Gender differences in the cognitive control of emotion: An fMRI study

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Abstract

The interaction of emotion and cognition has become a topic of major interest. However, the influence of gender on the interplay between the two processes, along with its neural correlates have not been fully analysed so far.

In this functional magnetic resonance imaging (fMRI) study we induced negative emotion using negative olfactory stimulation while male ($n = 21$) and female ($n = 19$) participants performed an n-back verbal working memory task. Based on findings indicating increased emotional reactivity in women, we expected the female participants to exhibit stronger activation in characteristically emotion-associated areas during the interaction of emotional and cognitive processing in comparison to the male participants.

Both groups were found to be significantly impaired in their working memory performance by negative emotion induction. However, fMRI analysis revealed distinct differences in neuronal activation between groups. In men, cognitive performance under negative emotion induction was associated with extended activation patterns in mainly prefrontal and superior parietal regions. In women, the interaction between emotion and working memory yielded a significantly stronger response in the amygdala and the orbitofrontal cortex (OFC) compared to their male counterparts.

Our data suggest that in women the interaction of verbal working memory and negative emotion is associated with relative hyperactivation in more emotion-associated areas whereas in men regions commonly regarded as important for cognition and cognitive control are activated. These results provide new insights in gender-specific cerebral mechanisms.
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1. Introduction

The interplay between cognitive and emotional processes has become a topic of major interest (Gray, Braver, & Raichle, 2002; Ochsner & Gross, 2005; Taylor & Fragopanagos, 2005; Vuilleumier, 2005). On the one hand, negative emotion induction has been reported to be associated with impaired performance in a verbal working memory task (Gray, 2001; Gray et al., 2002). However, the opposite pattern was detectable for spa-

tial stimulus material (Gray, 2001; Gray et al., 2002). Clinical studies, on the other hand, have attributed an attention-enhancing effect to stimulus-inherent emotional valence suggesting largely automated processing of emotional material as exhibited, for example, in phobia patients (Kopp & Altmann, 2005; Rinck & Becker, 2005, 2006).

The question of how the processes interact on a functional cerebral level is currently unresolved. As already stated by Gray et al. (2002) there are several possible models of neural interaction, taking into consideration both mutually modulating influences as well as the predominantly parallel processing of emotion and cognition. Several recent imaging studies examining the neural correlates of cognitive-emotional interaction in terms of the cognitive regulation of emotion found that up- and

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down-regulating (negative) emotion recruited mainly "cognitive areas" (i.e., prefrontal and anterior cingulate regions), known to play an important role in cognitive control. Thus, activation in "emotional areas", mainly the amygdala and the orbitofrontal cortex (OFC), was modulated up or down in concordance with the regulatory goal (Ochsner, Bunge, Gross, & Gabrieli, 2002; Ochsner & Gross, 2005; Ochsner et al., 2004; Ohira et al., 2006; Phan et al., 2005).

Hence, accumulating evidence suggests that emotion influences cognition and vice versa and that these reciprocal influences are associated with modifications in cerebral activation. Surprisingly, the influence of gender in the context of cognitive-emotional interaction has not been examined so far, despite numerous gender studies on the behavioural or functional cerebral level addressing emotional or cognitive processes separately.

Investigating cognitive processing in terms of verbal working memory, several studies have examined potential differaences between men and women. They found either no differences in behavioural performance between males and females (Bell, Willson, Wilman, Dave, & Silverstone, 2006; Goldstein et al., 2005) or higher accuracy in women as compared to men (Speck et al., 2000). With regard to cerebral activation, these studies revealed differences in terms of significantly stronger signal changes in women (in middle, inferior, and orbital prefrontal regions; Goldstein et al., 2005) as well as significantly greater mean activation in men (with a greater number of pixels activated in the right superior parietal and right inferior occipital gyrus, and a greater BOLD signal in the left inferior parietal lobe; Bell et al., 2006) as well as in terms of lateralization (with a more left-lateralized activation in women; Speck et al., 2000).

In relation to emotional processing, a comprehensive quantitative meta-analysis (Wager, Phan, Liberzon, & Taylor, 2003) found no general gender differences in brain activation patterns in response to emotions (apart from the fact that men seem to exhibit more lateralized activation whilst women's brainstem regions are seemingly more frequently activated). However, gender differences have been reported for the processing of emotion when induced by olfactory stimulation with women exhibiting a stronger signal in the left OFC independent of hedonic valence (Royet, Plailly, Delon-Martin, Kareken, & Segebarth, 2003).

Irrespective of these somewhat contradictory imaging findings, women are generally regarded as "more emotional" than men. They are more vulnerable to disorders that affect emotions (Sloan & Kornstein, 2003) and have been found to display stronger emotion-specific physiological responses during emotion processing (Kring & Gordon, 1998; Labouvie-Vief, Lumley, Jain, & Heinze, 2003). Men, on the other hand, have been shown to be better able to cognitively control negative emotions (Birditt & Fingerman, 2003) or to be more prone to use cognitive control strategies to counter negative affect (Thayer, Newman, & McClain, 1994). Hence, gender-associated differences with regard to cognitive-emotional interplay or the ability to cognitively regulate emotional states seem plausible and invite analysis.

Our study focused on two main aspects. First, gender differences in the processing and control of emotion during cognitive load was investigated. In most neuroimaging studies, gender has been and still is a rather neglected factor, a situation which should not go on unchallenged. Most results are generalized based on findings of only one gender or mixed samples, in which gender differences have not been analysed due to unequal or restricted sample sizes. The acknowledgement of possible gender differences is however a prerequisite for valid generalized results especially in a context where behavioural as well as cerebral sex differences have been reported. Only the exact characterization of the cerebral correlates of defined functions, taking moderating variables such as gender into account, can build a valid basis for the translation of basic research into clinical context. Second, emotion and cognition constitute the most central components of human life and have been shown to be closely intertwined. In most psychiatric disorders, such as depression or dementia, affective symptoms and impairments demonstrate impressively their influence on cognitive functionality as do cognitive impairments on mood and well-being, respectively. Hence, the investigation of cerebral correlates of (different) strategies of healthy males and females in the regulation of emotion in view of cognitive demands (with the consequence of a reduced or maintained performance level) may have clinical implications.

The present study is, to our knowledge, the first to examine potential gender differences in the interaction of emotion and cognition. For this purpose, we induced negative emotion by means of negative olfactory stimulation (with rotten yeast) while male and female participants performed a verbal working memory task. We relied on olfactory stimulation as it can easily be applied simultaneously with the cognitive task without further increasing the cognitive load. In preceding studies (Schneider et al., 1999, 2000, 2006) we found olfactory stimulation to be an effective method for emotion induction due to the tight anatomical connections between the olfactory system and the limbic cortex. A further major advantage of the olfactory emotion induction is the possibility of dissociating the two primary affective dimensions, intensity and valence. It therefore constitutes an effective standardized and validated method of mood induction. Following our preparatory study (Schneider et al., 2006) on a behavioural level, we hypothesized that participants would show a poorer performance during the more complex 2-back task as compared to the 0-back condition and that this difference would be aggravated by the effect of the negative olfactory stimulation, proving especially detrimental during the cognitively more challenging 2-back condition. Against the background of the experimental findings mentioned above, which indicated a stronger emotional reactivity in women compared to men, we also expected female participants to exhibit a significantly poorer performance under negative emotion induction as compared to their male counterparts.

Accordingly, for the fMRI analysis of the effect of emotion, we hypothesized stronger activation for females compared to males in typically "emotional" regions like middle temporal areas, the amygdala or the orbitofrontal cortex and other parts of the cortico-limbic system. We anticipated that these activations would also be more pronounced in females during the interaction of negative emotion and verbal working memory. Since men

were found to be more prone to counter negative emotion cognitively (Birditt & Fingerman, 2003; Thayer et al., 1994) male participants on the other hand would show significant activation in areas, which have repeatedly been associated with verbal working memory as well as cognitive control processes (i.e., prefrontal and parietal areas or the dorsal anterior cingulate).

2. Materials and methods

2.1. Subjects

Participants were closely screened for medical, neurological, and psychiatric history. The Structured Clinical Interview for DSM-IV (SCID-I, German version; Wittchen, Zaudig, & Fydrich, 1997) was performed to exclude lifetime diagnosis for axis I. Urine drug screenings guaranteed the preclusion of subjects with current drug abuse. Subjects with first-degree relatives with psychiatric disorders were excluded. Furthermore, the usual exclusion criteria for MRI were applied (e.g., metallic objects in the body, tattoos, disorders that affect cerebral metabolism). After a detailed description of the study, written informed consent was obtained. The local Institutional Review Board approved the protocol.

Before scanning, an olfactory screening with the Sniffin' Sticks Test (Hummel, Konnerth, Rosenheim, & Kobal, 2001), a multiple forced choice task which allows the differentiation between anosmia, hyposmia and normosmia, was performed to guarantee that all subjects had normal olfactory functioning. The German MWT-B (Lehrl, 1989) multiple-choice vocabulary test served for crystalline verbal intelligence estimation.

Forty right-handed (according to Edinburgh Inventory, Oldfield, 1971) healthy volunteers took part in the study, 19 women and 21 men. Fourteen of the male participants already have been included in the study of Habel et al. (2007). The male subjects had a mean age of 31.43 years (S.D. = 10.43), a mean education of 12.52 years (S.D. = 2.99) and a mean IQ of 111.38 (S.D. = 16.29; MWT-B). The female group had a mean age of 32.47 (S.D. = 10.77). Their education averaged 12.32 years (S.D. = 2.50) and their IQ constituted 114.53 (S.D. = 9.86). The two groups did not differ significantly in terms of age ($t = -.31$, df = 38, $p = .757$), mean education ($t = .24$, df = 38, $p = .814$) or verbal intelligence ($t = -.75$, df = 33.39, $p = .461$). There was also no significant difference in the ratio of smokers and non-smokers ($\chi^2 = .07$, df = 1, $p = .787$) with 4 smokers and 17 non-smokers in the male group compared to 3 smokers and 16 non-smokers in the female group.

2.2. Stimuli and tasks

Single black letters (A–Z) were presented in a pseudo-randomized order and appeared for 500 ms on a white background (via PRESENTATION software package; Neurobehavioral Systems Inc., San Francisco, CA). In the following 900 ms a fixation cross was shown in the middle of the screen (baseline phases). Activation phases demanded pressing a button (LUMItouch™, Lightwave Technologies, Richmond, B.C., Canada) with the right index finger to the predefined target letter X during the 0-back task (selective attention) and a response to any letter that matched the last but one letter seen during the 2-back task (attention and verbal working memory). For each run, letters were presented with a ratio of 60 non-targets to 35 targets in the 0-back and the 2-back conditions, respectively. 0-back and 2-back conditions alternated, always intermitted by the low-level baseline condition. The paradigm was arranged as a block design consisting of two runs (one per olfactory stimulation condition) of 8 min, each with 10 fixation baseline phases (18 s each) and 10 activation blocks of 0-back and 2-back phases (30 s each, Fig. 1).

Thus, both selective attention and working memory were assessed during the n-back task. Olfactory stimulation with either neutral ambient air or the nauseous odour of rotten yeast took place only during 0-back and 2-back conditions. Participants were instructed to continue breathing regularly through the nose without holding their breath. Each olfactory stimulus was applied for 3 s every 5 s (Fig. 1). Since a block design is susceptible to habituation effects, especially in the primary olfactory cortex (Poellinger et al., 2001) we decided against a continuous odour flow.

For the negative olfactory stimulation, the odour of rotten yeast was chosen (Zucco et al., 1989) since it is perceived as unpleasant but has no toxic side
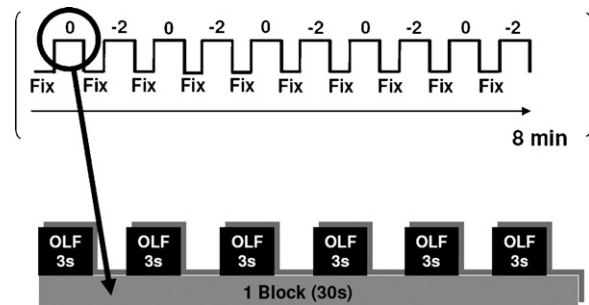

Fig. 1. fMRI block design consisting of two runs of 8 min each with 10 baseline fixation phases (Fix) lasting 18 s and 10 activation blocks (0-back/2-back) lasting 30 s each. During the activation phases, participants experienced either neutral or negative olfactory stimulation (depending on the run) every 5 s for 3 s (OLF). The order of the valence of stimulation was permuted across subjects.

effects. Furthermore, rotten yeast stimulates only the olfactory nerve of the olfactory system (which is closely linked to emotional areas) but not the trigeminal nerve, which amongst others mediates tactile sensations of the face unwanted in investigating brain activation during olfactory-induced emotion induction. Twenty grams of fresh, commercially available yeast were dissolved in 200 ml of water and kept at a constant temperature of 30 °C (86 °F) for 2 weeks. Ambient air served as neutral stimulus. Air and rotten yeast were applied through single tubes with an olfactometer as described earlier (Schneider et al., 1999, 2000) and delivered to the subjects' right nostril at constant temperature (30 °C/86 °F) and pressure (50 ml/s). The presentation order of air and rotten yeast was permuted across subjects.

After each of the two runs, subjects were asked to rate the respective odour using the Self Assessment Manikin (SAM; Lang, 1980), including a 10-point unipolar rating scale for intensity (1 = no perception, . . ., 10 = very intensive) and non-verbal visual manikins corresponding to 5-point bipolar rating scales for emotional valence (1 = very pleasant, . . ., 5 = very unpleasant) as well as arousal (1 = very nervous, . . ., 5 = very relaxed). Furthermore, the emotional self rating (ESR) scale was applied, a 5-point unipolar intensity scale (1 = not at all, . . ., 5 = extreme) for the specificity of the experienced emotion (Schneider, Gur, Gur, & Muenz, 1994).

2.3. Data acquisition

Imaging was performed on a 1.5 T Sonata MR scanner (Siemens Medical Systems) in the Institute of Neuroscience and Biophysics—Medicine, Research Centre Jülich. Structural images were acquired using an MP-RAGE three-dimensional T1-weighted sequence (voxel size: 1 mm × 1 mm × 1 mm, sagittal FoV: 256 mm × 256 mm, 160 slices, TR = 2.2 s, TE = 4 ms, TI = 1200 ms, alpha = 15°). Functional images were collected with echo-planar imaging (EPI) sensitive to BOLD contrast (T2*, voxel size: 3.125 mm × 3.125 mm × 3 mm, 64 × 64 matrix, FoV: 200 mm × 200 mm, 32 slices, 3 mm thickness, TR = 3.2 s, alpha = 90°). Slices covered the whole brain and were positioned transaxially parallel to the anterior–posterior commissural line (AC–PC). A specialised whole-brain EPI sequence was applied, providing optimised BOLD sensitivity in sub-cortical limbic brain regions as well as in cortical areas. Sub-cortical areas are affected by susceptibility-induced signal loss (Deichmann, Josephs, Hutton, Corfield, & Turner, 2002) which can be compensated by an echo time reduction of the EPI sequence. It is well-known from theory and experimental work that an echo time of approximately 60 ms is optimal for fMRI of the cortex at 1.5 T. However, the optimal echo time in sub-cortical regions such as the amygdala reduces to about 40 ms for AC-PC slice orientation (Stöcker et al., 2006). Therefore, the used EPI sequence performed a bottom-up slice-dependent variation of the echo time (TE) with an intermediate transition zone: the lower eight slices were scanned at a TE of 40 ms followed by a linearly increasing TE up to 60 ms in the next six slices and a constant TE of 60 ms in the remaining 18 slices (for further details see Stöcker et al., 2006). Two scanning runs of 154 functional image volumes were collected, with the initial four images excluded from subsequent analyses in order to remove the influence of T1 stabilization effects.

2.4. Data analysis

Performance of the 0-back and 2-back task was assessed by the mean number of correct reactions ('hits'). Repeated measures ANOVAs with the within-subject factors task (0-back, 2-back) and emotion (neutral, negative) and the between-subject factor gender were performed. Two female participants had to be excluded from the ANOVA because their behavioural data had not been recorded due to technical problems.

For the subjective scores of the SAM valence and intensity ratings, as well as the ESR rating, non-parametric Wilcoxon tests were calculated to find out whether participants' judgments differed between negative and the neutral olfactory stimulation or between females and males. Since previous studies of our own (Habel et al., 2007; Schneider et al., 2006) consistently confirmed the specificity of the emotion 'disgust' in response to rotten yeast, we restricted the analysis of the ESR ratings to its disgust subscale.

FMRI data analysis was accomplished via SPM2 software (Statistical Parametric Mapping; Wellcome Department of Cognitive Neurology, London, UK; http://www.fil.ion.ucl.ac.uk/spm). After realignment and stereotaxic normalization (2 mm × 2 mm × 2 mm), a 10 mm full-width-at-half-maximum (FWHM) Gaussian smoothing kernel was applied to optimize the signal-to-noise ratio and compensate for inter-subject anatomical variation. A 0.00781 Hz high-pass filter removed low frequency noise.

For further analysis the fixation baseline was subtracted from the activation contrasts (0-back and 2-back). Verbal working memory brain activation was analysed for each subject contrasting the 2-back against the 0-back condition. The effect of negative emotion induction was calculated by subtracting brain activation during neutral olfactory conditions (ambient air) from that during negative stimulation (rotten yeast). The interaction effect of emotion and cognition was specified contrasting the effects of working memory and negative emotion induction (i.e., [2-back negative–0-back negative] − [2-back neutral–0-back neutral]).

To investigate gender differences in brain activation during cognition and emotion respectively, at the second level, the intra-subject contrast images for emotion (negative versus neutral olfactory stimulation) and verbal working memory (2-back versus 0-back) were subjected to two-sample t-tests between males and females at a significance level of $p < .001$ uncorrected (extent threshold: five voxels).

ANCOVAs were calculated for the second order interaction effect of working memory and negative emotion, i.e. the intra-subject contrasts for the emotion by cognition interaction were subjected to an ANCOVA contrasting males and females. Unwanted effects of inter-individual differences in the decline of behavioural working memory performance due to negative emotional stimulation were monitored by including these differences as covariates of no interest (i.e., the number of hits during the neutrally stimulated 2-back condition minus the number of hits during the negatively stimulated 2-back condition; see also Habel et al., 2007). As the interaction between working memory and negative emotion was the focus of the present study, first order (i.e., within-subject) interactions were additionally computed by means of two emotion-by-cognition ANCOVAs for both groups separately (in addition to the direct ANCOVA gender comparison). For consistency, and to obviate bias, statistical significance was again determined at a significance level of $p < .001$ uncorrected (extent threshold: five voxels). Since a differentiation in activation and deactivation is hard to achieve, especially for group comparisons of complex interaction contrasts, parameter estimates from the corresponding ANOVAs are displayed for each condition (minus fixation baseline).

3. Results

3.1. Subjective and behavioural data

The analysis of perceived valence, intensity and arousal for the two odours by means of the SAM revealed that negative olfactory stimulation was successful with regard to emotion induction: participants rated the negative odour as significantly more unpleasant ($Z = -4.81$, $p < .001$) and intensive ($Z = -4.42$,

$p < .001$) than the neutral ambient air and their arousal was higher during the negative olfactory stimulation ($Z = -2.69$, $p = .007$). Also, on the ESR disgust scale the appraisal of yeast and air differed significantly ($Z = -4.42$, $p < .001$) revealing a greater feeling of disgust in response to the negative olfactory stimulation.

Males and females did not differ significantly in any of the mentioned sub-scales (Table 1) except for the perceived intensity of air. Here, males experienced the neutral stimulus as more intensive than the females did. There was no difference between the perceived valence, induced arousal, disgust experienced or the intensity of the negative odour between the sexes.

Mean number of hits fulfilled the assumptions for parametric testing (two-sample Kolmogorov–Smirnov Test, Levene's Test of Equality of Error Variances and Mauchly's Test of Sphericity/Greenhouse-Geisser, respectively). The repeated measures ANOVA with the within-subject factors task (0-back, 2-back) and emotion (neutral, negative) and the between-subject factor gender revealed a significant main effect for task ($F = 28.48$, d$f = 1$, 36; $p < .001$) and emotion ($F = 5.81$, d$f = 1$, 36; $p = .021$) as well as a significant interaction between task and emotion ($F = 6.13$, d$f = 1$, 36; $p = .018$). No significant effects were found for gender ($F = .06$, d$f = 1$, 36; $p = .817$), and its interaction with task ($F = .05$, d$f = 1$, 36; $p = .834$) or emotion ($F = 2.51$, d$f = 1$, 36; $p = .122$) or the interaction of all three factors (task × emotion × gender; $F = 1.29$, d$f = 1$, 36; $p = .263$).

3.2. fMRI Data

3.2.1. Verbal working memory

The two-sample t-test for the working memory contrast (2-back versus 0-back) revealed stronger activations in the lingual gyrus on both sides in males compared to females (*right*: $x = 10$, $y = -62$, $z = -6$, $k_E = 12$, $T = 3.52$, $p = .001$; *left*: $x = -10$, $y = -64$, $z = -6$, $k_E = 13$, $T = 3.51$, $p = .001$), whereas, the women showed stronger activations in a widespread network, namely the middle and posterior cingulate gyri, the left angular gyrus, bilateral middle temporal regions, inferior temporal areas on the left side as well as several bilateral frontal regions including the right inferior frontal gyrus (Table 2, Fig. 2).

3.2.2. Negative olfactory-induced emotion

While males did not exhibit a significantly stronger signal than females in any region for the contrast of negative emotion, females displayed stronger activation in the left superior temporal gyrus, the right inferior frontal gyrus and the left insula (Table 3).

3.2.3. Interaction of working memory and negative olfactory stimulation

In the group of female participants no significant activation was found in the ANCOVA for the interaction between verbal working memory and negative emotion (with the number of hits during the neutrally stimulated 2-back condition minus the number of hits during the negatively stimulated 2-back condition as

Table 1
Comparisons of the SAM subscales valence, arousal and intensity and the ESR subscale disgust (Wilcoxon test) between males and females: mean (±S.D.), Z-scores and p-values

Subscale	Induced emotion	Males, mean (±S.D.)	Females, mean (±S.D.)	Z	p
Valence (SAM)	Neutral	3.00 (±.45)	2.74 (±.93)	−1.31	.191
Valence (SAM)	Negative	4.33 (±.66)	4.11 (±1.10)	−.52	.601
Arousal (SAM)	Neutral	4.52 (±.81)	4.00 (±1.37)	−1.00	.317
Arousal (SAM)	Negative	3.57 (±1.17)	3.79 (±1.51)	−.90	.368
Intensity (SAM)	Neutral	3.05 (±2.13)	4.79 (±2.62)	−2.16	.031
Intensity (SAM)	Negative	7.95 (±2.11)	6.79 (±2.96)	−1.27	.206
Disgust (ESR)	Neutral	1.29 (±.56)	1.26 (±.56)	−.19	.852
Disgust (ESR)	Negative	2.95 (±1.28)	2.26 (±1.24)	−1.71	.087

Table 2
Working memory contrast (SPM2, two-sample t-test, $p < .001$ uncorrected, extent five voxels): stronger activation in females compared to males (MNI coordinates)

Region	Side	x	y	z	k_E	Max. SPM {T}	P_{uncorr}
Medial superior frontal gyrus, BA 6	L	−6	30	56	1344	6.02	<.001
Inferior frontal gyrus, BA 47	R	32	28	−20	6	3.58	<.001
Inferior frontal/frontal operculum	L	−44	14	20	16	3.80	<.001
Precentral gyrus, BA 6	L	−44	0	22	18	3.91	<.001
Precentral gyrus, BA 4	L	−60	−20	40	21	3.66	<.001
Middle cingulate gyrus, BA 24	R	14	−12	40	186	3.95	<.001
Posterior cingulate gyrus, BA 31	L	−8	−50	28	409	5.56	<.001
Middle temporal gyrus, BA 21	R	54	2	−20	94	4.31	<.001
Middle temporal gyrus, BA 21	L	−58	6	−28	30	4.08	<.001
Inferior temporal gyrus, BA 20	L	−56	−12	−28	43	4.06	<.001
Angular gyrus, BA 39	L	−48	−66	30	101	4.45	<.001

variable of no interest). In the male group, however, one-sample analysis yielded significant activation in several areas including the right precuneus, inferior parietal areas on the left side, the anterior, middle and posterior cingulate, the right thalamus as well as left dorsolateral and right inferior frontal areas (Table 4, Fig. 3).

The direct comparison of males and females for the interaction contrast resulted in more brain activation in the left inferior parietal lobe, right middle temporal gyrus and left superior occipital lobe in males (Table 5, Fig. 4) as opposed to more activation in the left amygdala and the right orbitofrontal cortex in females (Table 6, Fig. 5).
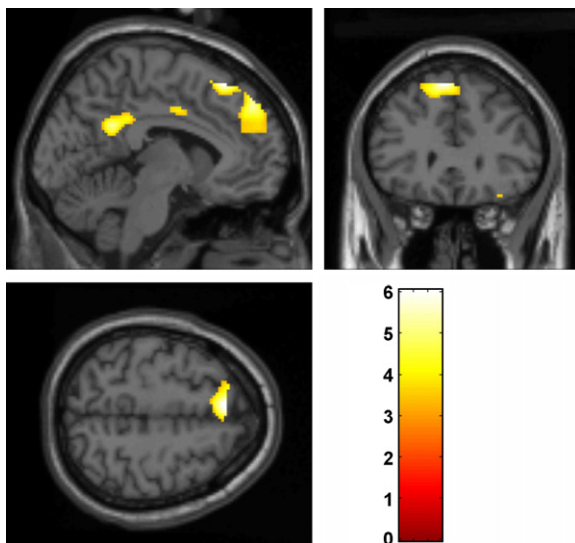

Fig. 2. Working memory contrast (two-sample t-test, $p < .001$ uncorrected, extent five voxels): stronger brain activation in females compared to males in the middle and posterior cingulate gyrus and medial prefrontal areas.
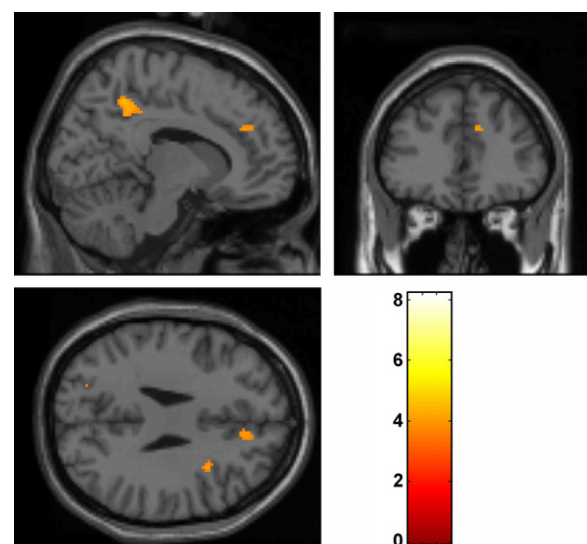

Fig. 3. Brain activation in the male group during the interaction of working memory and negative emotion (ANCOVA with the number of hits during the neutrally stimulated 2-back condition minus the number of hits during the negatively stimulated 2-back condition as variable of no interest; $p < .001$ uncorrected, extent five voxels): amongst others in the anterior cingulate gyrus and the precuneus.

Table 3
Contrast of negative emotion (SPM2, two-sample t-test, p < .001 uncorrected, extent five voxels): stronger activation in females compared to males (MNI coordinates)

Region	Side	x	y	z	k_E	Max. SPM {T}	P_{uncorr}
Inferior frontal gyrus, BA 45	R	54	20	16	10	3.55	.001
Superior temporal gyrus, BA 22	L	−66	−22	4	40	4.78	<.001
Insula	L	−38	−22	−2	5	3.48	.001

Table 4
Interaction between working memory and negative emotion ([2-back negative–0-back negative] − [2-back neutral–0-back neutral]) for the male participants (SPM2, ANCOVA, p < .001 uncorrected, extent five voxels, MNI coordinates)

Region	Side	x	y	z	k_E	Max. SPM {T}	P_{uncorr}
Middle frontal gyrus, BA 8	L	−26	30	36	48	4.23	<.001
Inferior frontal lobe/frontal operculum	R	34	10	28	15	3.95	<.001
Precentral gyrus, BA 4	L	−40	−22	62	82	4.30	<.001
Precentral gyrus, BA 4	L	−42	−10	62	14	4.29	<.001
Anterior cingulate gyrus, BA 32	R	12	38	28	23	3.98	<.001
Anterior cingulate gyrus, BA 32	L	−14	12	40	117	4.90	<.001
Middle cingulate gyrus, BA 24	R	18	−10	40	24	4.16	<.001
Middle cingulate gyrus	R	16	14	42	13	3.70	.001
Posterior cingulate gyrus, BA 29	L	−28	−46	6	34	3.98	<.001
Middle temporal gyrus, BA 37	R	42	−64	10	215	6.76	<.001
Postcentral gyrus, BA 3/4	L	−34	−24	40	68	4.01	<.001
Postcentral gyrus, BA 5	L	−26	−44	58	14	3.86	.001
Parietal lobe, BA 40	L	−32	−46	38	850	8.17	<.001
Supramarginal gyrus	R	30	−40	44	127	6.11	<.001
Precuneus, BA 7	R	12	−48	46	94	4.49	<.001
Superior occipital gyrus, BA 19	R	24	−80	36	196	4.89	<.001
Cerebellum	L	−8	−56	−26	5	3.96	<.001
Thalamus	R	20	−26	14	10	4.00	<.001
Insula	R	36	−24	24	25	4.12	<.001
Caudate	L	−4	6	16	19	4.07	<.001

Table 5
Interaction between working memory and negative emotion: stronger activation in males compared to females (SPM2, ANCOVA, p < .001 uncorrected, extent five voxels, MNI coordinates)

Region	Side	x	y	z	k_E	Max. SPM {T}	P_{uncorr}
Middle temporal gyrus, BA 39	R	46	−64	10	34	4.97	<.001
Supramarginal gyrus, BA 40	L	−32	−46	38	149	5.69	<.001
Superior occipital lobe	L	−22	−68	36	70	3.84	<.001

4. Discussion

The present study aimed at systematically examining gender-specific processing in association with the interplay of emotional and cognitive processes.

4.1. Performance data

Men as well as women performed significantly worse during negative olfactory stimulation, but only in the more complex

2-back condition. Our results correspond with earlier studies on female subjects and mixed gender samples (Bartolic, Basso, Schefft, Glauser, & Titanic-Schefft, 1999; Gray, 2001; Gray et al., 2002) as well as a recent study of our own (Schneider et al., 2006) in which significant impairments in verbal working memory performance in association with negative emotion experience were detectable.

However, the working memory performance of the female subjects did not, against all expectations, show signs of being significantly more impaired by emotion induction when com-

Table 6
Interaction between working memory and negative emotion ([2-back negative–0-back negative] − [2-back neutral–0-back neutral]): stronger activation in females compared to males (SPM2, ANCOVA, p < .001 uncorrected, extent five voxels, MNI coordinates)

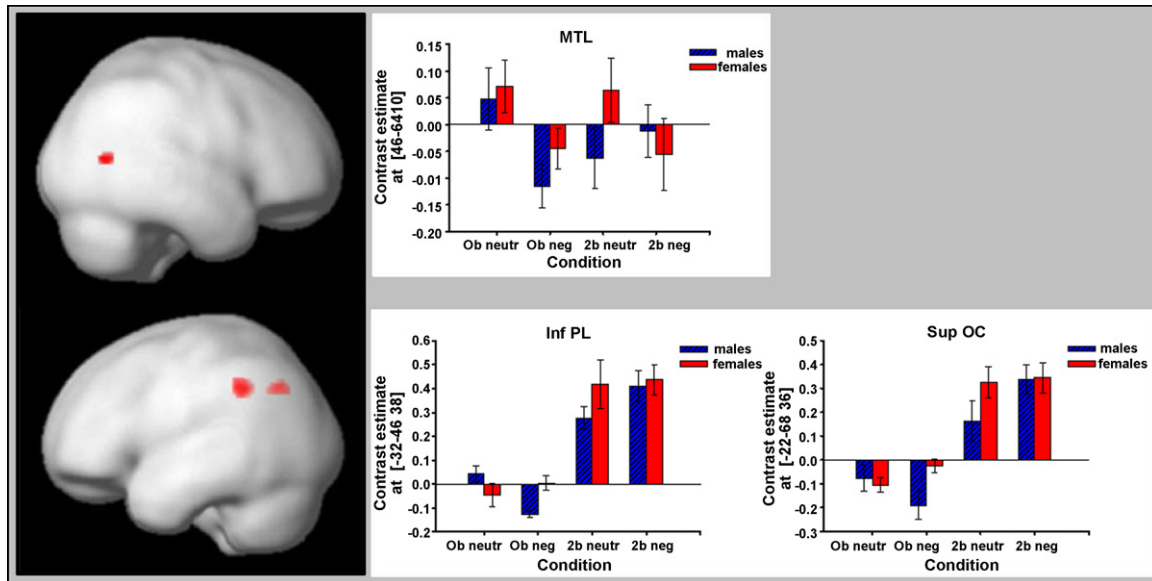| Region	Side	x	y	z	k_E	Max. SPM {T}	P_{uncorr}
Inferior orbitofrontal gyrus, BA 11	R	28	16	−22	5	3.55	<.001
Amygdala	L	−22	−2	−12	10	3.60	<.001

Fig. 4. Interaction of working memory and negative emotion (ANCOVA, $p < .001$ uncorrected, extent five voxels): significantly stronger activation in males compared to females in the right middle temporal gyrus, left inferior parietal lobe and left superior occipital lobe. Parameter estimates (±standard error) are displayed on the right. Fixation baseline was subtracted from all conditions.

pared with male counterparts. There are several possible reasons for this finding. Firstly, since according to subjective ratings both sexes experienced a similar intensity of negative emotion, this might have resulted in similar effects of emotion on working memory performance. Secondly, it is important to bear in mind that performance is not directly and exclusively linked to

processing efficiency (Gray et al., 2005). The same number of correct responses in two groups may be based on completely different brain activation patterns. Or, in other words, different activation mechanisms can in fact be associated with the same behavioural performance with different strategies leading to the same goal.
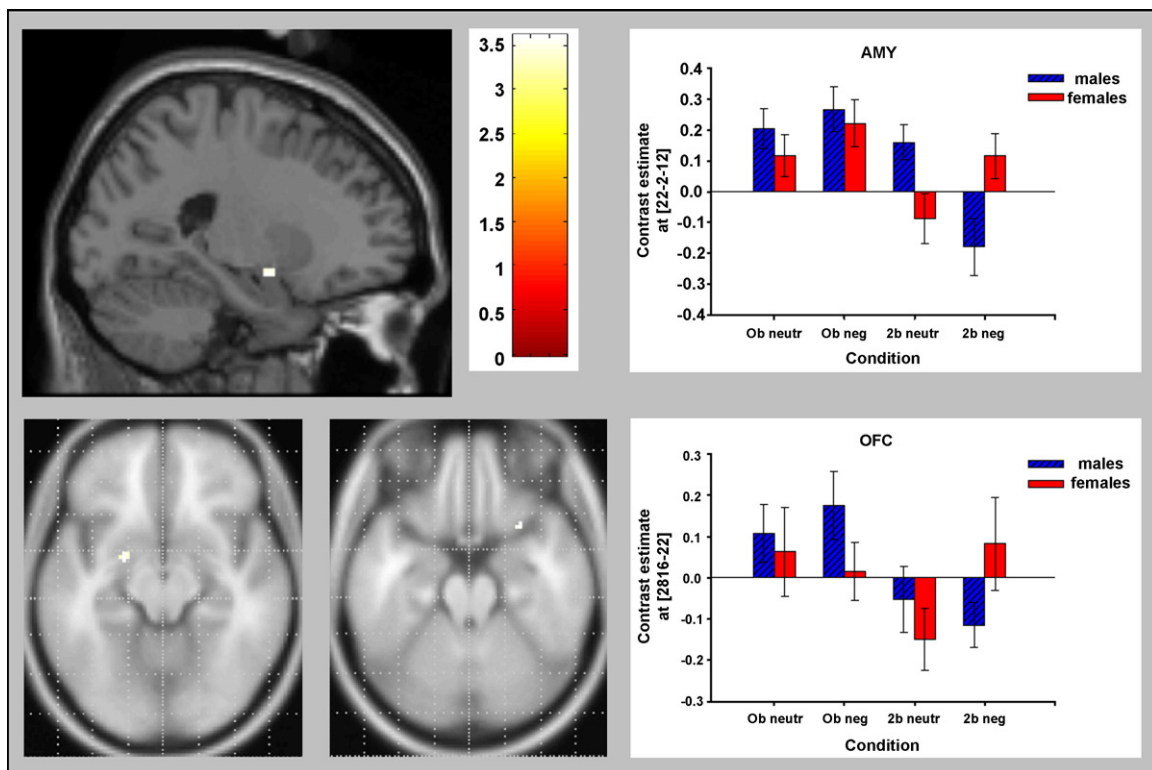

Fig. 5. Interaction of working memory and negative emotion (ANCOVA, $p < .001$ uncorrected, extent five voxels): significantly stronger activation in females compared to males in the left amygdala and the right orbitofrontal gyrus. Parameter estimates (±standard error) are displayed on the right. Fixation baseline was subtracted from all conditions.

4.2. FMRI data

4.2.1. Working memory

With regard to verbal working memory in particular, several relative activation differences were found, despite the lack of differences in behavioural performance between groups. While, men displayed stronger activation only in the lingual gyrus when compared to women, females showed significantly stronger activation in a network consisting of mainly right inferior and bilateral superior prefrontal, bilateral middle and left inferior temporal as well as posterior cingulate regions. This significantly stronger working memory-associated activation corroborates the assumption that female participants recruit several task-relevant regions (predominantly the superior PFC and the angular gyrus) to a significantly stronger degree than the male participants. Hence, the results presented indicate that in women, working memory processes for verbal material involve a more extensive network of brain regions. The similarity of performance between the groups moreover demonstrates that different strategies can lead to the same result.

Gender differences in working memory are contradictory. While Speck et al. (2000) reported comparable activation patterns in mainly prefrontal and parietal regions in men and women (more left-lateralized in women), Bell et al. (2006) found greater activation in males in several regions. Our findings support those of Goldstein et al. (2005) who applied an auditory verbal working memory task and found significantly more signal in women in middle, inferior, and orbital prefrontal regions despite no significant differences in performance between the sexes. The inconsistency of these studies seems to be mainly ascribable to methodological differences as Bell et al. applied a numerical working memory task and analyses in the study by Speck et al. differed from ours with regard to the contrasts performed (i.e., they contrasted 2-back versus baseline instead of 2-back versus 0-back).

4.2.2. Negative emotion

As assumed, negative emotion yielded significantly stronger brain activation in females than males in a region which is mainly associated with the processing of negative emotions; the insula has repeatedly been found to be critically involved in the processing of negative emotion, predominantly disgust (Schafer, Schienle, & Vaitl, 2005; Wright, He, Shapira, Goodman, & Liu, 2004). Moreover, present findings correspond with a recent study on gender differences in emotion perception which reported significantly more activation in females compared to males in superior temporal regions during negative emotion induction (Hofer et al., 2006).

4.3. Interaction between cognition and emotion—specific gender characteristics

Whilst female subjects revealed stronger activation for both main effects, the interaction of both processes revealed no activation for the one-sample t-test in the female group. The lack of significant activation during the interaction implies that in women emotional and cognitive processing run predominantly parallel—with little, if any, crossover activation. Thus, while exclusive cognitive processing (of verbal material) is strongly reticular involving a wide-spread bilateral cerebral network in women, the processing of cognition and emotion seems to run predominantly along separate pathways. The assumption that in women (structural or functional) connectivity between emotional and cognitive areas is rather weak could be a (somewhat speculative) conclusion from the present data.

In the male group, the analysis of the interaction between working memory and negative emotion exhibited an extensive fronto-parieto-cingulate network comprising mainly of dorsolateral prefrontal regions on the left side, the right inferior frontal lobe, left inferior parietal regions, the right precuneus and anterior, middle and posterior cingulate areas. Thus, our findings imply predominately parallel processes of emotion and cognition in females and mutually modulating processes in males.

In line with our expectations regarding the male participants, the interplay of emotion and cognition activated regions suggested a critical involvement in the cognitive control of emotion (Beauregard, Lévesque, & Bourgouin, 2001; Hariri, Bookheimer, & Mazziotta, 2000; Lévesque et al., 2003; Ochsner et al., 2002, 2004; Ohira et al., 2006; Phan et al., 2005). It has previously been noted that the anterior cingulate and the prefrontal cortex, mainly in dorsal medial and lateral prefrontal areas are activated during emotion regulation by cognitive reappraisal (Ochsner et al., 2002), during suppression of sadness via detachment (Lévesque et al., 2003) and controlled emotion suppression (Phan et al., 2005). These areas in the lateral PFC have been attributed with a high sensitivity for emotional-cognitive interaction (Perlstein, Elbert, & Stenger, 2002; Simpson et al., 2000). Moreover, the precuneus, which was activated significantly in males, has recently been found to correlate negatively with behavioural performance decrement in verbal working memory performance during negative emotion induction (Habel et al., 2007).

4.4. Interaction between cognition and emotion—gender differences

Interestingly, when directly comparing both groups for the interaction contrast a significantly stronger signal was detectable in males in the left inferior parietal cortex, a region generally regarded as important in the context of attention and working memory processes (for a review, see Naghavi & Nyberg, 2005). Moreover, this region has been found to be involved in olfactory working memory processing (Dade, Zatorre, Evans, & Jones-Gotman, 2001) as well as in tasks examining olfactory recognition memory (Cerf-Ducastel & Murphy, 2006). In addition, there was significantly stronger activation in large parts of the temporo-parieto-occipital association cortex. Thus, the direct group comparison indicated increased activation in the male participants in "perceptual-cognitive" regions, although there was, contrary to our expectations, no hyperactivity in any frontal region.

However, in line with our hypothesis, there was relatively greater activity in the amygdala (on the left side) and the right OFC (bordering at the insula) in the female participants during

working memory and negative emotion compared to working memory activation during neutral stimulation. Therefore, as opposed to the male participants, the female subjects exhibited stronger activity in regions known to be responsible for the processing of predominantly negative emotions (for a review, see Phan, Wager, Taylor, & Liberzon, 2004). Decreases in activation have been repeatedly observed here under successful emotion regulation (Beauregard et al., 2001; Lévesque et al., 2003; Ochsner et al., 2002; Phan et al., 2005) as well as constant activation levels under unsuccessful emotion regulation in psychiatric disorders (Davidson, Putnam, & Larson, 2000; Phillips, Drevets, Rauch, & Lane, 2003; Shin et al., 2004). As illustrated by the parameter estimates in Fig. 5, differences in activation levels in the amygdala and the OFC of males and females were closely linked to the working memory-task taking place under the influence of the two emotions. Interestingly, unlike the female participants, who showed activation in these regions during the interaction of verbal working memory and negative emotion, male subjects obviously inhibited or even deactivated these areas.

Hence, while the within-group analysis indicates the absence of an interaction between working memory and emotion in females, suggesting instead the predominantly parallel processing of the two, the direct group comparison suggests that in females (as compared to males) emotion-associated activation outweighs working memory-associated activation when both processes interact. It is important to note, however, that this effect results from the direct comparison of the two groups. In males as compared to females, on the other hand, the interaction is associated more strongly with cognition, where cognitive control seemingly outweighs emotion-associated activation.

One potential cause of gender differences in brain function currently under discussion is differential regional volumetric brain size. Women have been found to possess relatively larger bilateral volumes in several areas, mainly dorsolateral (BA 46), orbital (BA 47), inferior and superior frontal gyri (Goldstein et al., 2001; Luders et al., 2005; Schlaepfer et al., 1995). However, in the present study, differential activation was mostly lateralized and differed depending on the contrast analysed. Both findings argue against structural differences as the cause of the activation differences detected between the genders.

4.5. Concluding remarks and limitations of the study

These results provide initial evidence for the assumption that the interaction between emotion and cognition relies on differential processing mechanisms in men and women. This further underscores the importance of considering gender as a major factor of influence in neuroimaging findings on emotion and cognition as well as their interplay. In men, brain activation during verbal working memory performance under negative emotion induction compared to neutral emotion suggested a strong interaction of emotion and cognition as well as an increased cognitive control as compared to women. In females, emotional and working memory processes seem to run more parallel with relative hyperactivation in more "emotional" areas compared to males.

With regard to future studies on emotional-cognitive interaction, several aspects have to be taken into consideration. Although olfactory stimulation constitutes a very effective method for inducing emotion, for the purpose of comparison, the implementation of a different emotion induction method could prove informative. Furthermore, it must be noted that disgust, which has been the predominant emotion in our study, is only one aspect of negative emotional experience. Another limitation of our study is that the women involved were at different phases of their menstrual cycle. As hormonal levels may have an important influence on the activation of certain brain areas (Berman et al., 1997; Shaywitz et al., 1999) investigating such hormonal effects might be a promising avenue for future studies.

More detailed knowledge about gender-specific mechanisms for the effective cognitive regulation of negative emotion may be helpful in improving our understanding of human behaviour in general as well as for devising effective therapeutic measures in a clinical context.

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