3.58	158
Inferior temporal gyrus Parietal	Left	-42 -45 -12	3.83	
Superior parietal gyrus Occipital	Left	-24-72 42	3.56	70
Middle occipital gyrus	Left	-36 -72 3	3.40	18
( <b>2b)</b> Unpleasant vs. neutral (self)				
Frontal				
Inferior frontal gyrus Parietal	Left	-48 42 3	4.02	44
Precuneus	Left	-12 -48 12	3.05	20
Occipital Superior occipital gyrus	Right	9 – 99 18	3.30	10
Pleasant vs. neutral (self)				
Temporal				
Medial temporal pole	Left	-42 12 -36	4.05	17
Hippocampus	Right	2610-19	3.90	34
Fusiform gyrus	Right	51 – 48 – 12	3.06	15
Parietal	Right	31 -40 -12	5.00	13
Precuneus	Left	-9 - 5145	6.06	75
Occipital Middle occipital gyrus	Right	24 – 99 6	3.28	49
				49 72
Lingual Lingual	Left Right	-21 -42 0 15 -93 -9	4.13 3.76	72 49
Lingual	Right	13 – 33 – 3	5.70	43
(3b)				
Unpleasant (self) vs. unpleasant (no reference) Frontal				
Inferior frontal gyrus	Left	-39366	3.36	45
Temporal	ECIT	-33300	3.50	43
Medial temporal gyrus	Left	-45 - 426	3.81	67
Fusiform gyrus	Right	42 – 36 – 15	3.15	36
Parietal				
Precuneus	Left	-6-5427	3.28	32
Precuneus	Right	30 - 48 9	3.48	45
Inferior parietal gyrus	Left	-45 -39 36	3.34	29
Middle cingulate	Left	-6-2439	3.26	36
Occipital				
Middle occipital gyrus	Left	-15 - 930	3.57	49
Inferior occipital gyrus	Right	36 -84 -15	3.19	10
Thalamus	Left	-12 - 303	3.42	14
Pleasant (self) vs. pleasant (no reference) Frontal				
Inferior frontal gyrus	Left	-42 42 6	4.52	21
Temporal	Leit	-42 42 0	4.32	21
Medial temporal gyrus	Left	-51-12-15	4.77	81
Parietal Precuneus	Left	-27 -51 9	3.68	60
Inferior parietal gyrus				
Posterior cingulate Occipital	Left	3 – 52 24	3.63	51
Middle occipital gyrus	Left	-24-8115	2.95	21
Calcarine	Left	-18 -84-12	3.59	25
Calcarine	Right	0 – 57 12	3.11	10
Thalamus	Left	-9-18-6	3.32	43
		- 10 0	<del></del>	

Tables 2b-4b (Continued)

Brain region	Hemisphere	<i>xyz</i> {mm}	T-value	Cluster
(4b)				
Unpleasant (self) vs. unpleasant (other)				
Frontal				
Rolandic operculum	Left	-48 - 2118	3.32	45
Temporal				
Medial temporal gyrus	Left	-45 - 510	3.66	8
Pleasant (self) vs. pleasant (other)				
Frontal				
Inferior frontal gyrus	Left	-42 45 3	3.26	10
Temporal				
Medial temporal gyrus	Left	-51 - 12 - 15	4.77	81
Inferior temporal gyrus	Left	-48 - 18 - 27	3.02	20
Hippocampus	Right	9 - 3 - 12	3.57	46
Parietal				
Inferior parietal gyrus	Left	-57 -33 33	3.25	32
Posterior cingulate	Left	-15 - 4821	3.12	28

for unpleasant compared to neutral nouns, but activity in either of these regions did not differ significantly from unreferenced emotional nouns or from self-related unpleasant nouns (Table 5a, Figs. 1 and 2).

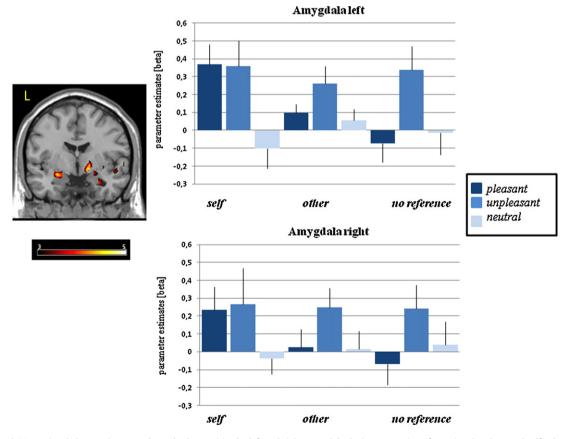
## 3.1.4. Effects of reference (neutral words)

During reading of neutral words activity in the MPFC (both dMPFC and vMPFC), the insula, the ACC and the amygdala did not show any suprathreshold activation regardless of whether words were related to the self, the other or of no particular self-other reference.

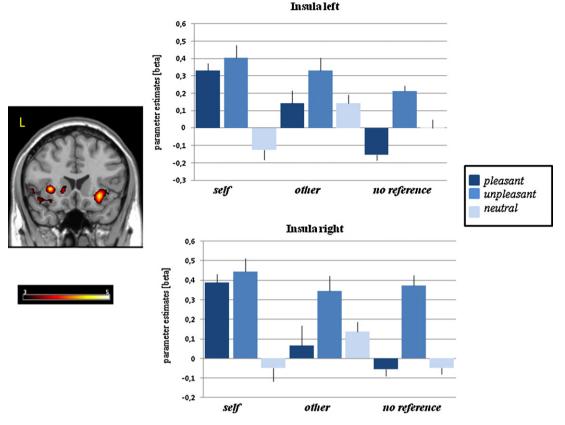
## 3.2. Behavioral data

## 3.2.1. Subjective ratings

Participants' ratings of valence and arousal for self-related, other-related and unreferenced emotional and neutral nouns are listed in Table 6. Valence ratings showed a significant main effect of the factor "Word Category" (F(2,42) = 150.31, p < 0.001): Pleasant words were rated as more pleasant than neutral words and unpleasant words as more unpleasant than neutral words. The interaction effect of the factor "Valence Category × Reference" was also significant (F(4,84) = 3.79, p < 0.01). Post-hoc test showed that self-related pleasant words were rated as more pleasant than other-



**Fig. 1.** Right panel: Mean signal changes (mean and standard errors) in the left and right amygdala during processing of emotional and neutral self-related, other-related and unreferenced nouns. The picture on the left (left panel) displays significant changes in the amygdala during processing of self-related emotional nouns, *p* < 0.005. Color bars represent *T*-values. (For interpretation of the references to color in text, the reader is referred to the web version of the article.)



**Fig. 2.** Right panel: Mean signal changes (mean and standard errors) in the left and right insula during processing of emotional and neutral self-related, other-related and unreferenced nouns. The picture on the left (left panel) displays significant changes in the insula during processing of self-related emotional nouns, *p* < 0.005. Color bars represent *T*-values. (For interpretation of the references to color in text, the reader is referred to the web version of the article.)

related (t(21)=4.38, p<0.001) or unreferenced pleasant words (t(21)=2.98, p<0.01). For arousal, only the main effect of "Word Category" showed a significant effect (F(2,42)=78.46, p<0.001), i.e., unpleasant and pleasant words were generally rated as more arousing than neutral words irrespective of their reference (self, other, no particular reference).

## 3.2.2. Memory-surprise free recall

After scanning participants remembered only a few of the presented words by surprise (M = 12.2, SD = 5.5). Of these, unpleasant nouns were generally better remembered than neutral words (unpleasant: M = 4.6, SD = 2.36, neutral: M = 2.25, SD = 3.3; unpleasant-neutral: t(21) = 3.35; p < 0.005) whereas pleasant nouns were remembered better when they were related to the self compared to both other conditions (pleasant<sub>self</sub>: M = 3.9, SD = 2.02; pleasant<sub>other</sub>: M = 0.9, SD = 0.60; pleasant<sub>no reference</sub>: M = 1.0,

SD = 0.50; pleasant<sub>self</sub> – pleasant<sub>other</sub>: t(21) = 5.14; p < 0.0001; pleasant<sub>self</sub> – pleasant<sub>no reference</sub>: t(21) = 5.75; p < 0.0001).

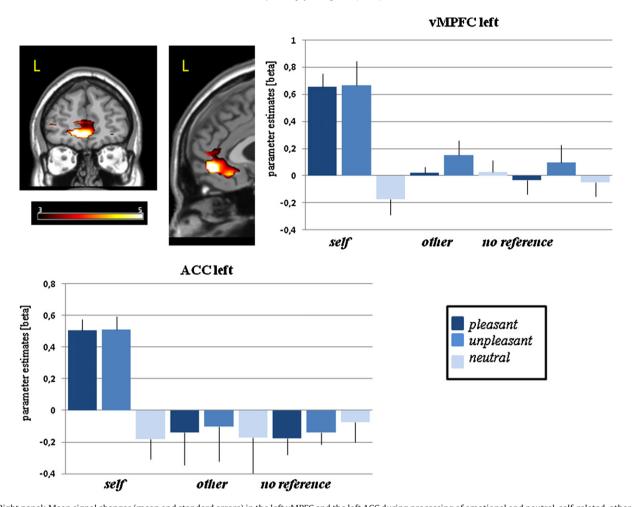
## 4. Discussion

The present study demonstrates how variations in stimulus reference (related to the self, vs. the other, vs. no particular reference) associated with emotion words influence brain activity patterns in emotion-related and self-related brain structures in a silent reading task. During reading, processing of unpleasant words compared to neutral and pleasant words increased amygdala and insula activation regardless of the stimuli's reference (self, other, no reference). This is consistent with earlier observations and human lesion studies (Adolphs, 2002) suggesting a specific role of the amygdala and the insula (e.g., Anders, Lotze, Erb, Grodd, & Birbaumer, 2004) in the processing of negative emotions. Regarding verbal stimuli greater activity changes in both the amygdala and the insula in response

**Table 6**Rating data (participants).

	Unpleasant	Pleasant	Neutral	
Self				
Valence	2.84 (0.36)	7.26 (0.16)	5.29 (0.10)	
Arousal	5.50 (0.34)	5.04 (0.35)	2.48 (0.31)	
Other				
Valence	2.96 (0.29)	6.25 (0.17)	5.05 (0.44)	
Arousal	5.11 (0.31)	4.52 (0.31)	2.46 (0.27)	
No reference				
Valence	2.40 (0.20)	6.66 (0.18)	5.12 (0.10)	
Arousal	5.66 (0.39)	4.75 (0.37)	2.54 (0.25)	

Notes: Valence and arousal ratings range from 1 (extremely negative valence, extremely low arousal) to 9 (extremely positive valence, extremely high arousal). Standard errors are in parentheses.



**Fig. 3.** Right panel: Mean signal changes (mean and standard errors) in the left vMPFC and the left ACC during processing of emotional and neutral, self-related, other-related and unreferenced nouns. The picture on the left (left panel) displays significant changes in these regions during processing of self-related emotional nouns, *p* < 0.005. Color bars represent *T*-values. (For interpretation of the references to color in text, the reader is referred to the web version of the article.)

to unpleasant words as opposed to pleasant or neutral words have been previously reported (e.g., Cunningham et al., 2004; Straube, Mentzel, & Miltner, 2005; Tabert et al., 2001). For pleasant nouns however, in the present study, amygdala and insula activation was preferentially increased when pleasant words were self-related, demonstrating that the role of the amygdala and also the insula in emotion processing might go well beyond the processing of negative emotions. In line with this assumption, many recent imaging studies showed that specifically the amygdala acts as dynamic relevance detector (Sander et al., 2005), responding in principle to both unpleasant and pleasant stimulations (for an overview see Zald, 2003), but taking into account information about a stimulus' personal relevance (N'Diaye et al., 2010; Modinos et al., 2009; Rameson et al., 2010; Yoshimura et al., 2009). Our findings regarding amygdala activation support these models of the amygdala as a system involved in relevance detection and furthermore suggest that, in addition to the amygdala, also other brain structures, like the insula, implicated in the processing of internal bodily signals (Craig, 2002, 2009; Critchley, Wiens, Rotshtein, Ohman, & Dolan, 2004), are involved in this type of emotional relevance processing.

It is unlikely that the above reported effects can be explained by differences in stimulus arousal or differences in word length. Unpleasant and pleasant words were carefully matched on several of these stimulus dimensions including arousal. In addition, emotional nouns were rated as equally arousing across the three conditions (self, other, no reference) by the participants of the present study. Regarding stimulus valence, participants judged pleasant nouns as more pleasant when they were related to the participant him- or herself, compared to when related to the other or when they had no personal reference. For unpleasant or neutral nouns no such reference-dependent valence effects were observed. This is consistent with a self-positivity bias in emotion processing (e.g., Diener & Diener, 1996; Mezulis, Abramson, Hyde, & Hankin, 2004; Pahl & Eiser, 2005). This bias has been consistently reported in response to trait adjectives in healthy subjects and has recently been shown to involve amygdala activation (Herbert et al., 2009; Sharot, Riccardi, Raio, & Phelps, 2007).

Enhanced amygdala and insula activation during reading of selfrelated emotion words encourages recent suggestions proposing a role of the amygdala (Anderson, 2007; Barrett, Bliss-Moreau, Duncan, Rauch, & Wright, 2007 for a brief overview), and the insula (Craig, 2009) in the processing of emotional experience and feelings. Both brain structures may contribute to emotional experience by providing the appropriate preconditions for its appearance, i.e., detecting the emotional relevance of a stimulus (amygdala) and associated stimulus-driven changes in internal bodily states (insula). However, neither of these functions might be sufficient for the appearance of self-related subjective feelings. Lesions of the amygdala (for an overview see Adolphs et al., 1994) or insula (for an overview see Jones, Ward, & Critchley, 2010) do not necessarily lead to impaired emotional experience, although both patient groups show selective impairments in emotion recognition from facial and vocal cues, also when these stimuli are considered as personally relevant (Adolphs et al., 1998; Jones et al., 2010). In accordance with these findings our data suggest that the amygdala and the insula are involved in the processing of emotional stimuli and of self-related emotional stimuli in particular, with self-related emotion words eliciting further activity increases in prefrontal brain structures like the ACC and the MPFC. The ACC has been demonstrated to be essential for the online monitoring of one's own mental, bodily and emotional state (Critchley, 2005). Furthermore, the MPFC has been shown to be specifically involved in self-processing (Lee & Siegle, 2009, for reviews) and to provide an important converging zone for the integration of information from the amygdala, the insula and the ACC.

MPFC activation has been observed in previous imaging studies in a variety of conditions such as evaluation of personality traits, appraisal of emotional stimuli from a first relative to a third person perspective (Lee & Siegle, 2009, for reviews) as well as during more specific tasks requiring participants to explicitly reappraise and regulate their feelings in response to emotionally evoking events by means of introspection (e.g., Ochsner et al., 2002; Ochsner, Knierim, et al., 2004; Ochsner, Ray et al., 2004). These results have led to the suggestion that in particular the MPFC modulates the subjective experience of emotions with the dorsal MPFC being generally more engaged in self-reflective evaluations and the ventral MPFC more in the monitoring and evaluation of one's feelings (e.g., Gusnard et al., 2001; Herwig, Kaffenberger, Jäncke, & Brühl, 2010; Jenkins & Mitchell, 2010; Zysset et al., 2003). In the present study MPFC activation comprised especially regions in the ventral MPFC and to a lesser degree also regions in the dorsal MPFC. Activity in the ventral and dorsal MPFC was more pronounced in the left hemisphere and enhanced during processing of self-related unpleasant and pleasant nouns relative to self-related neutral nouns as well as relative to other-related and unreferenced, emotional nouns. These activations occurred although, in the present study, participants were not instructed to appraise, reappraise or reflect upon the meaning of the presented stimuli in a particular manner, i.e., they were not explicitly instructed to evaluate the stimuli for their emotionality or their self-relevance and relatedness nor to up- or down-regulate their emotions while engaged in word reading. The only task given was to read the words silently and repeat them mentally while they appeared on the screen. These results demonstrate that in healthy subjects exposure to verbal stimuli describing own emotions enhances activity in the brain's self-processing structures important for the monitoring of internal, mental and bodily states (ACC) and the online evaluation of the own emotional experience and feelings (vMPFC) even in the absence of any task-induced selfor emotion processing instructions.

Results from whole brain analysis revealed further differences in brain activity patterns: There was a significantly greater increase in the posterior cingulate cortex and the precuneus and also in the left and/or right hippocampus for self-related emotional words (pleasant ones in particular) compared to other-related and unreferenced emotional words (see Tables 2b and 3b). Both the posterior cingulate cortex and the precuneus are involved in self-referential processing (Northoff & Bermpohl, 2004) and supposed to play an important role in attention and retrieval of self-related, emotional material from memory (e.g., Cavanna & Trimble, 2006; Maddock, Garrett, & Buonocore, 2003a; Maddock, Garrett, & Buonocore, 2003b). In line with this, self-related emotional nouns, pleasant ones in particular, were spontaneously remembered better than other-related or unreferenced pleasant words after scanning.

The above-illustrated results have a number of theoretical and practical implications. First, amygdala activation by emotional stimuli is modulated by stimulus reference consistent with the view of the amygdala as relevance detector. Second, our results demonstrate that insula activation is sensitive to these variations in stimulus reference as well. Third, our results suggest activation of brain areas belonging to the brain's emotion and self-networks,

i.e., ACC and MPFC besides amygdala and insula, to be specifically enhanced when emotional information becomes related to the self. The brain activations patterns found during processing of self-related emotional words might provide an important basis for the subjective experience of emotions as belonging to one's self (Barret, Mesquita, et al., 2007). Further studies using our paradigm in combination with an explicit emotion generation task could be extremely helpful to validate this assumption and further demonstrate how amygdala, insula, MPFC and ACC interact during the processing and generation of information related to one's own emotions. The present approach taken is novel but in support of neurophysiological models on emotion and the self (Northoff & Bermpohl, 2004; Schmitz & Johnson, 2007).

Practically, our design could be employed in certain patient groups with lesions of the amygdala, insula or MPFC. This could further our understanding on the role these brain structures play in the processing of self-related emotional stimuli. In affective disorders, such as depression (e.g., Grimm et al., 2009; Northoff, 2007), social anxiety (e.g., Blair, Geraci, Devido, McCaffrey, Chen, & Vythilingam, 2008), or alexithymia (Lane, Kaszniak, Ahern, & Schwartz, 1997), to name but a few, our paradigm could also prove sensitive and provide valuable insight into the neurophysiologic changes underlying the hypo- or hyperresponsiveness these patients demonstrate when they are confronted with emotion-laden, self-related material or when asked to identify and describe the own emotions.

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