Altered Brain Activity During Emotional Empathy in Somatoform Disorder

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Abstract: Somatoform disorder patients suffer from impaired emotion recognition and other emotional deficits. Emotional empathy refers to the understanding and sharing of emotions of others in social contexts. It is likely that the emotional deficits of somatoform disorder patients are linked to disturbed empathic abilities; however, little is known so far about empathic deficits of somatoform patients and the underlying neural mechanisms. We used fMRI and an empathy paradigm to investigate 20 somatoform disorder patients and 20 healthy controls. The empathy paradigm contained facial pictures expressing anger, joy, disgust, and a neutral emotional state; a control condition contained unrecognizable stimuli. In addition, questionnaires testing for somatization, alexithymia, depression, empathy, and emotion recognition were applied. Behavioral results confirmed impaired emotion recognition in somatoform disorder and indicated a rather distinct pattern of empathic deficits of somatoform patients with specific difficulties in “empathic distress.” In addition, somatoform patients revealed brain areas with diminished activity in the contrasts “all emotions”–“control,” “anger”–“control,” and “joy”–“control,” whereas we did not find brain areas with altered activity in the contrasts “disgust”–

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"control" and "neutral"–"control." Significant clusters with less activity in somatoform patients included the bilateral parahippocampal gyrus, the left amygdala, the left postcentral gyrus, the left superior temporal gyrus, the left posterior insula, and the bilateral cerebellum. These findings indicate that disturbed emotional empathy of somatoform disorder patients is linked to impaired emotion recognition and abnormal activity of brain regions responsible for emotional evaluation, emotional memory, and emotion generation. *Hum Brain Mapp* 33:2666–2685, 2012. © 2011 Wiley Periodicals, Inc.

Key words: fMRI; somatoform disorder; emotion; empathy

INTRODUCTION

Somatoform disorders, a group of complex diseases consisting of medically unexplained somatic symptoms [Hiller et al., 2010; Kirmayer et al., 1994; Pedrosa Gil et al., 2009; Stein and Muller, 2008], are linked to alexithymia-associated emotional dysfunctions as underlying psychological basis [Bach and Bach, 1996; Bailey and Henry, 2007; Bankier et al., 2001; Burba et al., 2006; Duddu et al., 2003; Grabe et al., 2004; Mattila et al., 2008; Pedrosa Gil et al., 2008; Wood et al., 2009].

In addition to alexithymia, which means diminished emotional awareness, somatoform patients also exhibit problems in emotion recognition (i.e., the correct labeling of emotions). Pedrosa Gil et al. [2009] found significant problems in the overall recognition of emotional faces in somatoform patients. Psychodynamic concepts of somatoform disorders suggest, that impaired emotion recognition in somatoform disorder is caused by the (unconscious) repression of emotions to avoid interpersonal conflicts [Bowlby, 1973; Maunder and Hunter, 2004; Waller and Scheidt, 2006].

Empathy refers to the ability of understanding and sharing emotions in social contexts [Decety and Jackson, 2004; Decety and Moriguchi, 2007; Lamm et al., 2007; Preston and de Waal, 2002]. According to a recent concept provided by Shamay-Tsoory [2011], two underlying systems can be distinguished: "emotional empathy" (i.e., the sharing of another's emotional state) and "cognitive empathy" (i.e., "the adoption of another's psychological point of view"). Regarding this, emotional empathy overlaps with other emotional processes such as "emotional contagion" (i.e., the sharing of another's emotional state without awareness that the own emotional state was induced by another individual, which differs from "emotional empathy," because in the latter a distinction between self and other is possible [Lamm et al., 2007; Preston and de Waal, 2002]) and "emotion recognition" [Nomi et al., 2008; Shamay-Tsoory, 2011].

With reference to the study of Pedrosa Gil et al. [2009], which demonstrated disturbed emotion recognition in somatoform disorder patients (see above), empathic deficits of somatoform disorder patients are likely. Even more, if one considers the connections between alexithymia and impaired emotional empathy [Decety and Moriguchi, 2007;

Guttman and Laporte, 2002; Williams and Wood, 2010]. However, empathic deficits in somatoform patients have not been investigated so far.

Furthermore, little is known about the neural mechanisms underlying the disturbed emotion processing (and empathy) of somatoform disorder patients. To our knowledge, only one recent study investigated brain activity of Korean patients suffering from Hwa-Byung, a Korean, culture-bound disorder, which resembles somatoform disorder with regard to medically unexplained symptoms [Lee et al., 2009; Min, 2008; Min and Suh, 2010; Min et al., 2009]. The authors reported increased activity in patients' lingual and fusiform gyrus during the perception of neutral, sad, and angry stimuli, and lower activity in the thalamus [Lee et al., 2009]. It is not known, whether the same mechanisms also apply to somatoform disorders.

However, emotional empathy and cognitive empathy have been investigated intensively in healthy subjects, and sets of relevant brain regions have been identified: During emotional empathy a brain network consisting of anterior cingulate cortex, anterior insula, superior temporal cortex, amygdala, and inferior frontal cortex is reliably involved [Carr et al., 2003; de Greck et al., 2011a; Fan et al., 2011; Jabbi et al., 2007; Wicker et al., 2003]. During cognitive empathy, the superior temporal sulcus, medial prefrontal cortex, the temporal poles, and the inferior frontal cortex are active [Hooker et al., 2008, 2010; Ochsner et al., 2004]. In addition, the neural correlates of emotion recognition have been investigated in healthy subjects. Here, a similar network including the amygdala, insula, inferior frontal cortex, but also the putamen and somatosensory cortex is active [Adolphs et al., 2000; Derntl et al., 2009; Gur et al., 2002; Sprengelmeyer et al., 1998]. As the study by Nomi et al. [2008] showed, both processes (i.e., emotion recognition and emotional empathy) induce neuronal activity in the same regions (including the inferior frontal gyrus, middle frontal gyrus, superior frontal gyrus, and others), underlining the close link between the emotion recognition and emotional empathy.

Since empathy is important for our survival and success in social environments [Blair, 2003; Decety and Moriguchi, 2007; Gallese et al., 2004] and deficits in empathy have been associated to impaired social functioning [Henry et al., 2008], it is crucial to learn more about the exact

relationship between disturbed emotion processing and empathic deficits in somatoform disorder. This study aimed to investigate the exact pattern of empathic dysfunctions in somatoform disorder patients and the underlying neural substrates. We applied an empathy task in which subjects were instructed to share the affective state of presented emotional faces. Facial stimuli displaying anger, disgust, joy, and a neutral state were applied; in addition, trial based evaluations of the subjective impression of empathic abilities were acquired. Moreover, fMRI allowed for simultaneously monitoring of empathy related neural responses. Further, clinical scales (Symptom Check List 90-R, Toronto Alexithymia Scale, Beck Depression Inventory), an empathy test (Interpersonal Reactivity Index), and an emotion recognition test (Tübinger Affekt Batterie, the German version of the Florida Affect Battery) were applied.

Hypotheses

We hypothesized that the applied behavioral questionnaires revealed disabilities in emotion recognition and emotional empathy of somatoform patients. In addition, we expected diminished neuronal activity in brain regions involved in emotion recognition such as insula, inferior frontal cortex, putamen, somatosensory cortex. Moreover, we were prepared to find diminished activity in brain regions involved in emotional empathy (such as anterior cingulate cortex, anterior insula, superior temporal cortex, amygdala, and inferior frontal cortex) or cognitive empathy (such as superior temporal sulcus, medial prefrontal cortex, the temporal poles, and the inferior frontal cortex). With regard to psychodynamic explanations of somatoform disorder, we hypothesized impaired empathic abilities and altered neural activity for specific emotions, rather than overall emotional deficits. In particular, we expected the largest problems in social emotions, such as anger and joy, whereas non-social emotions such as disgust or neutral expression should lead to fewer differences.

METHODS

Ethical Approval

The study was ethically approved by the Institutional Review Board of the Otto-von-Guericke University of Magdeburg/Germany. After a detailed explanation of the study, all subjects gave informed consent. The study was conducted at the Otto-von-Guericke University of Magdeburg/Germany.

Participants

We investigated 20 patients (gender: 12 females, 8 males; handedness: 19 right-handed, 1 left-handed; age: mean = 42.5, s.d. = 14.0). All patients suffered from a somatoform disorder as ascertained by a trained psychologist using the Structured Clinical Interview for DSM-IV (German version: SKID, [Wittchen et al., 1997]). More precise, 13 of the 20

patients fulfilled criteria of an undifferentiated somatoform disorder (DSM-IV: 300.81), 5 of the 20 patients had a pain disorder (DSM-IV: 307.80), and 2 of the 20 patients had a somatization disorder (DSM-IV: 300.81). All patients were recruited at the start of an inpatient psychotherapy. Patients were recruited from the Department of Psychosomatic Medicine and Psychotherapy of the Otto-von-Guericke-University Hospital in Magdeburg (11/20), from the Department of Psychotherapeutic Medicine of the Fachklinikum Uchtspringe (4/20), and from the Department of Psychosomatic Medicine and Psychotherapy of the AWO Hospital Jerichow (5/20). Six of the 20 patients were on psychotropic medication with duloxetine (1/20), duloxetine and trimipramine (1/20), opipramol (1/20), opipramol and paroxetine (1/20), doxepine (1/20), and hypericum (1/20) during the time point of the fMRI session.

Twenty gender and age matched healthy controls were also recruited in this study (gender: 12 females, 8 males; handedness: 16 right-handed, 2 left-handed, 2 both handed; age: mean = 37.0, s.d. = 10.6, $t(38) = 1.387$; $P_{\text{two-tailed}} = 0.173$). All subjects received financial compensation for their participation in the study.

Psychological Measures

We applied the following psychological measurements to control for differences between the patient group and the group of healthy subjects.

Somatization

Somatization was assessed using a German edition of the "Symptom Check List 90-Revised Version" (SCL-90-R, [Derogatis, 1977; Franke, 2002]). The SCL-90-R is a 90 item self-report questionnaire, which contains a number of subscales such as somatization, depression, and anxiety. Here, we focused on the somatization subscale. The SCL-90-R somatization score was collected from 16 control subjects and 19 somatoform patients.

Emotional awareness

To test for emotional comprehension and awareness, we applied a German edition of the "Toronto Alexithymia Scale-20" (TAS-20, [Bagby et al., 1994; Bressi et al., 1996]), a well-established self-descriptive questionnaire. TAS-20 scores were recorded for 19 healthy subjects and 20 somatoform patients.

Mood state

Subjective experience of depressive symptoms was assessed with a German edition of the "Beck Depression Inventory" (BDI, [Beck et al., 1961]). BDI scores were obtained from 18 healthy subjects and 20 somatoform patients.

Empathy

Empathy was assessed using the Interpersonal Reactivity Index (IRI, [Davis, 1983]). The IRI is a well-established

questionnaire, which allows to test for four different empathy categories: “empathic fantasy,” “empathic concern,” “empathic distress,” and “perspective taking.” IRI scores were collected from 19 healthy subjects and 20 somatoform patients.

Emotion recognition abilities

We used the “Tübinger Affekt Batterie” (TAB, [Breitenstein et al., 1996]), the German version of the “Florida Affect Battery” (FAB, [Bowers et al., 1999]) to test for emotion recognition abilities. We applied four subtests of the TAB: the TAB 3, which uses emotional face stimuli to test the ability to visually recognize different emotions; the TAB 5, which uses emotional face stimuli to check the ability to associate one emotional stimulus to a congruent other emotional stimulus; the TAB 8a, which uses spoken emotional sentences to test for the ability identify prosody and semantic content; and the TAB 8b, which uses spoken sentences as the TAB 8a, but applies a number of incongruent auditory stimuli (i.e., sentences with different prosody and emotional content). The emotion conditions applied in the TAB are: anger, joy, fear, sadness, and neutral. TAB scores were obtained from 14 healthy subjects and 20 somatoform patients.

Paradigm

We applied a paradigm that contained a combination of two tasks: a reward anticipation task and an empathy task. The tasks were separated from each other in a block wise manner. Due to the complexity of the study, here we report only results obtained from the empathy blocks. (See [de Greck et al., 2011b]) for the results obtained during the reward anticipation paradigm).

Experimental design

The fMRI experiment consisted of 6 blocks of 630s. Blocks 1, 3, and 5 were reward blocks; blocks 2, 4, and 6 were empathy blocks. Prior to the scanning subjects read detailed information about the paradigm with all the tasks and completed a couple of trial runs in order to familiarize them with the experiment. While lying in the scanner, the stimuli were displayed using the “Presentation” software package (Neurobehavioral Systems, Albany, CA), and were projected onto a matt screen via an LCD projector, which was visible through a mirror mounted on the head coil.

Empathy blocks

Every empathy block started with a short finger-tapping task. This task was included to have the later option of identifying each subject’s hand field of the primary motor cortex (due to complexity reasons, the results of this task cannot be reported here). This was directly followed by the actual empathy session, which started with the presen-

Figure 1.

Paradigm of the fMRI study. Every trial began with a 5 s lasting sole display of an emotional face or the presentation of a control stimulus. Subjects were instructed to empathize with the presented emotional face, which was expressed by the instruction phrase “please try to share the emotional state of the shown person.” Immediately after the presentation of the emotional face a subjective evaluation task was presented and subjects were asked to rate their ability to empathize with the preceding picture. For this, the subjects were trained to move a virtual bar of a visual analogue scale. Prior to the following empathy trial a short inter trial interval was presented, which lasted for 2 or 3 s. The facial stimuli included the emotion conditions anger, disgust, joy, and neutral emotional state. As control, stimuli served smoothed pictures with unrecognizable contents. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

tation of a short instruction lasting for 6 s. A total number of 40 empathy trials were presented in a random order. Figure 1 illustrates the task. After every eight empathy trials, a short pause of 6, 7, or 8 s duration occurred; during pauses the fixation cross was presented. At the end of each block, subjects were asked to evaluate their present feeling for contentedness as well as their impression of engagement in the empathy task, by virtually moving a bar on a visual analogue scale.

Stimuli

The emotional face stimuli were taken from the “Japanese and Caucasian Facial Expressions of Emotion

(JACFEE) and Neutral Faces (JACNeuF)-battery provided by Matsumoto and Ekman [Matsumoto and Ekman, 1988]. Of every emotion (namely anger, disgust, joy, and neutral) eight different facial stimuli were shown, resulting in a total number of 32 different facial stimuli. The emotions were presented by the same number of Caucasian and Japanese actors (Japanese face stimuli were included to keep the number of repeated presentations of each face stimulus as small as possible), half of them female, half of them male. As control stimuli served eight smoothed pictures with unrecognizable contents. Relying on a previous study, which implemented unrecognizable stimuli [Gerlach et al., 2002], we produced the control stimuli by transformation of the neutral stimuli using a smoothing procedure. We decided to implement unrecognizable stimuli (and not for instance neutral stimuli) to avoid any (even automatic) empathic responses. Since empathic responses might be induced by the mere presentation of facial stimuli, even without emotional expressions [de Greck et al., 2011a], and even without a specific instruction to empathize [Yamada and Decety, 2009], we favored unrecognizable stimuli over neutral stimuli. Another reason for us not to implement neutral stimuli was the possibility that the somatoform patients might have misrecognized neutral stimuli. The tendency to misrecognize facial stimuli is not only known for somatoform patients [Pedrosa Gil et al., 2009], but also for depressed patients [Csukly et al., 2009]. Subjects were instructed to rate the smallest empathy amount (zero) after the presentation of control stimuli. During the whole experiment, every emotional face stimulus was presented once in each block, and for three times during the entire experiment.

fMRI Data Acquisition

The fMRI data were collected in a 1.5T MR scanner (General Electric Sigma Horizon) via a standard circular polarized head coil. Using a midsagittal scout image, a stack of 23 slices was aligned parallel to the bicomissural plane. During each functional run 320 whole brain volumes were acquired (gradient echo EPI, TR = 2 s; TE = 35 ms; flip angle = 80°; Field of View = 200 × 200 mm²; slice thickness = 5 mm, inter-slice gap = 1 mm, spatial resolution = 3.125 × 3.125 × 5 mm³). Additionally, a T1 weighted image of every subject was acquired.

fMRI Data Analysis

Image processing and statistical analyses were carried out using the software package AFNI (<http://afni.nimh.nih.gov/afni/>, [Cox, 1996]). The first five volumes were discarded to compensate for saturation effects. All functional images were slice-time corrected with reference to the acquisition time of the first slice and corrected for motion artifacts by realignment to the first volume. The images were spatially normalized to a standard EPI-tem-

plate provided by AFNI ("TT_EPI") and resampled to 3 × 3 × 3 mm³. Finally, all functional images were smoothed with an isotropic 6 mm full-width half maximum Gaussian kernel. Only runs 2, 4, and 6 were included in the statistical analysis. T1-weighted images were normalized to a standard T1-template provided by AFNI ("TT_avg152T1").

For each subject, regressors of interest were created by the convolution of a gamma response function with the according stimulus time functions [Josephs et al., 1997]. At this, all relevant periods (namely all empathy periods, all evaluation periods, the pauses, and the free interval at the end of each session) were included in the model. In addition, six movement parameters resulting from the motion correction procedure, as well as nine regressors for the third degree polynomial model of the baseline of each block were included as regressors to account for any residual effects of head motion and baseline fluctuations, respectively.

Contrast images were calculated by employing linear contrasts to the parameter estimates for the regressors of each event. The resulting contrast images were then submitted to a second level random-effects analysis. Here, one-sample t-tests (including the 20 healthy subjects) and independent two sample t-tests (comparing the 20 somatoform patients and the 20 healthy subjects) were applied [Friston et al., 1995]. To control for the multiple testing problem, we performed a false discovery rate correction [Nichols and Hayasaka, 2003] and calculated family wise error probabilities. The anatomical localization and labeling of significant activations were assessed with reference to the standard stereotactic atlas of Talairach and Tournoux [1988] and by superimposition of the group contrast images on a mean brain generated by an average of each subject's normalized T1-weighted image.

In a second step, we performed a statistical analysis of the raw fMRI signals. Using the significant clusters from the different contrasts as regions of interest, we extracted fMRI signals from activations found in the second level analysis using sphere shaped regions of interest with a radius of 5 mm. fMRI raw data timecourses were processed using the software package PERL (<http://www.perl.org>). The timecourses were linearly interpolated and normalized with respect to a time window ranging from -6 to 30 s before and after the onset of each event. fMRI signal changes of every event were calculated with regard to the fMRI signal value of the onset of the according event. Mean normalized fMRI signal values from two following time steps (6–8 s after onset of the according event) were included in the statistical analysis. We used Repeated Measurements ANOVAs and independent t-tests to test for differences; Spearman correlations were applied to analyze the association of different clinical and emotional scores (namely the SCL-90-R-somatization score, the TAS-20 score, the BDI score, the IRI-empathic distress score, and the TAB-error rates for anger and joy, as well as overall TAB-error rates) with hemodynamic responses of our regions of interest.

Since six of the patients were on psychotropic medication with drugs, which might have affected their hemodynamic responses, we included additional statistical analyses using independent t-tests, which included the 20 healthy subjects and the 14 patients without medication.

RESULTS

Behavioral Results

Clinical results

As presented in Table I, somatoform patients exhibited increased somatization symptoms (SCL-90-R - somatization), increased alexithymia scores (TAS-20), and elevated depression scores (BDI).

Thirty-five percent of the acute patients (7/20) and none of the patients after psychotherapy had TAS-20 scores greater than 60; TAS-20 scores greater than 60 indicate alexithymia [Kooiman et al., 2000]. Moreover, 45% of the acute patients (9/20) and none of the patients after psychotherapy had BDI scores above 18; BDI scores above 18 indicate moderate or severe depression [Beck et al., 1961].

Empathy

Using an ANOVA, we found a significant effect of the factor group ($F(1,37) = 5.879$, $P = 0.020^*$), as well as a significant effect for the factor IRI-subcategory ($F(3, 111) = 4.957$, $P = 0.003^{**}$). In addition, we found a significant group $\times$ IRI-subcategory interaction ($F(3, 111) = 19.2786$, $P > 0.001^{**}$). Somatoform patients showed a significant difference in the "empathic distress" subcategory of the IRI, whilst all other subcategories prevailed no significant differences (see Table I and Fig. 2a).

Emotion recognition

The ANOVA showed a significant effect for the factors group ($F(1,32) = 8.4265$, $P = 0.007^{**}$) and TAB-subcategory ($F(4,128) = 18.514$, $P < 0.001^{**}$), whilst the interaction of group and TAB-subcategory failed significance ($F(4,128) = 0.841$, $P = 0.502$). Somatoform patients made overall significantly more mistakes in the TAB; with regard to the single emotional conditions, this was also the case for "anger," "joy," "sadness," and "fear." Somatoform patients performed as good as healthy subjects for the emotional condition "neutral," although (see Table I and Fig. 2b).

Trial-based intra-scanner ratings

After each empathy trial, subjects evaluated their subjective impression of empathy capability with regard to the stimulus presented in the preceding trial. The ANOVA did not show a significant effect for the factor group ($F(1,38) = 0.680$, $P = 0.4148$), but a significant effect for the factor emotion ($F(3,114) = 26.843$, $P < 0.001$). The interaction of group and emotion was not significant either ($F(3,114) = 1.9691$, $P = 0.1226$). (See Table I for details.)

Block-based intra-scanner ratings

At the end of each block, participants were asked to evaluate their subjective impression of engagement in the empathy tasks as well as their general contentedness. Statistical analysis revealed no significant differences between healthy subject and somatoform patients for intra scanner ratings of engagement in the empathy task and general contentedness. (See Table I for details.)

fMRI Results

Empathy regions of healthy subjects

The contrast of all emotions together compared with the control condition ("anger" + "disgust" + "joy" + "neutral expression") – "control" showed increased hemodynamic responses in a network of brain regions including the bilateral inferior frontal cortex, the right middle temporal cortex, bilateral amygdala, bilateral occipital cortex and bilateral cerebellum. The contrasts of each single emotion compared to the control condition led to increased hemodynamic responses in several regions, including the inferior frontal gyrus, amygdala, and occipital cortex (see Table II for details).

Empathy regions with diminished activity in somatoform patients

Comparing hemodynamic responses of somatoform patients and healthy controls, we found two regions with diminished hemodynamic responses for the contrast ["anger" + "disgust" + "joy" + "neutral expression"] – "control": the right parahippocampal gyrus and the left amygdala (see Table III and Fig. 3)

When looking for differences between both groups for empathy with single emotions, we found regions with significantly greater hemodynamic responses in controls when compared to patients only for "anger" – "control" (left postcentral gyrus, left superior temporal gyrus, bilateral parahippocampal gyrus, left posterior insula, left amygdala, left cerebellum; see Table III and Fig. 4) and "joy" – "control" (right parahippocampal gyrus, right cerebellum; see Table III and Fig. 5). We did not find brain regions with significant differences in hemodynamic activity for "disgust" – "control" and "neutral" – "control". None of the five contrasts revealed brain regions with increased hemodynamic responses in somatoform disorder patients.

Correlation of clinical scores and hemodynamic responses

We found a significant negative correlation of SCL-90-R-somatization scores and hemodynamic responses for the contrast "anger" – "control" in the left superior temporal gyrus (-33 , -15 , -27 ; $r_{\text{Spearman}} = -0.428$, $P_{\text{one-tailed}} =$

TABLE I. Behavioral results

	Group	<i>n</i>	Mean	95%-CI	<i>t</i>	<i>P</i> _[one-tailed]
Somatization (Symptom-Checklist-90-R-somatization)						
	h	16	42.2	37.8–46.6	4.718	<0.001**
	p	19	65.3	56.6–74.0		
Alexithymia (Toronto-Alexithymia-Scale-20)						
	h	19	36.7	32.8–40.6	6.115	<0.001**
	p	20	54.4	49.7–59.0		
Depression (Beck-Depression-Inventory)						
	h	18	3	0.7–5.3	8.217	<0.001**
	p	20	19.6	16.1–23.1		
Empathy (Interpersonal-Reactivity-Index)						
Empathic fantasy	h	19	23.1	20.7–25.5	0.233	0.816
	p	20	22.7	20.0–25.5		
Empathic concern	h	19	26.7	24.8–28.6	0.550	0.586
	p	20	25.9	23.6–28.2		
Empathic distress	h	19	19.3	16.7–22.0	6.483	<0.001**
	p	20	31.6	28.6–34.5		
Perspective taking	h	19	24.2	21.8–26.5	1.288	0.207
	p	20	22.4	20.7–24.1		
Emotion recognition (Tübinger-Affekt-Batterie)-Error rates						
Total	h	14	14.0%	9.5–18.6%	3.006	0.003**
	p	20	23.1%	18.6–27.7%		
Neutral	h	14	7.1%	2.8–11.5%	1.248	0.111
	p	20	10.7%	6.6–14.8%		
Anger	h	14	10.3%	6.4–14.2%	2.440	0.011*
	p	20	19.4%	12.5–26.2%		
Sadness	h	14	11.0%	5.2–16.7%	2.302	0.014*
	p	20	20.3%	13.9–26.8%		
Fear	h	14	20.1%	14.2–26.0%	2.242	0.016*
	p	20	30.3%	22.7–38.0%		
Joy	h	14	21.0%	11.3–30.6%	2.176	0.019*
	p	20	34.1%	25.7–42.5%		
Intra-scanner empathy ratings-trial based						
Total	h	20	63.6	56.2–71.0	[due to a lack of significant interactions in the ANOVA, t-tests were not calculated]	
	p	20	68.0	60.6–75.5		
Neutral	h	20	57.5	49.3–65.7		
	p	20	70.2	63.1–77.3		
Anger	h	20	59.2	48.6–69.8		
	p	20	62.3	50.9–73.7		
Joy	h	20	80.5	73.5–87.5		
	p	20	83.9	77.2–90.7		
Disgust	h	20	57.2	46.0–68.4		
	p	20	55.0	42.9–67.1		
Intra-scanner ratings-block based						
Engagement	h	20	68.0	61.1–74.9	0.809	0.424
	p	20	73.3	61.6–84.9		
Contentedness	h	20	63.6	54.8–72.3	0.429	0.670
	p	20	69.6	57.6–81.4		

Behavioral results of healthy subjects (h) and somatoform patients (p).

0.034*). All other correlations of SCL-90-R, TAS-20, and BDI scores with hemodynamic responses of any of the regions of interest did not reveal significant results. In addition, we did not find significant correlations of IRI empathic distress scores and hemodynamic responses for one of the regions of interest.

Correlation of emotion recognition error rates and hemodynamic responses in somatoform patients

We found significant negative correlations of TAB error rates for anger with hemodynamic responses of the contrast “anger” – “control” in somatoform patients in three

Figure 2.

Behavioral results. **(a)** Empathy: Empathy was assessed using the Interpersonal Reactivity Index (IRI), which provides the four categories “empathic fantasy,” “empathic concern,” “empathic distress,” and “perspective taking.” We found a significant difference between healthy subjects and somatoform patients only in the “empathic distress” subcategory ($t(37) = 6.483$, $P[\text{two-tailed}] < 0.001^{**}$). **(b)** Emotion recognition Overall performance in the Tübinger Affekt Batterie (TAB, subtests 3, 5, 8a, and 8b). Somatoform patients (P , $n = 20$) made significantly more errors compared to healthy controls (h , $n = 14$) in all emotions taken together as well as in the emotional subconditions “anger,” “sadness,” “fear,” and “joy.” We did not find differences between

somatoform patients and healthy subjects for the subcondition “neutral,” although. When looking for further differences between somatoform patients and controls (applying a post-hoc approach), we found that patients (but not controls) made significantly more mistakes in the subcondition “anger” compared to “neutral” (healthy: $t(13) = 1.162$; $P[\text{two-tailed}] = 0.266$; somatoform patients: $t(19) = 3.693$; $P[\text{two-tailed}] = 0.002^{**}$). The same was the case for “neutral” and “sadness” (healthy: $t(13) = 1.421$; $P[\text{two-tailed}] = 0.179$; somatoform patients: $t(19) = 2.759$; $P[\text{two-tailed}] < 0.012^*$). The error bars reflect the 95% confidence interval. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

regions: the left postcentral gyrus, the left superior temporal gyrus, and the left cerebellum (see Fig. 4 for details). TAB error rates for joy correlated negatively with hemody-

namic responses of the contrast “joy” – “control” in two regions, both located in the right cerebellum (see Fig. 5 for details). No positive correlations were found.

TABLE II. Empathy regions of healthy subjects

Region		x	y	z	T	n	$P_{[FWE]}$
All emotions (“anger” + “disgust” + “happy” + “neutral”) – “control”) $P_{[FDR]} = 0.05$, minimum cluster size 50 voxel							
Left	Inferior frontal cortex	–45	–12	24	5.690	345	<0.001
Right	Inferior frontal cortex	45	–6	15	4.562	223	0.016
Right	Dorsomedial prefrontal cortex	6	–54	21	4.878	53	0.999
Right	Middle temporal gyrus	45	39	0	5.989	55	0.998
Left	Precentral gyrus	–48	9	48	5.299	73	0.954
Right	Precentral gyrus	51	6	39	5.132	85	0.840
Right	Supplementary motor area	6	0	60	3.437	302	0.001
Right	Postcentral gyrus	21	45	66	5.212	88	0.807
Left	Amygdala	–12	12	–18	5.464	321	< 0.001
Right	Amygdala	21	6	–18	6.067	370	< 0.001
Right	Ventral striatum	15	–12	0	5.372	163	0.130
Left	Occipital cortex	–23	91	–19	7.051	543	< 0.001
Right	Occipital cortex	31	87	–19	6.476	618	< 0.001
Left	Cerebellum	–28	87	–23	7.010	543	< 0.001
Left	Cerebellum	–39	47	–29	5.524	543	< 0.001
Right	Cerebellum	44	75	–23	6.389	618	< 0.001
Right	Cerebellum	46	51	–27	4.873	618	< 0.001
Anger (“anger” – “control”) $P_{[FDR]} \leq 0.05$, minimum cluster size 50 voxel							
Left	Inferior frontal gyrus	–48	–24	18	4.942	94	0.096
Right	Inferior frontal gyrus	45	–6	18	4.758	157	< 0.001
Right	Supplementary motor area	6	3	60	5.866	144	0.004
Right	Precentral gyrus	51	6	42	6.219	83	0.160
Left	Postcentral gyrus	–48	6	48	5.854	50	0.741
Right	Postcentral gyrus	18	48	69	4.949	70	0.332
Left	Amygdala	–18	0	–18	7.259	120	0.019
Right	Amygdala	21	6	–18	5.249	96	0.084
Left	Occipital cortex	–39	81	–21	9.752	403	< 0.001
Right	Occipital cortex	33	87	–24	6.524	291	< 0.001
Right	Cerebellum	39	51	–33	5.018	56	0.600
Disgust (“disgust” – “control”) $P_{[FDR]} \leq 0.05$, minimum cluster size 50 voxel							
Left	Inferior frontal gyrus	–45	–27	0	5.855	187	0.002
Left	Supplementary motor area	–4	4	59	4.941	134	0.005
Right	Supplementary motor area	3	2	51	5.547	134	0.005
Left	Occipital cortex	–39	81	–21	10.037	273	0.002
Right	Occipital cortex	27	87	–21	7.625	281	0.002
Right	Cerebellum	39	45	–30	5.046	69	0.330
Joy (“joy” – “control”) $P_{[FDR]} \leq 0.05$, minimum cluster size 50 voxel							
Right	Superior temporal gyrus	28	–5	–19	3.911	263	< 0.001
Right	Supplementary motor area	9	0	60	4.852	64	0.344
Left	Amygdala	–24	15	–18	4.805	83	0.114
Right	Amygdala	19	10	–19	4.505	263	< 0.001
Left	Occipital cortex	–36	81	–21	8.171	273	< 0.001
Right	Occipital cortex	30	84	–24	6.724	413	< 0.001
Left	Cerebellum	–36	48	–27	5.437	60	0.406
Neutral (“neutral” – “control”) $P_{[FDR]} \leq 0.05$, minimum cluster size 50 voxel							
Left	Inferior frontal gyrus	–48	–21	12	5.234	164	0.012
Right	Supplementary motor area	3	0	60	6.564	193	0.003
Right	Amygdala	21	8	–15	5.166	57	0.901
Left	Occipital cortex	–39	81	–21	10.762	410	< 0.001
Right	Occipital cortex	39	75	–24	6.472	402	< 0.001

Active clusters of healthy subjects ($n = 20$). x , y , and z coordinates belong to the peak voxel of the cluster and refer to the Talairach and Tournoux stereotactical space. T -values refer to the peak voxel; n represents the number of voxels in the cluster; $P_{[FWE]}$ describes the family wise error of a cluster of the given size.

TABLE III. Empathy regions with different activity in somatoform disorder patients

All emotions (“anger” + “disgust” + “happy” + “neutral”) – “control”)								
Somatoform patients < healthy subjects, $P_{[\text{uncorrected}]} \leq 0.001$, minimum cluster size 10 voxel								
Region		x	y	z	T	n	$P_{[\text{FWE}]}$	$T_{[20/14]}^*$
Right	Parahippocampal gyrus	30	54	–3	4.851	22	0.664	4.149
Left	Amygdala	–24	–3	–24	5.051	19	0.828	4.129
*All $T_{[20/14]}$ values correspond to $P_{[\text{uncorrected}]} \leq 0.001$								
Somatoform patients > healthy subjects, $P_{[\text{uncorrected}]} \leq 0.001$, minimum cluster size 10 voxel no region								
Anger (“anger” – “control”)								
somatoform patients < healthy subjects, $P_{[\text{uncorrected}]} \leq 0.001$, minimum cluster size 10 voxel								
Region		x	y	z	T	n	$P_{[\text{FWE}]}$	$T_{[20/14]}^*$
Left	postcentral gyrus	–15	39	66	4.294	21	0.899	3.223
Left	superior temporal gyrus	–33	–15	–27	4.165	15	0.998	3.616
Left	parahippocampal gyrus	–33	18	–24	4.319	15	0.998	3.656
Right	parahippocampal gyrus	18	21	–15	4.736	13	0.999	4.972
Left	posterior insula	–36	33	15	4.653	13	0.999	4.375
Left	Amygdala	–21	–3	–21	4.913	17	0.978	5.047
Left	Cerebellum	–36	81	–24	4.635	14	0.999	4.646
*All $T_{[20/14]}$ values correspond to $P_{[\text{uncorrected}]} \leq 0.0029$								
Somatoform patients > healthy subjects, $P_{[\text{uncorrected}]} \leq 0.001$, minimum cluster size 10 voxel no region								
Disgust (“disgust” – “control”)								
Somatoform patients < healthy subjects, $P_{[\text{uncorrected}]} \leq 0.001$, minimum cluster size 10 voxel no region								
Somatoform patients > healthy subjects, $P_{[\text{uncorrected}]} \leq 0.001$, minimum cluster size 10 voxel no region								
Joy (“joy” – “control”)								
Somatoform patients < healthy subjects, $P_{[\text{uncorrected}]} \leq 0.001$, minimum cluster size 10 voxel								
Region		x	y	z	T	n	$P_{[\text{FWE}]}$	$T_{[20/14]}^*$
Right	Parahippocampal gyrus	30	54	–3	4.533	22	0.472	3.601
Right	Cerebellum	33	84	–27	4.811	11	0.997	4.455
Right	Cerebellum	21	87	–30	4.131	10	0.999	5.061
*All $T_{[20/14]}$ values correspond to $P_{[\text{uncorrected}]} \leq 0.0011$								
Somatoform patients > healthy subjects, $P_{[\text{uncorrected}]} \leq 0.001$, minimum cluster size 10 voxel no region								
Neutral (“neutral” – “control”)								
Somatoform patients < healthy subjects, $P_{[\text{uncorrected}]} \leq 0.001$, minimum cluster size 10 voxel no region								
Somatoform patients > healthy subjects, $P_{[\text{uncorrected}]} \leq 0.001$, minimum cluster size 10 voxel no region								

Active clusters of the contrasts “all emotions” – “control,” “anger” – “control,” “disgust” – “control,” “joy” – “control,” and “neutral” – “control”; voxel-based independent samples t-test comparing healthy subjects ($n = 20$) and somatoform patients ($n = 20$). x , y , and z coordinates belong to the peak voxel of the cluster and refer to the Talairach and Tournoux stereotactical space. T -values refer to the peak voxel; n represents the number of voxels in the cluster; $P_{[\text{FWE}]}$ describes the family-wise error of a cluster of the given size; $T_{[20/14]}$ reflects the T score of the same peak voxel using a contrast, which included the 20 healthy controls and the 14 nonmedicated patients.

a right parahippocampal gyrus [30, 54, -3] **b left amygdala [-24, -3, -24]** **Figure 3.**

Brain activity during empathy. The comparison of healthy subjects and somatoform patients revealed two brain regions with significant differences in hemodynamic responses for the contrast ["anger" + "disgust" + "joy" + "neutral expression"] – "control" ($P_{\text{uncorrected}} = 0.001$, minimum cluster size 10 voxel): the right parahippocampal gyrus (**a**) and the left amygdala (**b**). The left picture illustrates the exact location of the region of interest. The center picture shows the mean hemodynamic responses of healthy subjects (h , $n = 20$) and patients (p , $n = 20$) during empathy. In the right picture, each patient is presented by a dot; its x-value representing his average error rate

in the TAB and its y-value representing his mean fMRI signal during empathy. Activation maps are superimposed on a normalized mean image of all 40 participants (patients and healthy control subjects). The figure shows disturbed neuronal activity of somatoform patients in the right parahippocampal gyrus and the left amygdala. The figure also suggests that there is no association of overall emotion recognition deficits and brain activity during empathy in both regions. (The error bars reflect the 95% confidence interval; P -values are "one-tailed.") [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

DISCUSSION**Summary of Findings**

Behaviorally, somatoform patients showed abnormal scores in several self-report questionnaires, including the Symptom-Checklist-90-R (SCL-90-R), the Toronto-Alexithymia-Scale 20 (TAS-20), and the Beck-Depression-Inventory (BDI). Moreover, somatoform patients scored higher in the

"empathic distress" subscale of the Interpersonal-Reactivity-Index (IRI) when compared to the healthy control group. Scores of somatoform patients in the "empathic fantasy," "empathic concern," and "perspective taking" subscale of the IRI did not differ significantly from scores of the healthy control group. Emotion recognition of somatoform patients in the Tübinger Affekt Batterie (TAB) was impaired when compared to healthy subject with regard

Figure 4.

Brain activity during empathy with angry faces Seven brain regions of somatoform disorder patients showed diminished hemodynamic responses compared to healthy subjects for the contrast “anger” – “control” ($P_{\text{uncorrected}} = 0.001$, minimum cluster size 10 voxel): the left postcentral gyrus (a), the left superior temporal gyrus (b), the bilateral parahippocampal gyrus (c, d), the left posterior insula (e), the left amygdala (f), and the left cerebellum (g). Alike Figure 3, the left picture illustrates the exact location of the region of interest. The center picture shows the mean hemodynamic responses of healthy subjects (h , $n = 20$) and patients (p , $n = 20$) during empathy with anger. In the right picture, each patient is presented by a dot; its x-value representing his average error rate in the TAB during anger

and its y-value representing his mean fMRI signal during empathy with anger. Activation maps are superimposed on a normalized mean image of all 40 participants (patients and healthy control subjects). Somatoform patients’ TAB error rates during anger predicted diminished hemodynamic responses during anger of three brain regions: the left postcentral gyrus, the left superior temporal gyrus, and the left cerebellum. The more problems a patient had in recognizing anger, the smaller his hemodynamic activity during empathy with anger in those three regions. (The error bars reflect the 95% confidence interval; P -values are “one-tailed.”) [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Figure 4 (Continued).

to all tested emotions except "neutral." Noteworthy, somatoform patients but not healthy subjects performed worse in trials using anger and sad stimuli compared to neutral stimuli. In addition, somatoform patients reported equal subjective impression of empathic capabilities during the fMRI experiment.

The fMRI analysis revealed diminished responsiveness of brain regions during empathy in three of the five con-

trasts: "all emotions" – "control," "anger" – "control," and "joy" – "control," whereas we found no significant regions for the contrasts "disgust" – "control" and "neutral expression" – "control." Two regions showed diminished activity in somatoform patients in the contrast "all emotions" – "control": the right parahippocampal gyrus and the left amygdala. Hemodynamic responses in these regions did, however, not correlate with the overall error rates in the

a right parahippocampal gyrus [30, 54, -3]

b right cerebellum [33, 84, -27]

c right cerebellum [21, 87, -30]

Figure 5.

TAB. Several regions showed diminished neuronal activity in the contrast “anger” – “control,” including the left postcentral gyrus, the left superior temporal gyrus, the bilateral parahippocampal gyrus, the left posterior insula, the left amygdala and the left cerebellum. TAB error rates for anger correlated with hemodynamic responses during empathy with anger in the left postcentral gyrus, the left superior temporal gyrus and the left cerebellum. During empathy with joyful faces, somatoform patients showed diminished responsiveness in three regions: the right parahippocampal gyrus and two regions in the right cerebellum. TAB error rates for joy correlated with hemodynamic responses during empathy with joy in both cerebellar regions.

Brain Activity During Empathy in Healthy Subjects

Empathy lead to increased neuronal activity in a number of brain regions in healthy subjects, which included the bilateral inferior frontal cortex, bilateral amygdala, right supplementary motor area, right postcentral gyrus, and other regions. These results are in accordance with previous studies investigating the neural correlates of empathy [Blair et al., 1999; Breiter et al., 1996; Carr et al., 2003; de Greck et al., 2011a; Jabbi et al., 2007; Morris et al., 1996; Nomi et al., 2008; Phillips et al., 1997; Sprengelmeyer et al., 1998].

Comorbidity of Somatoform Patients

Somatoform patients not only exhibited increased somatization scores (as ascertained by the SCL-90-R), but also reported more depressive (BDI) and alexithymic symptoms (TAS-20). This finding is in line with several studies about somatoform disorder, which concordantly reported a high comorbidity of somatoform symptoms, depressive symptoms and alexithymic symptoms [Bailey and Henry, 2007; Hanel et al., 2009; Waller and Scheidt, 2004]. Whilst we found significant correlations of hemodynamic responses of several regions and error rates in the TAB, as well as a significant correlation of SCL-90-R scores with

hemodynamic responses of the left superior temporal gyrus during anger, we did not find any significant correlations of depressive or alexithymic symptom scores with hemodynamic responses. This supports the conclusion that our results are associated with impaired emotion recognition and somatization, rather than depression and alexithymia.

Diminished Neuronal Modulation in Somatoform Disorder

Our results differ from those of a previous study conducted by Lee et al. [2009], who investigated patients suffering from Hwa-Byung, a mental disorder bound to the Korean culture, which resembles somatoform disorder with regard to medically unexplained symptoms. In their fMRI study using emotional faces, Lee et al. found several brain regions with stronger activity in Hwa-Byung patients (compared to a group of healthy controls); these regions included the lingual gyrus, the fusiform gyrus and the inferior occipital gyrus. The authors described only one region with stronger activity in healthy controls during angry faces, the right thalamus. Besides several differences with regard to the study design (for instance Lee et al. used an epoch-related design and their participants were instructed to merely watch the facial stimuli), differences in the psychodynamic mechanisms underlying somatoform disorder and Hwa-Byung could explain the differences in brain activity: in Hwa-Byung, patients suffer from medically unexplained symptoms which are caused by the initial suppression of anger, followed by an exaggerated anger response [Lee et al., 2009; Lin, 1983; Min, 2008]. Lee et al. [2009] suggest that a lack of emotional control is responsible for the increased activity in the lingual gyrus, fusiform gyrus, and inferior occipital gyrus (and the decreased activity of the right thalamus) during the processing of emotional faces. The psychodynamic mechanisms underlying somatoform disorders are different, however, since somatoform disorders are explained by a chronic suppression of specific emotions in order to protect relevant relationships [Bowlby, 1973; Maunder and Hunter, 2004; Waller and Scheidt, 2006]. Diminished modulation of

Figure 5.

Brain activity during empathy with joyful faces Three brain regions showed diminished hemodynamic responses of somatoform disorder patients compared to healthy subjects during the contrast “joy” – “control” ($P_{\text{uncorrected}} = 0.001$, minimum cluster size 10 voxel): the right parahippocampal gyrus (a), and two regions of the left cerebellum (b, c). Alike Figure 3 and 4, the left picture illustrates the exact location of the region of interest. The center picture shows the mean hemodynamic responses of healthy subjects (h , $n = 20$) and patients (p , $n = 20$) during empathy with joy. In the right picture, each patient is presented by a dot; its x-value representing his average error

rate in the TAB during joy and its y-value representing his mean fMRI signal during empathy with joy. Activation maps are superimposed on a normalized mean image of all 40 participants (patients and healthy control subjects). Somatoform patients' TAB error rates during joy predicted diminished hemodynamic responses during joy of both cerebellar regions. The worse a patient's performance during the detection of joy, the smaller his hemodynamic activity during empathy with joy. (The error bars reflect the 95% confidence interval; P -values are “one-tailed.”) [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

brain activity in several regions of somatoform disorder patients in our study is in accordance with this concept.

Empathic Deficits, Impaired Emotion Recognition and Abnormal Brain Activity in Somatoform Disorder

The intra-scanner ratings of subjective empathy experience and the IRI results suggest that somatoform patients do rather not present a global alteration of empathic disabilities but a distinct problem with a specific empathic process: "empathic distress". Individuals, who score high on "empathic distress" in the IRI, describe themselves as to be easily affected and overwhelmed by negative emotional states of others. The TAB results show that somatoform patients have more difficulties in the recognition of all applied emotions except "neutral" (when compared to healthy control subjects).

The fMRI results show that brain activity of somatoform patients is abnormal for anger and joy, whilst we found no differences for the emotions disgust and neutral expression. These findings are in accordance with our initial hypothesis based on psychodynamic concepts of somatoform disorder, which explain somatoform disorder by the repression of emotions to avoid interpersonal conflicts [Bowlby, 1973; Maunder and Hunter, 2004; Waller and Scheidt, 2006]: somatoform patients showed abnormal brain activity only during social emotions such as anger and joy, whereas brain activity was normal during disgust and neutral expression. However, we are cautious with this interpretation because the behavioral results indicate that both groups felt better able to empathize with angry and happy faces compared to faces showing disgust and neutral expression.

Nevertheless, our findings fit into the psychodynamic concept of somatoform disorder in additional ways: (i) Somatoform patients showed normal empathic abilities in most of the applied behavioral empathy tests and only exhibited distinct changes in their empathic abilities connected to empathic distress. Negative emotions of others are experienced comparatively stronger and somatoform patients tend to experience them as overwhelming, which might trigger suppressing mechanisms [Waller and Scheidt, 2004]. (ii) Brain regions which showed diminished neural activity in somatoform patients included brain regions which are associated to emotional experience (amygdala), evaluation of social emotions (superior temporal gyrus), and emotional memory (parahippocampal gyrus). Diminished neuronal activity in these regions might reflect inhibition of emotion processing in these regions.

What can we infer from the regions, which showed altered neuronal activity in somatoform patients? The location of these regions (i.e., parahippocampal gyrus, amygdala, postcentral gyrus, superior temporal gyrus, posterior insula, cerebellum) is in accordance with the conclusion

that somatoform patients do not only suffer from disturbed emotion recognition—a process which is associated with activity in amygdala and somatosensory cortex [Adolphs et al., 2000; Derntl et al., 2009; Gur et al., 2002]—but also from disturbances of other processes such as emotional empathy and emotional memory. Emotional empathy is known to induce activity in the superior temporal sulcus region [Carr et al., 2003; de Greck et al., 2011a; Hoerker et al., 2008; Hooker et al., 2008], this region showed disturbed neuronal activity in somatoform patients. Emotional memory is associated with neuronal activity in the parahippocampal gyrus [Smith et al., 2004; Sterpenich et al., 2006], another region, which showed diminished modulation in somatoform patients. Interestingly, in a recent study by Loughhead et al., activity in the parahippocampal gyrus was positively correlated with the degree of conflict related to autobiographical episodes [Loughhead et al., 2010]. Disturbed activity in the parahippocampal gyrus in somatoform patients is hence in line with the assumption that somatoform patients suffer from disturbed processing of emotional memory, a conclusion which is in accordance with psychodynamic concepts concerning somatoform disorder. However, since we did not investigate emotional memory in this study, this conclusion has to be preliminary.

Whilst we found negative correlations of emotion recognition error rates and hemodynamic responses of the left postcentral gyrus, left superior temporal gyrus, left posterior insula, and the bilateral cerebellum, other regions including the bilateral parahippocampal gyrus and the amygdala lacked this correlation. These results support our conclusion that the empathic deficits of somatoform patients cannot be completely reduced to impaired emotion recognition.

Our results suggest further that the cerebellum plays a role in the empathic dysfunctions of somatoform patients during anger and joy. A region in the left cerebellum showed diminished activity the contrast "anger" – "control," and two regions in the right cerebellum showed diminished activation in the contrast "joy" – "control." Hemodynamic responses of all three cerebellar regions correlated negatively with error rates for the according emotions in the TAB. The cerebellum is known to play a role in emotion regulation [Schutter and van Honk, 2005] and is involved in the processing of emotional faces [Fusar-Poli et al., 2009] and emotional stimuli in general [Berpohl, et al., 2006]. Furthermore, the cerebellum plays a role in the processing of autobiographic memory [Svoboda et al., 2006].

What new insights do our results reveal about the relationship of empathy and emotion recognition and their impairment in somatoform disorder? Empathy describes the induction of a congruent emotion in one individual caused by the emotional state of another individual [Decety and Jackson, 2004; Preston and de Waal, 2002]. Emotion recognition means the correct labeling of an emotion presented by a target individual [Pedrosa Gil et al., 2009].

For both processes, the generation of a specific emotional state (congruent to the emotional state of the target) is essential [Adolphs et al., 2000; Preston and de Waal, 2002]. Regarding this, the generation of an emotional state can be induced (i) by external stimuli—for instance by emotional contagion, a process which involves neuronal activity in particular in the inferior frontal gyrus and the inferior parietal cortex [Keysers and Gazzola, 2006; Kramer et al., 2010; Nummenmaa et al., 2008; Shamay-Tsoory, 2011]—or (ii) by a stimulus from the internal world—for instance the induction of emotion by autobiographic memory, which involves neuronal activity in particular in the parahippocampal gyrus [Damasio et al., 2000; Smith et al., 2004; Sterpenich et al., 2006]. The two processes have in common that they engage further activity in somatosensory cortices, such as the postcentral gyrus and insula to generate a full blown emotional response [Adolphs et al., 2000; Banissy et al., 2010; Damasio et al., 2000; Immordino-Yang et al., 2009; Nummenmaa et al., 2008; Rudrauf et al., 2009].

Relying on these concepts, the following interpretation is consistent with our data: Somatoform disorder patients suffer from deficits in emotion recognition and show abnormal brain activity during empathy, because they cannot generate the congruent emotional state within themselves. Why are somatoform patients not able to do so and how can we support this conclusion? Relying on psychodynamic concepts, a possible explanation for impaired emotion generation of somatoform disorder patients is that these patients have learnt to unconsciously suppress specific emotions in order to protect relevant relationships [Bowlby, 1973; Maunder and Hunter, 2004; Waller and Scheidt, 2006]. In addition, as our behavioral results show, somatoform disorder patients describe more empathic distress, they are afraid to be overwhelmed by emotions, which probably inhibits emotion generation processes. With regard to our fMRI findings, another explanation for impaired emotion generation of somatoform patients is the disturbed activity of the parahippocampal gyrus, which does not provide the necessary biographical memory to generate the emotional state. In addition, our study showed diminished modulation of the somatoform patients' postcentral gyrus and insula; both regions do not provide the somatosensory information necessary for sufficient emotion generation and emotional experience.

Limitations

We would also like to address a few limitations of our study. The group of patients was rather heterogeneous, consisting of different forms of somatoform disorders. In addition, we are aware of the discussion about the heterogeneous concept of somatoform disorders in general [Kroenke, 2006; Mayou et al., 2005; Voigt et al., 2010]. However, since we focused on the empathic processing

of emotional stimuli, which is independent of the individual symptoms of each patient, we decided to include any patient who fulfilled the criteria of a somatoform disorder. Further, in the fMRI contrasts comparing somatoform patients and healthy subjects, we did not apply corrections for multiple comparisons. Our results are thus preliminary and await replication in other studies. Nonetheless, we found significant correlations of hemodynamic responses and error rates in the TAB in several regions (left postcentral gyrus, left superior temporal gyrus, bilateral cerebellum), which confirm the involvement of these regions. Moreover, six of our patients were on psychotropic medication. However, we implemented additional voxel based contrasts comparing the 14 nonmedicated patients and the 20 healthy controls, in which we found comparable T scores of the peak voxels of the regions of interest. These results strongly suggest that differences in neuronal activity between healthy controls and somatoform patients are not due to medication effects; nonetheless, we can not completely exclude a bias caused by the psychotropic medication. Another limitation regards the empathy task of our study. We applied an empathy task, which focused on intentional emotional empathy, which is only a small aspect within the range of empathic responses. In future studies it might be of interest to investigate further empathic processes, such as emotional contagion or in particular empathy for pain. Finally, due to time restraints, the variety of emotions applied in our study was limited. In addition, our paradigm did not allow disentangle empathic processes from other emotional processes such as emotion recognition or emotion generation; such a comparison would be another promising endeavor. In future studies it might also be interesting to explore brain function of somatoform patients during empathy with other emotions, such as fear or in particular sadness, which were not included in our study.

CONCLUSIONS

Impaired emotion recognition of somatoform disorder patients is linked to abnormal brain activity during emotional empathy in brain regions responsible for emotional evaluation, emotional memory, and emotion generation.

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