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Distinguishing specific sexual and general emotional effects in fMRI—Subcortical and cortical arousal during erotic picture viewing

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Sexual activity involves excitement with high arousal and pleasure as typical features of emotions. Brain activations specifically related to erotic feelings and those related to general emotional processing are therefore hard to disentangle. Using fMRI in 21 healthy subjects (11 males and 10 females), we investigated regions that show activations specifically related to the viewing of sexually intense pictures while controlling for general emotional arousal (GEA) or pleasure. Activations in the ventral striatum and hypothalamus were found to be modulated by the stimulus' specific sexual intensity (SSI) while activations in the anterior cingulate cortex were associated with an interaction between sexual intensity and emotional valence. In contrast, activation in other regions like the dorsomedial prefrontal cortex, the mediodorsal thalamus and the amygdala was associated only with a general emotional component during sexual arousal. No differences were found in these effects when comparing females and males. Our findings demonstrate for the first time neural differentiation between emotional and sexual components in the neural network underlying sexual arousal.

Introduction

Sexual excitement is characterized by feelings of specific sexual intensity as well as by a strong general emotional arousal and feeling of pleasure. Any neural investigation that targets the neural network underlying this specific sexual intensity (SSI) is confronted with the problem of differentiating it from other structures mediating general emotional processing. This distinction of separate structures is highly pertinent to an ongoing debate on different accounts of emotion processing: Proponents of the "basic emotion theory" would suggest on the basis of animal findings and translational observations, that a limited set of hard wired, distinct basic emotions exists across human and non-human animals (Panksepp, 1998). These encompass different executive systems such as rage, fear and lust. Such primary emotive systems would be based on hierarchically organized circuits that are genetically imprinted and orchestrate certain affective neurodynamic responses (Panksepp, 1992). While this view would try to discern systems mediating SSI from other basic systems, the dimensional approach relies on processes of cognitive appraisal attributing a general emotional arousal (GEA) and hedonic valence to an emotional experience. While some have questioned the existence or applicability of the "basic emotion" approach (Ortony and Turner, 1990), there is evidence that both views may apply on different system levels (Panksepp, 1992).

Recent studies investigating the neural correlates of human sexual arousal revealed a broad network of cortical and subcortical brain regions that are activated during the processing of visual erotic stimuli. Cortical regions comprise of a parieto-occipito-temporal network, mainly consisting of the superior and inferior parietal lobes (SPL, IPL), the lateral occipital cortex (LOC), as well as the medial prefrontal cortex (MPFC), anterior cingulate cortex (ACC) and insula. Subcortical regions include the ventral and dorsal striatum, the amygdala and the hypothalamus (Arnow et al., 2002; Ferretti et al., 2005; Karama et al., 2002; Moulier et al., 2006; Mouras et al., 2003; Paul et al., in press; Ponseti et al., 2006; Redoute et al., 2000; Stoleru et al., 1999; see also Mouras, 2007, and Mouras and Stoleru, 2007, for an extensive overview).

To specify the role of each of these regions during sexual arousal (SA), prior investigations attempted to relate them to distinct components of a multidimensional model of SA. According to this model, cognitive, motivational, autonomic and emotional components contribute to SA (Redoute et al., 2000; Stoleru et al., 1999). Cognitive components include processes of early appraisal of a stimulus as sexual incentive and direction of attentional focus to a sexual target. Related

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neural activity was assumed to be mediated mainly by activations in temporo-occipito-parietal regions as well as in the orbitofrontal cortex (Mouras, 2004; Mouras et al., 2003). On the basis of correlational findings between markers of penile tumescence and concurrent neural activity, the autonomic component of SA was related in particular to activations in the insula, hypothalamus and anterior cingulate (Arnow et al., 2002; Ferretti et al., 2005; Moulier et al., 2006; Redoute et al., 2000). On the other hand, motivational components including adaptation of motor responses were related to activations in the basal ganglia (Redoute et al., 2000). The involvement of the medial thalamus, ventral striatum (VS) and amygdala was related to the emotional dimension of hedonic value, i.e., pleasantness or valence, or to general emotional arousal (GEA) during SA (Ferretti et al., 2005; Karama et al., 2002; Redoute et al., 2000).

One should, however, be aware that all the above regions are also activated by non-erotic emotional stimuli. Recruitment of attentional resources leads to higher activations in temporo-parieto-occipital regions for more emotionally arousing stimuli (Ishai et al., 2004; Lang et al., 1998; Pessoa et al., 2002b). This recruitment is mainly modulated by the amygdala and prefrontal cortex (Desimone and Duncan, 1995; Lane et al., 1998; Pessoa et al., 2002a; Vuilleumier et al., 2001; Vuilleumier and Pourtois, 2007; Vuilleumier et al., 2004). The involvement of the MPFC and the ACC in non-erotic emotional processing is also well documented (Grimm et al., 2006; Phan et al., 2002). Therefore, their attribution to a distinct and specific autonomic component of SA together with the anterior insula and hypothalamus may be questionable. Although measures of penile tumescence suggested the involvement of these particular brain structures in the erectile response of sexual arousal (Arnow et al., 2002; Ferretti et al., 2005; Moulier et al., 2006), concurrent neural activations could still be attributable to somatosensory integration of erection as well as to the pleasant feeling associated with its perception (Mouras, 2004).

Given that the very same regions are activated during both erotic and non-erotic emotional processing, control of GEA during SA is particularly important in the identification of neural activity specifically related to SSI during SA. Neural specificity in particular brain regions would be indicated by occurrence of higher activations in stimuli inducing higher SSI and the independence of this activation from dimensions of valence or GEA. In order to achieve such neural differentiation, neuroimaging studies attempted to reduce differences between erotic and non-erotic visual control stimuli in these general emotional dimensions by introducing control conditions of humorous or sports clips (Arnow et al., 2002; Redoute et al., 2000). However, these stimuli still differed in general emotional dimensions like induced feeling of pleasure (Mouras et al., 2003).

The challenge persists to examine which parts of the described subcortical–cortical network display additional activity during processing of erotic stimuli without being modulated by emotional valence or GEA. Past investigations often used long dynamic video clips to induce sexual excitement. Although the long duration ensures induction of sexual feelings, it also allows several emotional states to occur within one clip, which makes it rather difficult to efficiently control for GEA or valence (Janssen et al., 2003). Short presentations of still pictures may be matched more easily and more accurately for induced emotional states. Furthermore, the bodily content of erotic pictures has to be manipulated independently of SSI to account for activations related to the processing of human body parts. This would require the introduction of both sexual-bodily and non-sexual-bodily stimuli. Recent investigations demonstrated that human body parts by themselves activate regions which are implicated in part in SA (Downing et al., 2001; Downing et al., 2007; Peelen and Downing, 2007). Since SA induced by visual erotic stimuli inherently involves the processing of bodies and body parts, neural investigation needs to distinguish activations mediating SSI from those related to the processing of body parts.

Aims and hypotheses

Based on previous imaging findings, we tried to elicit neural activity in the subcortical–cortical network modulated by SSI as opposed to GEA. Sexual stimuli can be considered strong incentives and sexual activity a rewarding situation (Fisher et al., 2006). Considering its pivotal role in reward mechanisms (Knutson and Wimmer, 2007; Yacubian et al., 2007), the ventral striatum was hypothesized to show an effect for SSI independent of GEA or emotional valence. A further specific effect of sexually intense pictures was considered for the hypothalamus given the well described effects of both hypothalamic lesions and electric stimulation on sexual behavior in animals (Karama et al., 2002; McKenna, 1999) as well as its role in initiating specific autonomous responses during SA (Ferretti et al., 2005; Georgiadis and Holstege, 2005).

In addition to those regions being specific to SSI, we investigated regions of the subcortical–cortical network that allow for interaction between processes of SSI and GEA and those regions whose activation during SA might be modulated only by GEA. Using functional magnetic resonance imaging (fMRI), we presented carefully matched erotic and emotional, non-erotic, as well as non-erotic, non-emotional (neutral) visual stimuli. In addition, subjects evaluated these stimuli in a post-scanning session according to their subjective experience of SSI, GEA and emotional valence. Subjective ratings were then used to guide analyses of fMRI data.

Methods

Experimental design

Twenty-one heterosexually oriented subjects (11 males and 10 females) were asked to view and passively experience a total of 256 bodily-erotic, emotional and neutral photographs taken from the International Affective Picture System (Lang et al., 2005). Age range was 21–36 years (mean: 25.73, median: 24) for males and 22–28 years (mean: 23.9, median: 23) for females. Erotic (bodily) pictures depicted partially or completely naked people of both sexes alone or in couples of men and women in a context of positive or negative valence. Mean number of people per picture was 1.94 (±0.70) and did not differ between positive and negative bodily pictures. Non-bodily-emotional pictures showed one or more humans in sports scenes or other social interactions as well as emotionally arousing non-human motives in a positive or negative context.

Bodily erotic and non-bodily, emotional picture categories were matched for standard ratings of arousal, dominance and valence as provided by the IAPS catalogue (Lang et al., 2005). Neutral and emotional pictures were matched for dominance and mean valence ratings, while emotional pictures had higher arousal values. Mean valence of emotional stimuli was very low for negative and very high for positive stimuli while neutral stimuli always had intermediate valence levels.

Runs consisted of either non-bodily-emotional and neutral (4 runs) or non-bodily-emotional and bodily (erotic) stimuli (4 runs) and were presented in a pseudorandomized order. Each run consisted of a total of 32 images and had a total length of 8 min 32 s. Stimulus duration was intended to address two main concerns. While SA in earlier

studies was induced either by short movies or pictures of at least 20–30 s, the shortest duration shown to evoke penile tumescence was 10 s (McConaghy, 1989). Aiming to be especially sensitive to early components of SA such as cognitive and emotional evaluation, imaging studies investigating effective emotional stimulation use shorter stimulus durations which reliably induce an emotional response and support sufficient specificity of the investigated emotional process. Consequently, a presentation duration of 5 s was chosen, which has been shown to reliably invoke subjective experience of SA (measured on a 1–9 item scale) and found to be short enough to maintain a certain emotional state (Heinzel et al., 2006). Pictures were presented in a randomized order across runs and subjects were asked to promptly press a button at the appearance of each picture to monitor their vigilance in the scanner, as assessed by reaction times.

In order to control for the possible influence of preceding attention on the experience of the presented stimuli, half of the pictures were preceded by an expectancy period of 4.5 s indicating the type of the subsequently presented picture. Expected and unexpected pictures (see below) were balanced for the number of positive and negative erotic and emotional or neutral pictures, the total number of pictures, and IAPS values. Following an approach described by Bermpohl et al. (2006), the expectancy period was indicated by the presentation of a white arrow on a dark background. Downward arrows indicated sexual, upward arrows emotional and rightward arrows neutral expectancy. After the picture presentation, a fixation cross (intertrial interval) was presented for a duration of 8 s. Arrows and fixation cross were of equal size, color and luminance and were centered on a black background. Prior to the experimental session, subjects were familiarized with the paradigm by completing a test run consisting of 32 trials.

Behavioral and subjective evaluation

Reaction times were defined as the time between picture onset and subsequent button press during the fMRI experiment. Subjective ratings of the pictures were conducted outside the scanner after the fMRI session using a visual analogue scale. This approach was preferred to an intra scan assessment to avoid judgment related cognitive influence which can confound neural activity during emotional perception (Blair et al., 2007; Grimm et al., 2006; Mitchell et al., 2007; Northoff et al., 2006; Taylor et al., 2003). Ratings of experienced SSI, GEA and valence were acquired. Subjects were asked to rate their own personal experience instead of cognitively evaluating the erotic and emotional properties of the stimuli. During analysis of behavioral data, average scores of ratings were calculated for the whole group. For intra-scan reaction times and reports of GEA, SSI and valence, analyses of covariance (ANOVA) containing the factors stimulus category (bodily or non-bodily-emotional), stimulus subcategory (positive or negative) and mode of presentation (unexpected or expected) were calculated for main effects and interactions. Gender of subject was entered as a between subjects factor. Since many stimuli depicted couples that induce high sexual intensities (Hamann et al., 2004), ratings of all stimuli were regarded together and no further analysis was performed on gender effects on the viewing of opposite sex stimuli.

Imaging–scanning procedures

Data acquisition was conducted on a 1.5 Tesla General Electric Signa scanner using a standard headcoil. Imaging procedures included collection of (a) structural high resolution images (rf-spoiled GRASS sequence 60 slices sagittal, 2.8 mm thickness), (b) T1 weighted anatomic images coplanar with the functional images (23 slices, aligned to the plane connecting the anterior and posterior commissure axis covering the whole head in oblique axial orientation), (c) inversion recovery T1 weighted echo planar images coplanar with the functional images and (d) echo planar functional images sensitive to BOLD contrast (257 sequential acquisitions, 23 slices with 3.125 mm in-plane resolution, 5 mm thickness, 1 mm gap; T2* weighted gradient echo sequence: TR 2 s, TE 40 ms). The first seven images were discarded due to T1 saturation effects. During image acquisition, stimuli were projected on a mirror mounted on the headcoil using a LCD projector.

Image analysis

Image preprocessing and statistical analyses were carried out using MATLAB 6.5.1 and SPM2 (SPM2 software package; Wellcome Department of Cognitive Neurology, London, UK; see http://www.fil.ion.ucl.ac.uk/spm2.html). A total of 2000 (8×250) volume images were realigned to the first image to correct for head movement between scans, mean-adjusted by proportional scaling, resliced and normalized into standard stereotactic space (resulting in an isotrophic 3 mm resolution). The cut-off for subjects showing translational head movement was set to 2 mm and for rotational movement to 1°. No subject had to be excluded. Image normalization was performed using the MNI (Montreal Neurological Institute) template provided by SPM. Spatial transformation included both linear and non-linear dimensions and used the non-linear sampling algorithm provided with SPM2. Data were thereafter expressed in terms of standard stereotactic coordinates in the x, y and z axes. Transformed functional data sets from each subject were smoothed with a Gaussian kernel of 8 mm (full-width half-maximum) for the group analysis to meet the statistical requirements of the General Linear Model and to compensate for normal variation in individual brain size, shape and sulcal/gyral anatomy across subjects. Subject-specific low frequency drifts in signals were removed by a high pass filter of 128 s.

For each subject, a design matrix modeling of emotional and erotic or emotional and neutral IAPS pictures was defined. For the analysis of effects of preceding expectancy, unexpected and expected viewing of the stimulus categories were modeled as separate events. This enabled us to compare the main contrasts for stimuli presented in an "expected mode" (after expectancy cues) or in an unexpected mode (after fixation).

Besides these experimental conditions, regressors for the baseline condition (fixation cross) and expectancy periods were entered into a design matrix including a total of 7 regressors. To investigate effects of positive and negative subcategories of erotic and emotional stimuli and to make explicit use of their sexual and emotional properties, these were modeled separately in a third design matrix on single subject level. Specific effects were tested by applying appropriate linear contrasts to the parameter estimates for each condition, resulting in a t-statistic for each voxel. Analysis of effects for the whole group of all subjects and for groups of males and females was performed in a second level, random effects model on a whole brain level (Friston et al., 1999).

We report, if not explicitly mentioned otherwise, differences in activated regions that survived a threshold of $p < 0.001$, corrected for multiple comparisons using FDR correction (false discovery rate; Genovese et al., 2002) for clusters consisting of at least 10 contiguous voxels ($k = 10$) for main contrasts, and a conjoint p-threshold of $p < 0.05$ (FDR-corrected) for conjunction analyses or serial subtraction contrasts (interactions) of more than one contrast at the second level.

Table 1
Mean ratings (±SD) are reported for all bodily, non-bodily-emotional and non-bodily neutral picture categories, as well as for positive and negative subcategories

Stimulus category	SSI		GEA		Valence	
	Mean	SD	Mean	SD	Mean	SD
Bodily-emotional	4.06	1.12	6.38	1.31	4.70	0.30
Positive	5.93	1.27	6.07	1.5	6.95	0.76
Negative	2.19	1.27	6.70	1.17	2.46	0.76
Non-bodily-emotional	1.16	0.46	5.75	1.32	4.41	0.36
Positive	1.25	0.76	5.00	1.56	6.32	0.73
Negative	1.07	0.18	6.56	1.23	2.50	0.74
Neutral	1.12	0.23	2.61	1.03	5.14	0.30

Subjects were asked to rate "How sexually intense" (1–9), "How emotionally intense" (1–9) and "What kind of emotion" (valence with 1: very negative to 9: very positive) they experienced the picture.

The strategy of analysis aimed to first reveal several regions involved in SA and then specify their involvement in more specific aspects as SSI or GEA. First, BOLD effects of all positive bodily pictures greater than those of all positive non-bodily stimuli were assessed by a linear contrast. This contrast was further performed separately for expected and unexpected stimuli and contrast images of both contrasts were compared on a second level, random effects, paired *t*-test. Gender effects in the main contrast were tested on the second level, performing a two sample *t*-test of subjects' contrast images.

To investigate specific neuronal effects of differences in SSI between stimulus categories, specific contrasts were chosen according to effects revealed by behavioral results in a next step. One contrast could compare a stimulus type rated higher for SSI (S=higher SSI), higher for GEA (E=higher GEA) and higher for valence (P=more pleasant) to a less sexually intense (s=lower SSI), less emotionally arousing (e=lower GEA) and less pleasant (p=less pleasant) stimulus ([SEP>sep]). This contrast was then entered into a conjunction analysis (Nichols et al., 2005), with a contrast of the type [S>s] that compared two stimuli which differed in their ratings of SSI but not in GEA or valence. Activations in common areas revealed by this conjunction analysis were interpreted as being related to greater sexual intensity common in both contrasts but not as (common) effects of greater GEA or valence. Characterization of a stimulus subtype as more or less emotionally arousing or sexually intense was done according to the behavioral results and was always relative to the other stimulus subtype entered in the contrast (Fig. 4a).

The linear relationship between subjective ratings and neural activations was then tested adding subjects' ratings of SSI, GEA and valence for each stimulus as parametric regressors (Lewis et al., 2007; Nagai et al., 2004). This new design matrix consisted of regressors of interest for bodily and non-bodily stimuli which were then modulated by three parametric regressors of first polynomial order for individual subjective ratings of SSI, GEA and valence. Effects of all parametric regressors were then tested in a second level random effects model (Friston et al., 1999). This analysis aimed to reveal a parametric (linear) modulation by SSI, GEA or valence in regions showing effects either for SSI, GEA or valence.

Effects of greater GEA within areas activated during sexual arousal were tested by a conjunction of [bodily>non-bodily pictures] and [non-bodily>neutral pictures], identifying common activations for higher GEA but not SSI. The interaction of specific sexual intensity and valence was tested by a serial subtraction search for higher effects of valence in bodily stimuli than in non-bodily-emotional stimuli.

Second level analyses of more than one contrast per subject were corrected for non-sphericity. For resulting regions of interest, neural responses were extracted and transformed to percentage signal changes for our regressors of interest in each subject using the MarsBar toolbox (Brett et al., 2002). Temporal patterns were investigated by time course analyses applying a finite impulse response model (FIR) which does not make an assumption on the resulting signal changes after stimulus

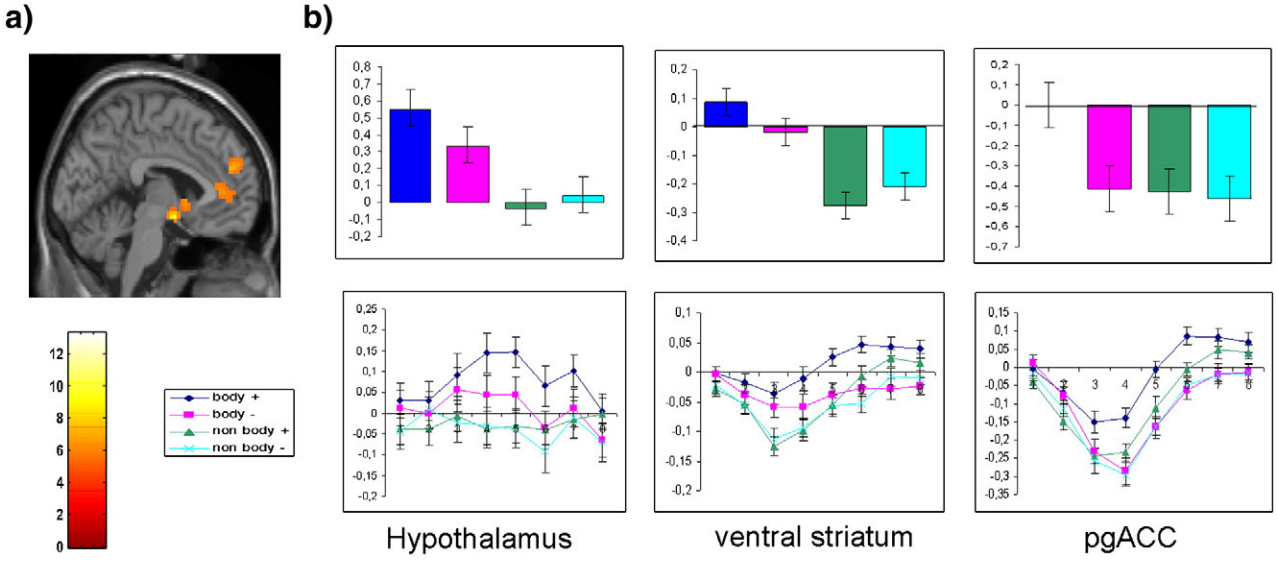

Fig. 1. Main regions of sexual stimulus perception controlling for emotional stimulus perception. (a) The sagittal brain section shows activity in hypothalamus, VS, pgACC and DMPFC to be higher in positive bodily (erotic) than positive non-bodily (emotional) pictures at a corrected threshold of $p<0.001$ and a voxel threshold of $k>10$. (b) Bar diagrams in the upper panel show percentage signal changes in these regions for all four stimulus conditions (positive (+) and negative (−) bodily and non-bodily stimuli). The lower panel shows corresponding time courses for each condition for the next 8 acquisition time points (16 seconds) after stimulus onset. For DMPFC, see also Fig. 5.

Table 2
Effects of positive bodily (i.e., erotic) pictures when compared to positive non-bodily (emotional) pictures ($p<0.001$, corrected, $k>10$) and when additionally compared to negative bodily pictures

Region	[positive bodily>positive non-bodily]		Conjunction: [positive bodily>positive non-bodily]^ [positive>negative bodily]		Signal correlation with sexual intensity	
	(*x*, *y*, *z*)	*Z*-values	(*x*, *y*, *z*)	*Z*-values	(*x*, *y*, *z*)	*Z*-values
VS	−9, 9, 3;	4.53;	0, 12, −3;	3.98;	−3, 15, −3;	4.82;
	9, 6, 6;	5.85;				
Hypothalamus	−3, 12, −9;	4.54	−2, 11, −11;	3.98;		
	6, 0, −12;	4.88;				
ACC	0, 39, 6;	4.84;	0, 39, 6;	4.84;	−6, 48, −9;	6.05;
VMPFC	3, 57, 3;	4.94;	3, 57, 3;	4.90;		
DMPFC	6, 51, 30;	4.85;				
LOC	−51, −78, 0;	7.36;				
	54, −72, 0;	7.69;	54, −72; −6;	3.93;		
SPL	−36, −60, 57;	4.84;			33, −39, 48;	5.05;
	27, −60, 60;	5.05;				
Precuneus	3, −66, 36;	5.71;	3, −66, 48;	4.43;		
FFA	42, −45, 24;	6.32;				
Ventral tegmentum	−3, −6, −9;	4.53;				
Amygdala	18; −3; −15;	4.43;				

The conjunction revealed common regions in both contrasts at $p<0.05$ (corrected, $k>10$). Correlation of activations with individually reported sexual intensity for each bodily picture as revealed by parametric analysis is reported at $p<0.001$ (corrected, $k>10$).
VS: ventral striatum, ACC: anterior cingulate cortex, VMPFC: ventral medial prefrontal cortex, DMPFC: dorsal medial prefrontal cortex, LOC: lateral occipital complex, SPL: superior parietal lobe, FFA: fusiform face area.

presentation. Parameter estimates were calculated for 8 time bins of 1TR (=2 s) length for each regressor of our design matrix.

Results

Subjective ratings

A (2×2×2) ANOVA for reported SSI revealed significant main effects for stimulus category (*bodily or non-bodily-emotional*) and stimulus subcategory (positive or negative stimuli) but not for the mode of presentation (*expected or unexpected*) at $p<0.001$. Although balanced by IAPS standard ratings of pleasantness and arousal, ANOVAs on reported GEA and valence showed significant main effects of all three factors at a lower level of $p<0.01$. As shown in Table 1, positive bodily, i.e., erotic, pictures where rated not only higher for specific sexually intensity than positive non-bodily pictures, but also more pleasant and more emotionally arousing, while negative bodily and non-bodily pictures only differed in their sexual intensity ratings (see also Fig. 4a). No effects were found for gender when entered as a between subjects factor in the analysis.

Behavioral performance

An ANOVA on reaction times (RT) revealed significant effects for the mode of presentation, with significantly faster RTs for expected than for unexpected pictures ($p<0.001$), while no significant effects ($p>0.05$) were found for the factors stimulus category and stimulus subcategory or subjects' gender or for any interaction. Effects of general

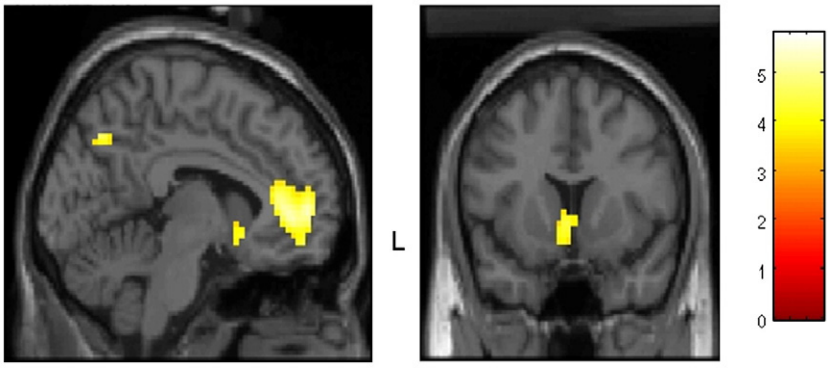

Fig. 2. Specific effects of positive bodily picture viewing. Regions revealed by the conjunction of the contras [positive bodily>positive non-bodily pictures] and [positive bodily>negative bodily pictures] at a corrected threshold of $p<0.05$, $k>10$. Common activations, reflecting common effects of positive erotic experience controlled for the general display of naked people, were found in pgACC, VS, anterior hypothalamus and precuneus (see also Table 2).

attentiveness for the main picture conditions (positive and negative bodily and non-bodily-emotional pictures) could thus be ruled out.

fMRI data

Distinction between sexual and emotional processing

Categorical approach. Positive bodily, i.e., erotic, pictures induced higher activity than positive non-bodily-emotional pictures in the ventral striatum (VS) and hypothalamus as well as in the perigenual anterior cingulate (pgACC), dorsal (DMPFC) and ventral (VMPFC) medial prefrontal cortex, precuneus, left and right occipital cortex (LOC) including the right fusiform face area (FFA) and bilateral superior parietal lobes (SPL) ($p<0.001$, corrected, $k>10$; see Fig. 1 and Table 2 for z-values and peak coordinates as well as for regions significant at a corrected $p<0.05$, $k>10$). The contrast between positive and negative bodily stimuli yielded similar regions and the conjunction of both contrasts, identifying brain regions that are specific for positive bodily, e.g., erotic, stimuli as distinguished from negative bodily and from positive non-bodily stimuli, revealed common activations in the VS and the Hypothalamus as well as in pgACC, VMPFC, precuneus and right LOC ($p<0.05$, corrected, $k>10$; Fig. 2 and Table 2).

To exclude effects of preceding attention, we separately tested the main contrast [positive bodily>positive emotional pictures] for stimuli with and without preceding expectancy. The above mentioned target regions of sexual arousal (VS, Hypothalamus, pgACC) did not show stronger effects in the expected modes when compared to the unexpected mode ($p>0.05$, corrected, for detailed analyses of expectancy effects in other regions; see Walter et al., in press).

Finally, none of these regions showed a significant gender difference ($p>0.05$ corrected) for neuronal effects in the main contrasts [bodily>non-bodily-emotional stimuli] or [positive bodily>positive non-bodily stimuli]. On an exploratory level, at a lower threshold of $p<0.05$ uncorrected, neither the amygdala nor the hypothalamus showed differential activation between males and females.

Behaviorally driven approach. Analysis of parametric modulation of regional signal intensities during bodily picture viewing by subjective ratings of specific sexual intensity identified the pgACC, the VS, extending into the medial preoptic area of the anterior hypothalamus (MPOA) and further into the right SPL ($p<0.001$ corrected, $k>10$, Fig. 3 and Table 2). The higher sexually intense a bodily stimulus was rated by a subject, the higher the signals were detected in these regions. In contrast to these regions, we did not observe parametric modulation in the posterior hypothalamus by SSI. Furthermore, we did not observe any correlating regions for emotional valence or GEA at this level of statistical significance ($p<0.001$, corrected). While at a lower level of $p<0.05$, corrected, we observed parametric modulation of signal intensities in the pgACC by emo-

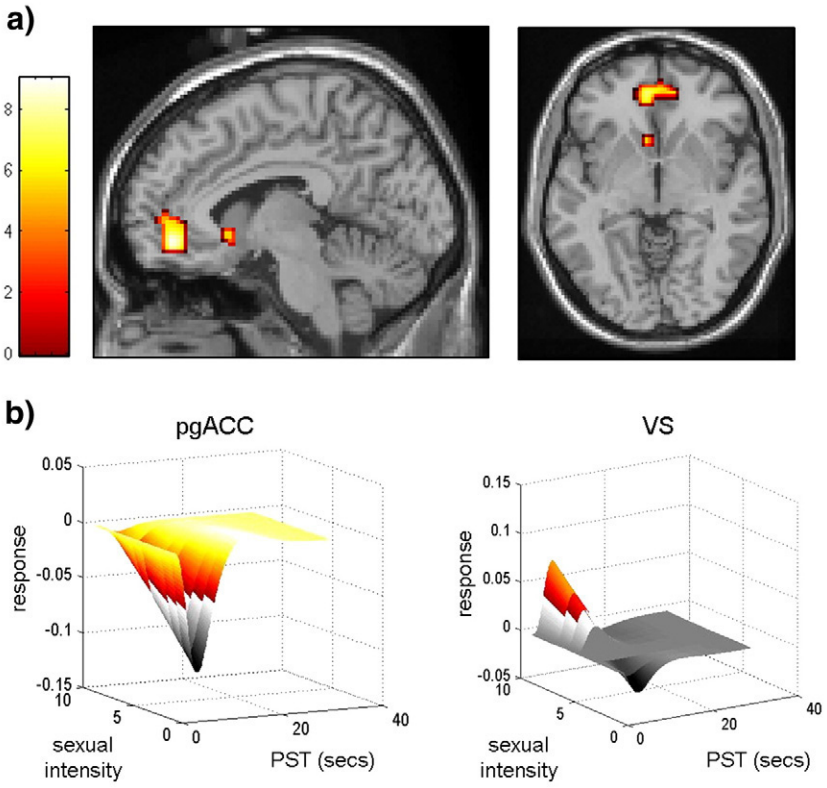

Fig. 3. Correlation of neural responses and subjective ratings. (a) Brain sections show effects of bodily stimuli in the VS and the pgACC, extending into the VMPFC, that were found to be positively modulated by reported ratings of sexual intensity when entered as parametric regressors ($p<0.001$, corrected, $k>10$). The lower panel in (b) shows the parametric modulation of responses for one representative subject to illustrate this finding. The modeled changes in hemodynamic responses function are therefore plotted as a function of peristimulus time (PST, stimulus onset at $t=0$) and individually reported sexual intensity. The anterior cingulate responded with strongest signal decreases for bodily stimuli with low sexual intensity while highly sexually intense stimuli were correlated with near resting state activity. In the VS in contrast, stimuli with highest sexual intensity ratings elicited highest signal increases (compare also Figs. 1 and 4).

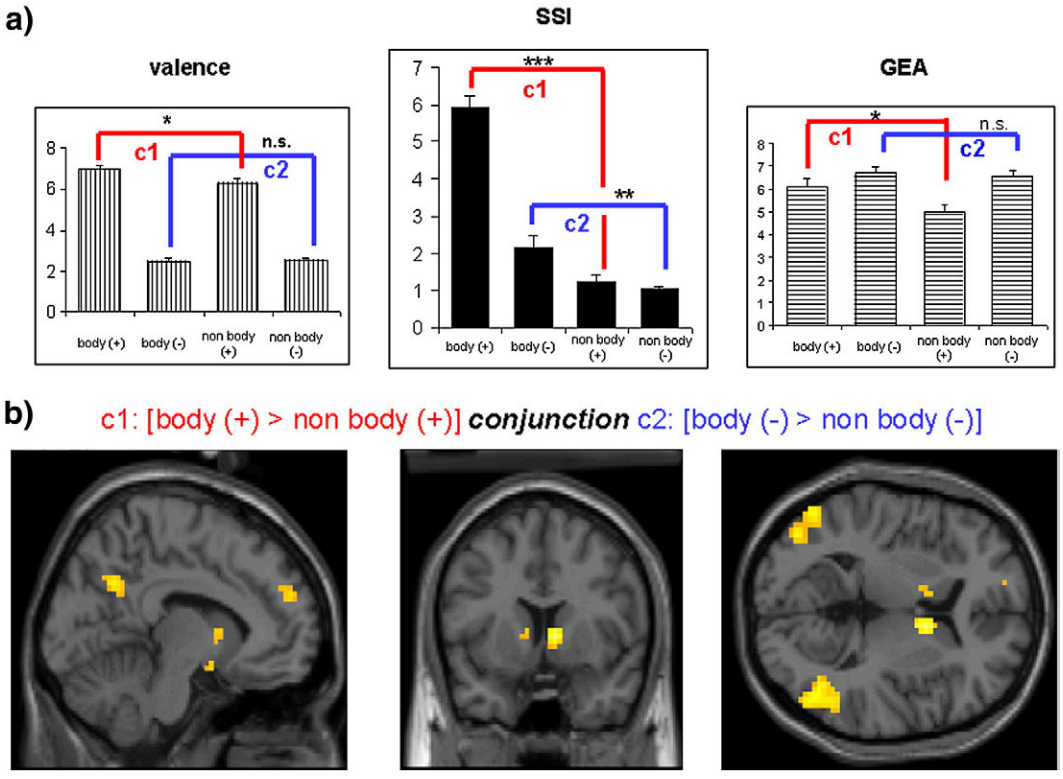

Fig. 4. Conjunction analysis on the basis of intensity ratings. (a) Comparison of subjective effects: Bar diagrams plot mean ratings for SSI, GEA and valence for all four stimulus conditions. Both positive (+) and negative (−) bodily picture sets were rated more sexually intense than respective non-bodily pictures sets but only positive bodily pictures were also rated more pleasant (higher valence) and more emotionally arousing than positive non-bodily-emotional pictures. For exact values, compare Table 1 and behavioral results. The comparisons between stimulus categories are color coded, and the same colors indicate the comparison of BOLD responses between these stimulus categories. Underlying differences in subjective ratings for the conjoined contrasts below are indicated by red and blue color bars and indexed for the two contrasts c1 and c2 that compare the same stimuli for (a) and (b). (b) Comparison of neural effects: The commonality of higher SSI in behavioral ratings was reflected by the conjunction of both functional stimulus contrasts, looking for common differential activations at a corrected $p<0.05$, $k>10$. Common differences in activations, which can be traced back to differences in SSI but not in GEA or valence, were found in the VS, hypothalamus, DMPFC and precuneus. Differences in GEA or valence were not present in conditions in either contrast and are thus not represented by this conjunction.

tional valence, but no modulation by GEA. Similar patterns were found for males and females when analyzed separately (Supplementary Fig. 1).

Control for emotional valence and intensity in erotic stimuli. In view of our behavioral data, we conducted a further conjunction analysis where we conjoined the contrast [positive bodily > positive non-bodily pictures] with the one [negative bodily > negative non-bodily pictures]. As can be seen in our behavioral data, both contrasts showed significant effects of SSI whereas this was not the case for valence or GEA, which did not differ in negative pictures (Fig. 4a). Resulting common regions thus mirror the specific effects of sexual intensity so that we were able to specifically control for effects of emotional valence and GEA in positive bodily, e.g., erotic, stimuli. This analysis revealed foci in the hypothalamus and VS as well as in the DMPFC, precuneus, SPL, FFA and LOC ($p<0.05$, corrected; Fig. 4b and Table 3).

Common and interacting regions between sexual and general emotional processing

Common regions in sexual and general emotional processing. Regions that showed higher activity in bodily-emotional (i.e., positive and negative) compared to non-bodily-emotional (i.e., positive and negative) picture conditions and a higher activity in non-bodily-emotional compared to neutral conditions were re-

Table 3
Effects specific for differences in sexual intensity ($p<0.05$, corrected, $k>10$)

Region	Conjunction: [positive bodily > positive non-bodily] ^ [negative bodily > negative non-bodily]	
	Coordinates (x, y, z)	Z-values
VS	−9, 9, 6;	3.44;
	9, 9, 3;	4.64;
Hypothalamus	−9, 3, −13;	3.73;
DMPFC	−6, 51, 27;	3.93;
LOC	−51, −75, −6;	5.33;
	54, −66, 0;	5.03;
SPL	−33, −57, 54;	4.79;
	33, −57, 57;	4.86;
Precuneus	9, −63, 39;	4.21;
FFA	45, −42, −24;	3.81;

VS: ventral striatum, DMPFC: dorsomedial prefrontal cortex, LOC: lateral occipital complex, SPL: superior parietal lobe, FFA: fusiform face area.

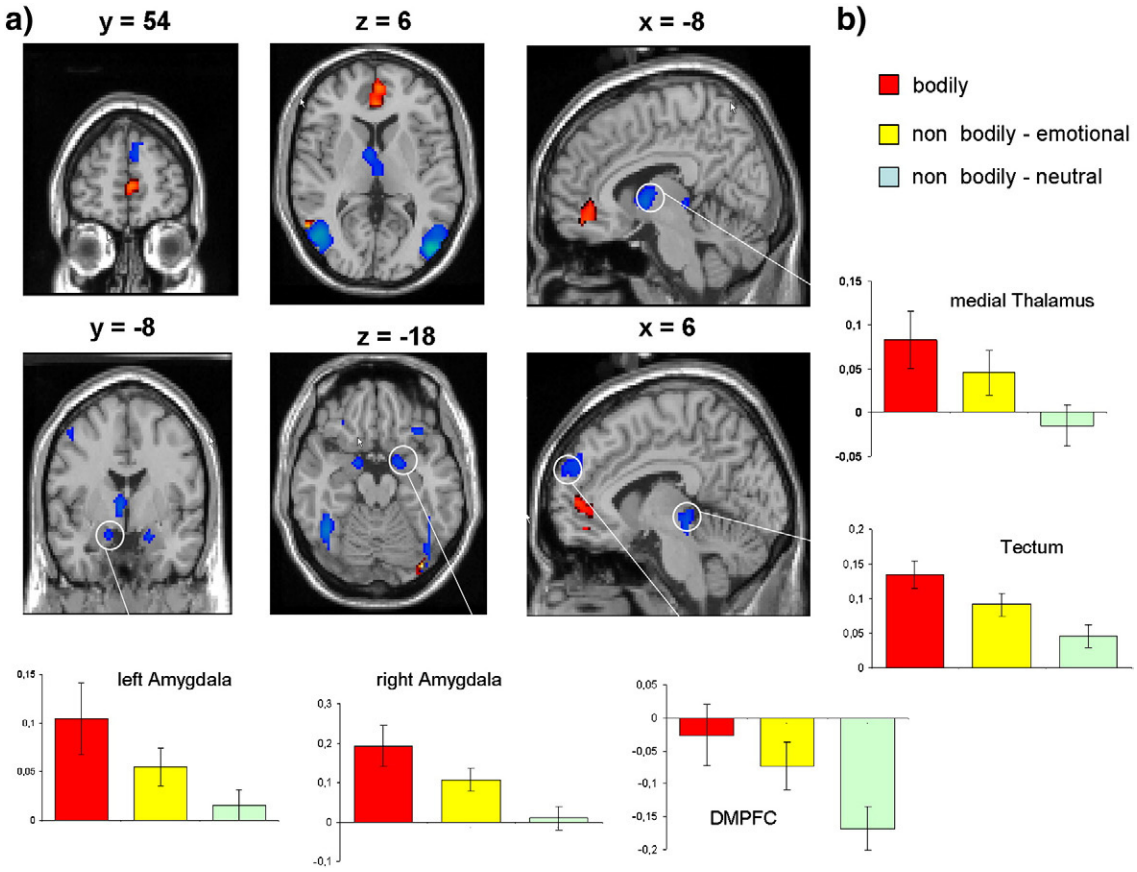

Fig. 5. Common and interacting regions in sexual and emotional processing. (a) Red voxels indicate regions with a significant interaction in processing of sexual arousal and valence, as revealed by the contrast [positive>negative bodily-emotional pictures]>[positive>negative non-bodily-emotional pictures] at $p<0.05$, corrected, $k>10$. Significantly stronger effects in the first contrast were found in the pgACC and bilateral occipital cortex (LOC) (see also Table 4 and bar diagrams in Figs. 1 and 4 for comparison of neural and behavioral effects in pgACC). Blue voxels indicate significant regions for the conjunction of the contrasts [bodily>non-bodily-emotional pictures] and [non-bodily-emotional>non-bodily neutral pictures] at $p<0.05$, corrected, $k>10$. In resulting regions, including amygdala, DMPFC, LOC, tectum and thalamus, activity during non-bodily emotion processing was found to be lower than during processing of bodily stimuli but higher than during neutral picture presentation, reflecting rather general effects of emotional intensity. (b) Bar diagrams plot mean percentage signal changes for bodily, non-bodily-emotional and neutral conditions in these common regions.

vealed by the contrast [all bodily-emotional>all non-bodily-emotional pictures] conjoined with the contrast [all non-bodily-emotional stimuli>all neutral stimuli]. Significant commonalities indicating common effects of GEA were found for the DMPFC, bilateral amygdala, right medial thalamus, dorsal midbrain and bilateral FFA and LOC ($p<0.05$ corrected, k>10, see the blue colored voxels in Fig. 5 and Table 4). To demonstrate signal increases and decreases, we show mean percentage signal changes for all conditions in DMPFC, amygdala, right medial thalamus and dorsal midbrain.

Interaction between sexual and general emotional processing

Regions showing a higher difference between positive and negative stimuli in the bodily-emotional conditions when compared to the non-bodily-emotional conditions, with positive stimuli yielding higher signal intensities than negative stimuli, were tested with the serial subtraction [positive>negative bodily stimuli]>[positive>negative non-bodily stimuli]. Significant differences were found in the pgACC (extending into the VMPFC) and LOC ($p>0.05$ corrected, see red colored voxels in Fig. 5a and Table 4 as well as % signal changes in Fig. 1 for the pgACC).

Discussion

The present study aimed to investigate the neural correlates of specific sexual intensity independent of confounding variables like involvement of general emotional dimensions and bodies. This was achieved by carefully controlling for these factors in both design and analysis. We replicated patterns of activations in a large set of regions previously reported during SA, and we disentangled neuronal mechanisms mediating SSI from activity related to processes of GEA or valence. Neuronal effects in the VS and hypothalamus were independent of differences in emotional valence or GEA, while activation in the pgACC depended on an interaction of SSI and valence.

This distinction was further supported by a correlation between neural activity in the VS and MPOA and SSI ratings alone, and a correlation between activity in the pgACC and SSI as well as valence ratings. The interaction between SSI and emotional valence was

Table 4
Common regions for bodily and non-bodily-emotional picture viewing ($p<0.05$, corrected, $k>10$)

Region	Conjunction: [bodily-emotional > non-bodily-emotional] ^ [non-bodily-emotional > non-bodily neutral]	
	Coordinates (x, y, z)	Z-values
Amygdala	−15, 3, −18;	3.72;
	18, 0, −18;	4.00;
Thalamus	9, 0, 0;	4.48;
Dorsal midbrain	3, −24, 0;	4.00;
LOC	−48, −81, 0;	6.88;
	51, −69, 0;	6.17;
FFA	42, −45, −24;	4.78;
Inferior frontal gyrus	39, 33, −9;	4.08;
DMPFC	−6, 54, 30;	3.54;

LOC: lateral occipital cortex, FFA: fusiform face area, DMPFC: dorsomedial prefrontal cortex.

restricted to the pgACC and LOC, while a main effect of GEA independent of SSI was found for the DMPFC, amygdala, medial thalamus and midbrain. Our findings support earlier models of SA favoring involvement of certain brain regions in distinct components of sexual arousal.

Specific involvement of hypothalamus and VS

Recent imaging findings of hypothalamic activity during SA and particularly during penile erection led researchers to discuss its involvement especially in autonomous aspects of behavioral responses to erotic stimuli (Karama et al., 2002; Mouras, 2004; Redoute et al., 2000). However, given its fundamental role in mediating all kinds of autonomous, i.e., hormonal responses, it could not be excluded that hypothalamic activation during SA reflected a rather more general emotional arousal.

Our findings demonstrate for the first time that the hypothalamus is specifically involved in processing sexual intensity in humans independent of general emotional dimensions or bodies. This complements recent behavioral and neurohormonal findings. The hypothalamus has been shown to be specifically involved in copulatory behavior and erection in many animals (McKenna, 1999; Meisel, 1983; Meisel and Mullins, 2006). In humans, paraventricular hypothalamic secretion of oxytocin was reported to be increased during SA in males and females (Carmichael et al., 1987, 1994). In a recent study, Ferretti et al. (2005) found highest hypothalamic responses during the onset of penile erection in males, suggesting its particular involvement in triggering a behavioral response to a condition that is specifically sexually intense. In contrast to other regions like the insula and somatosensory cortex, hypothalamic activity was not elevated during sustained erection when compared to phases were no erection was recorded (Ferretti et al., 2005). Georgiadis and Holstege (2005) related hypothalamic activity to a specific neural process of sexual intensity rather than to actual sexual performance. This involvement of the hypothalamus in the initial phase of sexual arousal (Ferretti et al., 2005; Moulier et al., 2006), as opposed to the course of sexual performance, would favor its detection in designs using short-term visual stimulation. This was the case in our study, while other studies focusing on longer periods of sexual arousal, did not find reliable hypothalamic activations using blocked designs (Mouras, 2006). However, as we did not directly compare both long and short stimulus types, this remains to be tested by further studies.

The relation of hypothalamic activation to reported specific sexual intensity was also suggested by Karama et al. (2002). They further found this behavioral measure to sufficiently account for neural differences in activations between males and females, when the female group of their study reported erotic stimuli being less sexually intense. We could confirm this finding as, even on a considerably liberal statistical threshold, we did not find different hypothalamic activations when no differences of reported SSI existed between genders.

Considering the rewarding nature of sexual incentives, our findings, especially in the ventral parts of striatum, may be interpreted as mirroring implicit reward processing. The nucleus accumbens has been found to be essential during reward processing (Knutson and Wimmer, 2007; Wrase et al., 2007; Yacubian et al., 2007). In contrast to other regions like the anterior insula, activations in the VS, i.e., nucleus accumbens, were found to be involved in reward processing irrespective of its emotional value (Jensen et al., 2007). Erotic stimuli could therefore present a highly salient incentive in their own right. This is supported by our finding of a strong, isolated correlation of signal intensities with sexual intensity as rated by our subjects.

Ventral striatal activity is strongly influenced by dopaminergic transmission. While antidopaminergic effects of antipsychotics result in reduced libido and erectile impairment in males, the opposite effect can be observed during pharmacological administration of dopamine agonists (see also Arnow et al., 2002). Dopaminergic inputs originate mainly in the ventral tegmental area (VTA), which was recently found to be involved in the mediation of expectancy of novel visual or somatosensory stimuli (Fairhurst et al., 2007; Wittmann et al., 2007). This finding suggests an attentional modulation by stimulus salience dependent on the context of presentation. However, in our target regions of sexual intensity, namely the hypothalamus and VS, no differences were observed for effects of SSI, when relevant contrasts of expected and unexpected picture conditions were compared. It should also be noted that the reported regions receive also non-dopaminergic inputs.

Both the hypothalamus and VS thus have been previously hypothesized to be key players of specific erotic processing as opposed to mediating structures through elevated but unspecific emotional arousal that normally accompanies sexually arousing situations. To our knowledge, this study is the first to demonstrate this specificity of neural activity on the basis of behavioral and subjective data. This was accomplished by carefully matching for effects of emotions and body during sexual arousal.

Still, our findings should not be interpreted as suggesting that activity in the VTA-VS continuum would be restricted to sexual processes. Instead, it should be pointed out that other affective processes handling, e.g., rewarding or stressful, situations have been shown to activate these regions. The framework of our study only allows to relate activations during sexually arousing conditions to SSI and not to unspecific emotional dimensions such as GEA or valence. However, these dimensions describe aspects that are conceptualized in cognitive-attributional emotion theories while SSI would share more characteristics with primary emotive systems such as the expectancy command system (Panksepp, 1982) or the behavioral activation system (Gray, 1987). In addition to the distinct effects of sexual intensity in the VS and hypothalamus, we found other cortical areas that mediate either general emotional arousal within SA or an interaction of SSI and valence. In a more speculative way, our findings

might allow basic emotion views to primarily prevail in some subcortical regions while more general dimensional views may better reflect the function of higher cognitive systems and related cortical networks.

Interaction of sexual and emotional processes in the ACC

In contrast to the above regions, an interaction of specific sexual intensity and its hedonic value can be proposed for the pgACC. On the one hand, the pgACC showed the strongest parametric modulation of neural activity by reports of sexual arousal. On the other, isolated sexual intensity alone could not promote a higher neural activity in our conjunctional analysis. Further parametric effects of valence were found in the pgACC when the statistical threshold was lowered to $p<0.05$, corrected. The rostral anterior part of the ACC, mainly covering BA 24, receives specific projections from the shell of the nucleus accumbens in primates (Devinsky et al., 1995; Kunishio and Haber, 1994). This region is considered the "affective" subdivision (Bush et al., 2000; Vogt et al., 1992). Support for this view comes from a large set of imaging studies (George et al., 1995; Lane et al., 1997; Phan et al., 2002), as well as projections from the accumbens to the medial thalamus and to limbic as well as paralimbic areas (Devinsky et al., 1995; Russchen et al., 1985; Vogt, 2005).

We consider the pgACC to be a key structure in mediating previously reported interactions of emotional valence and sexual arousal (Bancroft et al., 2003; Lykins et al., 2006; Peterson and Janssen, 2007). The pgACC was found to be the only region with overlapping correlations of reported sexual intensity and emotional valence with neural responses, supporting its role in maintaining an emotional tone in response to internal or external stimuli and generating adapted behavior (Bechara and Naqvi, 2004; Ferretti et al., 2005). Activity in the pgACC was recently further related to personal relevance of stimuli (Phan et al., 2004, 2002) or more explicitly to self-relatedness (Frith and Frith, 1999; Northoff and Bermpohl, 2004). Heinzel et al. (2006) report the ventral part of the medial prefrontal cortex including the pgACC to be specifically related to subjective reports of self relatedness during visual presentation of bodily erotic stimuli.

Effects of general emotional processing

Considering that sexually arousing stimuli are also emotionally arousing, one may expect additional effects in regions which have been previously found to be activated during general emotional processing.

Extensive research revealed the human amygdala to be a core region of emotional processing. However studies of SA have been less consistent in reported effects, including several positive (Ferretti et al., 2005; Hamann et al., 2004; Karama et al., 2002) and negative findings (Arnow et al., 2002; Bocher et al., 2001; Moulier et al., 2006; Stoleru et al., 1999) as well as evidence of deactivations (Georgiadis and Holstege, 2005; Holstege et al., 2003). Inconsistencies have previously been assumed to be related to either low magnitudes of BOLD responses (Moulier et al., 2006), late deactivations common for consummatory phase of erection (Hamann et al., 2004) or even contrary effects of vigilance and sexual responses (Georgiadis and Holstege, 2005; Georgiadis et al., 2006). Due to the specific setup of our experiment, we cannot contribute to the discussion of amygdala responses during later phases of SA. However, in the early phase, we found robust activations. These were unspecific in that they also appeared in non-erotic control conditions when compared to neutral stimuli and disappeared when SSI was controlled for differences in GEA or valence. Consistent with earlier findings (Canli et al., 2002; Hamann and Mao, 2002), amygdala activations could be related to GEA which normally occurs in sexually arousing situations (Canli and Gabrieli, 2004). This would be supported by the finding of Hamann et al. that pictures of opposite-sex nudes did not lead to different amygdala responses, in contrast to pictures of sexual interactions of couples, which were reported to be also more physically arousing (Hamann et al., 2004).

In the same vein, the medial thalamus could be related to GEA during SA as suggested by Karama et al. (2002). In their study, the authors compared explicitly erotic film excerpts to neutral ones, the latter lacking the potential to induce emotional or erotic reactions. They found activations in the mediodorsal thalamic nucleus. For a comparable peak voxel localization, we did not only replicate their finding, but further confirmed their interpretation of this region as being especially related to general emotional processes during SA. This interpretation is supported by anatomical interconnections of the medial and midline nuclei in corticolimbic loops with the MPFC (Siwek and Pandya, 1991), ventral pallidum (Haber et al., 1985) and amygdala (Aggleton and Mishkin, 1984) in human and non-human primates. All these structures could also be related to GEA during SA. These interconnections further include the dorsal midbrain (Velayos and Reinoso-Suarez, 1982) which was also related to GEA by the same conjunction analysis (Fig. 5).

Higher signal intensities in the DMPFC during erotic as compared to non-erotic emotional situations could in the same way be interpreted as representing mainly higher GEA. Contrary to this interpretation, activations were also observed when no difference in emotional valence or GEA was found (Table 3). It should be noted that this conjunction of contrasts comparing positive and negative bodily picture conditions relative to non-erotic conditions of positive or negative valence (Fig. 4) could not be controlled for display of naked humans. Furthermore, sexual interaction of couples has to be regarded as a highly specific social constellation. This has to be taken into account as pictures of persons and social interactions have been reported to elicit strong effects in the DMPFC (Amodio and Frith, 2006; Iacoboni et al., 2004; Mitchell et al., 2002, 2005). This interpretation would be supported by the absence of effects in the DMPFC when the comparison between positive and negative bodily stimuli was entered into the conjunction (Fig. 2 and Table 2). Combining findings from these two conjunctions, we suggest that DMPFC activations are related to higher order processing of socially relevant stimuli, which could also be of particularly high self-relevance. This last notion would be supported by studies reporting effects in the DMPFC for either explicit self relatedness (Phan et al., 2004) or implicit self relatedness during emotional conditions (Heinzel et al., 2006). This early effect of still erotic pictures might, however, be substantially different from DMPFC activations which were specifically correlated with penile tumescence in a later phase of SA (Moulier et al., 2006).

In both DMPFC and ACC, effects were found to modulate the extent of deactivations. This is consistent with previous studies that find robust but unspecific signal decreases in the medial prefrontal cortex (including the rostral ACC) during a large variety of tasks, while showing highest activity at rest (Gusnard and Raichle, 2001). These negative BOLD responses have previously been found to correlate with local concentrations of the inhibitory transmitter GABA (Northoff et al., 2007). Consistent with recent findings (Heinzel et al., 2006), the degree of self relatedness of an external stimulus would thus be correlated with the amount of deactivation,

with highest self-related stimuli leaving activations closest to baseline (Northoff et al., in press).

Finally, emotional stimuli also included non-human stimuli and therefore also depicted fewer human faces than the bodily stimuli. At the same time, faces in neutral pictures showed low emotional expressions. While the present study focused on the distinction of processes related to SSI or GEA, we have to assume that FFA activations during SA may be related to an interaction of face perception and emotions. There is increasing evidence that this interaction might be mediated by connections between the amygdala and visual areas, the FFA in particular (see also Vuilleumier, 2005). However, due to our design, we cannot investigate such processes. Selected IAPS pictures included different views on human faces, and subjects were further free to orient their spatial attention on the whole scene. Thus, face perception as well as possible modulating effects of emotions on face perception cannot be ruled out or disentangled from other motivational aspects attributed to the FFA such as internally generated motivation like hunger or thirst (LaBar et al., 2001; Parsons et al., 2000). Still, according to our results, FFA activations during SA were not observed when controlling for confounding effects of body or emotion (Table 2 and Fig. 4).

At least an interaction of SSI, emotional dimensions and human bodies have to be taken into account for a small cluster of 38 voxels in the right LOC. Activation here remained in both conjunctions which should rule out confounding effects of bodies, GEA, or valence. However, in contrast to the pgACC, no correlation was found for reported GEA, SSI or valence. Furthermore, the interaction analysis of SSI and valence as well as the conjunction of common effects of GEA yielded significant effects in LOC. Bearing in mind the complexity of such an interaction, this finding should be discussed in terms of an "extrastriate body area" (Downing et al., 2001) and reported attentional top-down modulation of visual association areas by emotional relevance (Corbetta et al., 1993; Mouras et al., 2003; Stoleru et al., 1999). This emphasizes the distinction of sexual-bodily and non-sexual-bodily processes in the brain, with mere perception of bodies per se leading to activation rather in visual association cortex than in primary "sex regions".

It should, however, be noted that in our study we cannot make any inference about a specific relation of any of these regions to other aspects of sexual arousal such as penile tumescence in males or comparable genital responses in females. To allow subjects to experience erotic and non-erotic stimuli as undisturbed as possible, we did not obtain measures of erectile responses. In contrast, we concentrated on an early phase, which did not result in full erection but could be matched to GEA or valence more easily. Furthermore, by focusing on this early component of SA, we revealed global mechanisms found in both genders. Although we did not find differences in either subjective ratings or neural responses, we acknowledge that this observation has to be limited to this early phase of SA. Possible gender-specific differences in responses during the course of ongoing sexual arousal, including orgasm, could therefore not be covered by our study.

Conclusion

Focusing on subjective erotic experience in males and females, we compared patterns of differential activation between several regions previously related to a brain network of sexual arousal. Using stimuli of short duration, we could relate activations in the ventral striatum and hypothalamus to SSI independent of induced GEA or valence. An interaction of SSI and emotional valence was found for the rostral anterior cingulate, while activation during SA in other regions could be related to non-specific components of SA including GEA or more complex features of emotional scenes. Due to our methodological design using subjective ratings to guide neural analysis, we were able, for the first time, to neurally differentiate distinct effects of SSI from those related to emotional dimensions or body parts that are inherently involved in sexual arousal.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.neuroimage.2008.01.040.

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