

Provided for non-commercial research and education use.  
Not for reproduction, distribution or commercial use.



**This article appeared in a journal published by Elsevier. The attached copy is furnished to the author for internal non-commercial research and education use, including for instruction at the authors institution and sharing with colleagues.**

**Other uses, including reproduction and distribution, or selling or licensing copies, or posting to personal, institutional or third party websites are prohibited.**

**In most cases authors are permitted to post their version of the article (e.g. in Word or Tex form) to their personal website or institutional repository. Authors requiring further information regarding Elsevier's archiving and manuscript policies are encouraged to visit:**

**<http://www.elsevier.com/copyright>**



Contents lists available at SciVerse ScienceDirect

## Journal of Psychiatric Research

journal homepage: [www.elsevier.com/locate/psychires](http://www.elsevier.com/locate/psychires)

## Risk or resilience? Empathic abilities in patients with bipolar disorders and their first-degree relatives

Eva-Maria Seidel<sup>a,b,\*</sup>, Ute Habel<sup>b</sup>, Andreas Finkelmeyer<sup>b,c</sup>, Alexander Hasmann<sup>d</sup>, Matthias Dobmeier<sup>d</sup>, Birgit Derntl<sup>a,b</sup>

<sup>a</sup> Institute for Clinical, Biological and Differential Psychology, Faculty of Psychology, University of Vienna, Vienna, Austria

<sup>b</sup> Department of Psychiatry, Psychotherapy and Psychosomatics, Medical School, RWTH Aachen University, Aachen, Germany

<sup>c</sup> Institute of Neuroscience, Newcastle Biomedicine, Newcastle University, Newcastle-upon-Tyne, England, UK

<sup>d</sup> Department of Psychiatry, Psychosomatic and Psychotherapy, University of Regensburg, Regensburg, Germany

### ARTICLE INFO

#### Article history:

Received 23 July 2011

Received in revised form

11 November 2011

Accepted 14 November 2011

#### Keywords:

Empathy

Endophenotype

Relatives

Bipolar disorder

### ABSTRACT

Endophenotypes are intermediate phenotypes which are considered a more promising marker of genetic risk than illness itself. While previous research mostly used cognitive deficits, emotional functions are of greater relevance for bipolar disorder regarding the characteristic emotional hyper-reactability and deficient social-emotional competence. Hence, the aim of the present study was to clarify whether empathic abilities can serve as a possible endophenotype of bipolar disorder by applying a newly developed task in bipolar patients and their first-degree relatives. Three components of empathy (emotion recognition, perspective taking and affective responsiveness) have been assessed in a sample of 21 bipolar patients, 21 first-degree relatives and 21 healthy controls. Data analysis indicated significant differences between controls and patients for emotion recognition and affective responsiveness but not for perspective taking. This shows that in addition to difficulties in recognizing facial emotional expressions, bipolar patients have difficulties in identifying emotions they would experience in a given situation. However, the ability to take the perspective of another person in an emotional situation was intact but decreased with increasing severity of residual hypomanic and depressive symptoms. Relatives performed comparably bad on emotion recognition but did not differ from controls or patients in affective responsiveness. This study is the first to show that deficient emotion recognition is the only component of empathy which forms a possible endophenotype of bipolar disorder. This has important implications for prevention strategies. Furthermore, changes in affective responsiveness in first-degree relatives show a potential resilience marker.

© 2011 Elsevier Ltd. All rights reserved.

### 1. Introduction

Higher order emotional competencies, e.g. empathy, are important prerequisites for successful social interaction. In bipolar disorder disruptions of social functioning have been consistently reported (e.g., Begley et al., 2001; Kessler et al., 2006). These deficient social competencies may result from a dysfunctional ability to understand and react to emotional expressions of other people.

The majority of previous studies examining social-emotional competencies in bipolar disorder focused on emotion recognition, albeit showing inconsistent results. Some studies observed

significant impairments in general emotion recognition accuracy (Addington and Addington, 1998; Bozikas et al., 2006; Derntl et al., 2009a; Getz et al., 2003). Others reported only emotion-specific deficits (Summers et al., 2006; Yurgelun-Todd et al., 2000) and some even showed unaffected emotion recognition abilities (Lawrence et al., 2004; Vaskinn et al., 2007; Venn et al., 2004).

However, emotion recognition is only one component considered to be important for empathic competencies. According to most models of empathy one can derive at least three components (Decety and Jackson, 2004): emotion recognition, perspective taking (cognitive empathy) and affective responsiveness (emotional empathy). This definition takes into account that empathy not only entails understanding others but also understanding and regulating our own emotional reactions. In order to comprehensively analyze all three components we applied a newly developed task (Derntl et al., 2010, 2009b).

\* Corresponding author. Institute for Clinical, Biological and Differential Psychology, Faculty of Psychology, University of Vienna, Liebiggasse 5, 1010 Vienna, Austria.

E-mail address: [eva-maria.seidel@univie.ac.at](mailto:eva-maria.seidel@univie.ac.at) (E.-M. Seidel).

Previous studies regarding perspective taking abilities in bipolar disorder indicate a deficit in so-called theory of mind tasks (Bora et al., 2005; Kerr et al., 2003; Lahera et al., 2008; Olley et al., 2005). Directly comparing cognitive and emotional theory of mind a recent study (Montag et al., 2010) showed that euthymic bipolar patients are only affected in the cognitive but not in the emotional component.

Regarding affective responsiveness, there is evidence of increased responsiveness to emotional stimuli in bipolar disorder when using self-report measures (Henry et al., 2008) or mood induction (M'Bailara et al., 2009; Roiser et al., 2009).

As bipolar disorder is highly heritable (for a review see Goodwin and Jamison, 1990) a promising research strategy to shed light on pathophysiological mechanisms is the identification of endophenotypes, i.e. behavioral deficits which are heritable and present in family members in attenuated form. Despite the increased risk not all genetically predisposed individuals will develop the disorder. Therefore, a differentiation of risk and resilience factors is desirable. Previous studies examining neuropsychological endophenotypes of bipolar disorder focused on cognitive endophenotypes. However, these reflect only one part of the etiological puzzle that underlies the extreme emotional dysregulation of the disorder. Besides processing speed, working memory (Glahn et al., 2010), problem solving and interference control (Doyle et al., 2009), deficient response inhibition seems to be the most prominent cognitive endophenotype (Bora et al., 2009).

In the domain of emotion, Kruger et al. (2006) showed that activation in the ventral medial prefrontal cortex in response to sad mood induction differentiated siblings (increase) and patients (decrease) suggesting a capacity for resilience in terms of emotion regulation. Using the same mood induction paradigm, a recent study (Houshmand et al., 2010) showed that the induction of sadness is faster and more intense in unaffected siblings and patients compared to controls suggesting emotional hyperresponsiveness as an endophenotype of bipolar disorder.

In light of previous studies, we hypothesized deficits in emotion recognition but unaffected emotional perspective taking in bipolar patients. Further we assumed increased affective responsiveness in patients which can positively and negatively influence the identification of the respective emotion in oneself. In line with the endophenotype concept, we expected that relatives show an intermediate performance between controls and patients suggesting empathic competencies as a potential endophenotype for bipolar disorder. To the best of our knowledge, the present study is the first attempt to explore empathic competencies as a possible endophenotype of bipolar disorder by applying a newly developed task in bipolar patients and their unaffected first-degree relatives. This study design enabled us to differentiate between trait-like empathic deficits that are related to familial risk from those that are consequences of the disorder.

## 2. Methods

### 2.1. Sample

Twenty-one stable bipolar outpatients (9 females) meeting the DSM-IV criteria for bipolar disorder (according to the German version of the Mini International Neuropsychiatric Interview, MINI (Sheehan et al., 1998)), 21 first-degree relatives of these patients (11 females) and 21 healthy controls (10 females) participated in this study. The study was carried out in accordance with the latest version of the Declaration of Helsinki. All subjects gave written informed consent and the study was approved by the ethics committee of the University of Regensburg.

Bipolar patients who did not show any other psychiatric or neurological illness and had no substance abuse for the last six months

were recruited from the outpatient unit of the Department of Psychiatry, Psychosomatic and Psychotherapy at the University of Regensburg. Ten bipolar patients fulfilled the DSM-IV criteria for bipolar I disorder while 11 patients fulfilled the criteria for bipolar II disorder. Patients were diagnosed by their treating physician (MD) and diagnosis was confirmed by the MINI Interview performed by a trained independent rater. Mean age of onset was 39.62 (SD = 10.01, range 18–53) and mean illness duration was 8.33 (SD = 5.51, range 1–21). To assess affective symptoms, the German versions of the Young Mania Rating Scale (YMRS, Young et al., 1978) and the Montgomery Asberg Depression Rating Scale (MADRS, Montgomery and Asberg, 1979) were applied. On the YMRS, the symptom ratings did not reach clinically relevant scores (Cut-off = 12, Mean = 1.48, SD = 1.25, range 0–4) and there was only a mild symptom severity on the MADRS (Cut-off = 19, Mean = 6.67, SD = 5.54, range 0–9). At the time of testing all patients were taking the prescribed medication to ensure mood stabilization (antidepressant [ $n = 1$ ], neuroleptic [ $n = 2$ ], mood-stabilizer [ $n = 6$ ], antidepressants + neuroleptic [3], antidepressant + mood-stabilizer [ $n = 1$ ], mood-stabilizer + neuroleptic [ $n = 6$ ], combination of all three [ $n = 2$ ]).

The group of relatives included 21 unaffected full biological first-degree relatives of these patients with no history of psychiatric or neurological illness as well as no substance abuse (screened with the MINI). The non-psychiatric control group consisted of 21 healthy adults with no history of psychiatric or neurological illness as well as no substance abuse in themselves and in their first-degree relatives. The control group was recruited by advertisements. Demographic characteristics and test scores are shown in Table 1.

### 2.2. Materials and procedure

In the present study we relied on the same set of tasks we applied previously in schizophrenia patients (Derntl et al., 2009b) as well as in a study examining gender differences with functional magnetic resonance imaging (Derntl et al., 2010). Prior to these studies, stimuli were rated by 55 healthy adults and only those stimuli correctly identified by over 70 percent of the sample were used further. An illustration of the three tasks is shown in Fig. 1.

#### 2.2.1. Emotion recognition and age discrimination

We presented 60 colored Caucasian faces depicting five basic emotions (happiness, sadness, anger, fear, and disgust) and neutral expressions (see Fig. 1A). Half of the stimuli were used for emotion recognition, the other half for an age discrimination control task. Stimuli were selected from a standardized stimulus set (Gur et al., 2002) that has been frequently used as neurobehavioral probes (e.g., Derntl et al., 2008, 2011, Habel et al., 2007, 2010; Seidel et al., 2010a,b). The age discrimination task was introduced as a control task to assess the general capacity to process facial features. Facial

**Table 1**

Demographic characteristics, neuropsychological test and questionnaire data of patients, relatives and controls.

Variable	Patients	Relatives	Controls	<i>F</i>	<i>p</i>
Gender (M:F)	12:9	10:11	11:10	–	–
Age	46 (11.485)	38.43 (17.72)	41.67 (9.129)	1.718	0.188
Years of education	14.14 (2.670)	12.71 (2.53)	14.81 (4.285)	2.263	0.113
Verbal IQ	108.62 (14.379)	105.76 (12)	111.90 (9.9)	1.626	0.111
IRI total score	28.19 (7.67)	31.86 (4.64)	35.1 (5.71)	6.499	<b>0.003</b>
Fantasy	11.67 (3.18)	12.52 (2.80)	14.25 (3.41)	3.582	<b>0.034</b>
Perspective taking	13.52 (2.34)	14.90 (2.70)	15.35 (1.53)	3.692	<b>0.031</b>
Distress	12.00 (2.93)	11.05 (2.84)	9.70 (2.51)	3.554	<b>0.035</b>
Empathic concern	40.09 (7.38)	42.43 (4.49)	44.80 (5.03)	0.73	0.929

Note. Standard deviations appear in parentheses. Significant differences are shown in bold.

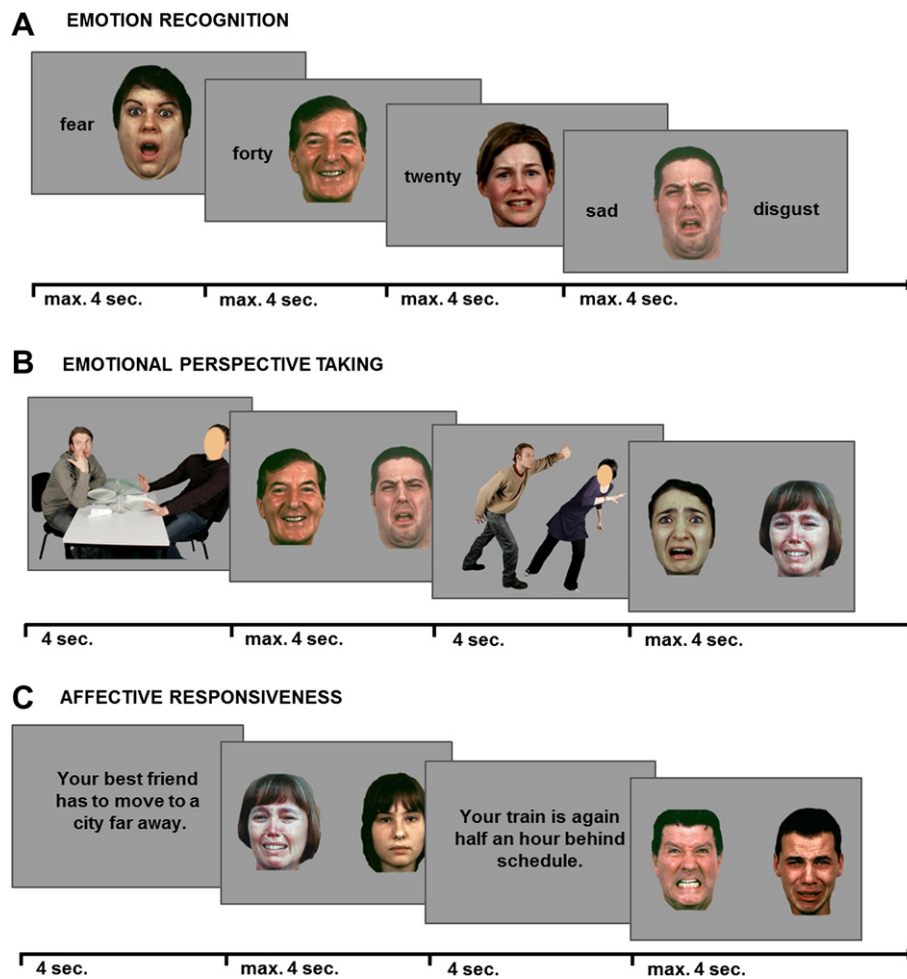


Fig. 1. Illustration of the three empathy tasks.

expressions were presented maximally for 5 s. For emotion recognition subjects had to determine the correct emotion by selecting from two emotion categories. In the control trials, subjects had to judge which of two age decades was closer to the poser's age.

### 2.2.2. Emotional perspective taking

Participants were presented with 57 pictures (for 4 s) depicting two interacting Caucasians thereby portraying five basic emotions and neutral scenes (10 stimuli per condition for disgust, happy and neutral; 9 stimuli for sadness, anger and fear). The face of one person was masked and participants were asked to infer the corresponding emotional expression of the masked face (see Fig. 1B). Responses were made by selecting between two different emotional facial expressions or a neutral expression presented after each scene. Facial alternatives were taken from the same pool of stimuli described above. One option was correct and the other was selected at random from all other choices.

### 2.2.3. Affective responsiveness

We presented 60 short sentences describing real-life situations which are likely to induce basic emotions (the same emotions as described above), and situations that were emotionally neutral (10 stimuli per condition). Participants were asked to imagine how they would feel if they were experiencing those situations (see Fig. 1C). Stimuli were presented for 4 s and response format was the same as for emotional perspective taking.

### 2.2.4. Empathy questionnaire and neurocognitive test

All participants completed one test tapping crystallized verbal intelligence (MWT-B, (Lehrl, 1996)), as a measure of premorbid crystallized intelligence and the German version of the Interpersonal Reactivity Index (IRI, (Davis, 1983)) as a self-report measure of empathic abilities.

### 2.3. Statistical analysis

Statistical analyses were performed according to our previous study (Derntl et al., 2009b) using SPSS Statistics 17.0 and level of significance was set at  $p = 0.05$ . Percent correct were analyzed using Generalized Estimating Equations (GEE; SPSS command GENLIN) accounting for non-normality of the dependent measure and/or violations of sphericity. For each empathy task, a full-factorial model was computed with emotion as within-subject factor, and group (bipolar vs. relative vs. control) as between-subjects factor. Analyses of emotional perspective taking and affective responsiveness tasks further included performance on emotion recognition and the respective other task as covariates to control for influences of response format on results and influences of responsiveness and perspective taking on each other. Due to the fact that each control subject answered all happy trials correctly in the affective responsiveness task, the happy condition was excluded from the analysis of this task. To compare performance among the empathy tasks and age discrimination, we computed an additional model using GEE with task (4 levels) as within-subject

factor, and group as between-subject factor. In this model, performance was aggregated over all emotions.

Reaction times were analyzed using repeated-measures ANOVAs with emotion as within-subject factor and group as between-subject factor. Statistical tests involving the emotion factor employed Greenhouse–Geisser correction if the sphericity assumption was not met.

Group differences regarding age, education, empathy questionnaires and verbal intelligence were assessed using univariate ANOVAs. Correlations were computed using the Pearson coefficient. Including gender as a second between-subject factor did not produce significant differences regarding accuracy or reaction time (all  $p$ -values  $> 0.105$ ).

### 3. Results

#### 3.1. Emotion recognition

There was a trend for differences in the accuracy of emotion recognition between the three groups (Wald- $\chi^2 = 5.692$ ,  $df = 2$ ,  $p = 0.058$ ) with the control group being more accurate than patients ( $p = 0.047$ ) and relatives ( $p = 0.036$ ), while patients and relatives did not differ from one another ( $p = 0.979$ , see Fig. 2). Recognition differed between emotion qualities (Wald- $\chi^2 = 61.338$ ,  $df = 5$ ,  $p < 0.001$ ) with highest accuracy for happiness and lowest for sadness. This effect was not moderated by group ( $p = 0.288$ ).

Also, reaction times differed between the three groups ( $F(2,60) = 61.476$ ,  $p < 0.001$ ) with controls responding faster than patients ( $p < 0.001$ ) and relatives ( $p < 0.001$ ) whereas patients and relatives did not differ ( $p = 0.759$ ). Reaction times differed between emotion qualities ( $F(5,300) = 12.873$ ,  $p < 0.001$ ) with fastest responses to happy and slowest responses to fearful expressions. This effect was not moderated by group ( $p = 0.141$ ). See Table 2 for means (SD) of all groups.

#### 3.2. Age discrimination

Performance analysis showed a trend for a group difference (Wald- $\chi^2 = 5.349$ ,  $df = 2$ ,  $p = 0.070$ ), such that controls tended to outperform patients ( $p = 0.034$ ). Relatives did not differ from controls ( $p = 0.256$ ) and patients ( $p = 0.391$ ). Age discrimination turned out to be easiest in neutral faces and worst in angry faces (Wald- $\chi^2 = 146.474$ ,  $df = 5$ ,  $p < 0.001$ ). This effect was not moderated by group ( $p = 0.524$ ).

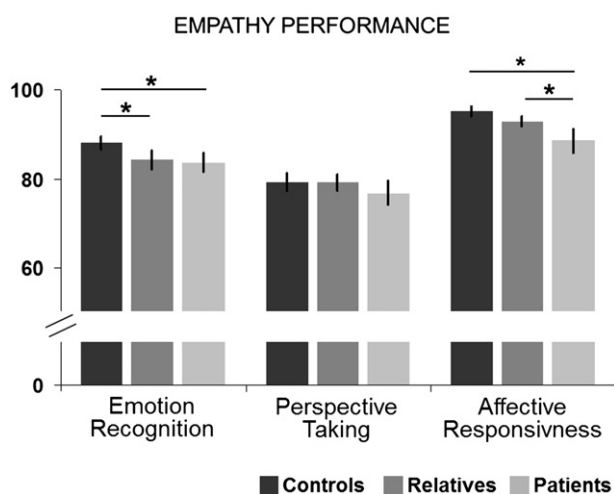


Fig. 2. Performance (% correct) in emotion recognition, emotional perspective taking and affective responsiveness in bipolar patients, their first-degree relatives and healthy controls.

Table 2

Mean accuracy (% correct) and reaction times (ms) of the empathy tasks. Standard deviations are given in parentheses.

Task		Patients	Relatives	Controls
Emotion recognition	% Correct	83.65 (9.42)	84.29 (9.32)	88.06 (6.88)
	RT	2181.6 (220.2)	2158.5 (303.1)	1448.1 (194.5)
Age recognition	% Correct	73.18 (10.57)	76.03 (9.98)	78.41 (4.90)
	RT	2416 (429.6)	2156.2 (377.6)	1456.7 (173)
Perspective taking	% Correct	76.90 (12.76)	79.03 (8.45)	79.29 (9.31)
	RT	1672.8 (372.9)	1680.1 (266.6)	1213.3 (326.5)
Affective responsiveness	% Correct	88.61 (12.42)	92.86 (5.53)	95.16 (4.80)
	RT	1454.1 (309.4)	1416.1 (270.3)	1128.4 (261.4)

We observed differences between the three groups in reaction times ( $F(2,60) = 43.186$ ,  $p < 0.001$ ) with controls responding faster than patients ( $p < 0.001$ ) and relatives ( $p < 0.001$ ). However, reaction times of relatives did not differ from patients ( $p = 0.601$ ). Responses were fastest for age discrimination in neutral faces and slowest for sad faces ( $F(5,300) = 5.089$ ,  $p < 0.001$ ). This effect was not moderated by group ( $p = 0.121$ ). See Table 2 for means (SD) of all groups.

#### 3.3. Emotional perspective taking

Controlling for emotion recognition and affective responsiveness performance, accuracy for emotional perspective taking was highest for happy stimuli and lowest for disgust (Wald- $\chi^2 = 95.037$ ,  $df = 5$ ,  $p < 0.001$ ). There was no group difference ( $p = 0.841$ ) and the difference between emotion qualities was not moderated by group ( $p = 0.916$ ) emerged (see Fig. 2).

Analysis of reaction times demonstrated no difference between emotion qualities ( $p = 0.233$ ) or groups ( $p = 0.679$ ). However, there was an interaction between group and emotion ( $F(10,290) = 2.147$ ,  $p = 0.021$ ). Post hoc emotion-specific ANOVAs indicated that response times of patients and relatives were slower than controls' for all emotional conditions (all  $p$ -values  $< 0.002$ ) whereas response times of patients and relatives did not differ significantly (all  $p$ -values  $> 0.215$ ). See Table 2 for means (SD) of all groups.

#### 3.4. Affective responsiveness

Controlling for emotion recognition and perspective taking performance and excluding happy situations, a group difference (Wald- $\chi^2 = 9.971$ ,  $df = 2$ ,  $p = 0.007$ ) occurred. Controls ( $p = 0.004$ ) as well as relatives ( $p = 0.047$ ) outperformed patients. However, relatives did not differ from controls ( $p = 0.164$ ) (see Fig. 2). Accuracy in affective responsiveness was highest for neutral stimuli, and lowest for anger (Wald- $\chi^2 = 58.271$ ,  $df = 4$ ,  $p < 0.001$ ). This effect was not moderated by group ( $p = 0.114$ ).

Reaction times did not differ for the five emotions ( $p = 0.989$ ) or between groups ( $p = 0.678$ ) and no interaction between group and emotion ( $p = 0.125$ ) occurred. See Table 2 for means (SD) of all groups.

#### 3.5. Task comparisons

Comparing the over all accuracy across all tasks (including age discrimination) revealed differences between the three empathic competencies (Wald- $\chi^2 = 231.211$ ,  $df = 3$ ,  $p < 0.001$ ) with lowest accuracy in age discrimination, followed by emotional perspective taking, emotion recognition and affective responsiveness. Also differences between groups occurred (Wald- $\chi^2 = 7.225$ ,  $df = 2$ ,  $p = 0.027$ ) with controls outperforming patients ( $p = 0.018$ ). Relatives did neither differ from controls ( $p = 0.130$ ) nor patients ( $p = 0.262$ ). The difference between tasks was not moderated by group ( $p = 0.102$ ).

### 3.6. Empathy questionnaire

We observed a group difference in the total score of the IRI ( $F(2,59) = 6.499, p = 0.003$ ) with lower scores in patients compared to controls ( $p = 0.002$ ) whereas relatives did neither differ from patients ( $p = 0.174$ ) nor controls ( $p = 0.289$ ). Moreover, we observed a group difference ( $F(2,59) = 3.389, p = 0.040$ ) in the empathy sum-score (fantasy + empathic concern + perspective taking) with lower scores in patients compared to controls ( $p = 0.035$ ) whereas relatives did not differ from patients ( $p = 0.589$ ) or controls ( $p = 0.584$ ). Also group differences occurred regarding the subscales fantasy ( $F(2,59) = 3.582, p = 0.034$ ), perspective taking ( $F(2,59) = 3.692, p = 0.031$ ) and personal distress ( $F(2,59) = 3.554, p = 0.035$ ) in contrast to empathic concern ( $p = 0.929$ ): Patients showed lower scores than controls for fantasy ( $p = 0.032$ ), perspective taking ( $p = 0.036$ ) and higher scores for personal distress ( $p = 0.030$ ). Again, relatives did not differ from controls (all  $p$ -values  $>0.251$ ) or patients (all  $p$ -values  $>0.155$ ). Correlating accuracy in our empathy tasks and scores on the IRI revealed a positive correlation of the subscale fantasy and emotional perspective taking ( $r = 0.456, p = 0.044$ ) in controls only.

### 3.7. Clinical characteristics

Correlation of symptom severity and performance on the empathy tasks showed that severity of depressive ( $r = -0.442, p = 0.045$ ) and manic symptoms ( $r = -0.552, p = 0.009$ ) was negatively correlated with performance in emotional perspective taking. Moreover, a marginally significant negative correlation of the number of previous episodes and performance on the age discrimination emerged ( $r = -0.431, p = 0.051$ ). Regarding illness duration, we observed a significant positive correlation with reaction time in the emotion recognition task ( $r = 0.517, p = 0.016$ ). Moreover, trends of associations of illness duration with accuracy in emotion recognition ( $r = -0.388, p = 0.083$ ) and with reaction times in the emotional perspective taking task occurred ( $r = 0.402, p = 0.071$ ).

## 4. Discussion

The present study examined which core component of empathy may serve as a possible endophenotype of bipolar disorder. There were three principle findings: First, deficient emotion recognition seems to be the only component of empathic competencies which might constitute a potential endophenotype of bipolar disorder. Second, emotional perspective taking seems to be state-dependent as it is negatively influenced by residual manic and depressive symptoms. Third, performance of first-degree relatives in affective responsiveness shows a potential resilience marker.

The ability to recognize emotional facial expressions seems to be comparably reduced in euthymic bipolar patients and their first-degree relatives, which is in accordance with our predictions. This was also reflected in significantly longer reaction times. Moreover, accuracy and reaction times were correlated with illness duration. Previous studies showed that acute (e.g., Getz et al., 2003) as well as remitted patients (e.g., Derntl et al., 2009a) are characterized by a deficit in emotion recognition. Our results add to the literature that emotion recognition is a promising candidate endophenotype of bipolar disorder which is state-independent and similarly pronounced in patients and their first-degree relatives. This has important implications for prevention strategies. We assume that emotion recognition difficulties are associated with the well-known psychosocial problems of bipolar patients (Zarate et al., 2000) that persist even after symptom recovery. Offering emotion recognition training programs (e.g., Wolwer et al., 2005)

for patients as well as in high-risk groups will improve social-emotional competencies and will reduce psychosocial stress, which is often reported as a trigger for onset or relapse (Post and Leverich, 2006).

Adding to the difficulties in emotion recognition, bipolar patients also seem to be impaired when inferring non-emotional information from other people's faces (age discrimination). While previous studies did not report general face processing deficits in bipolar disorder (Addington and Addington, 1998; Bozikas et al., 2006; Getz et al., 2003), the use of emotional facial expressions for age discrimination may have affected face processing in our sample due to the characteristic emotional hyper-reactability.

Consistent with previous studies (Montag et al., 2010) and our hypothesis, we did not observe reduced accuracy in emotional perspective taking in euthymic bipolar patients. However, reaction time data showed that controls responded faster than patients and relatives. This indicated that patients and relatives required longer for adopting the perspective of someone else and inferring the emotional state of this person by taking into account the social context. Compared to recognizing emotions only from facial displays, social contextual information seems to be easier to interpret for bipolar patients and their relatives. However, we observed a decline in performance with increasing severity of residual depressive and hypomanic symptoms in patients. This suggests that difficulties in emotional perspective taking are state-dependent changes in bipolar disorder. In contrast, deficits in cognitive perspective taking have been consistently observed, but there was no association with depressive or manic symptom severity, (e.g., Bora et al., 2005; Olley et al., 2005; Wolf et al., 2010).

In addition to difficulties in recognizing facial emotional expressions, bipolar patients have difficulties in identifying emotions they would experience in a given situation as indicated by the affective responsiveness task. Previous mood induction studies (e.g., M'Bailara et al., 2009; Roiser et al., 2009) showed that bipolar patients are characterized by an increased responsiveness to emotional stimuli. One can assume that bipolar patients more strongly responded to the mood induction component of the task. A higher emotional arousal can either improve or interfere with the ability to correctly identify one's own feeling. Here, the alexithymia concept (Taylor and Bagby, 2004), i.e. problems to identify, describe, and work with one's own feelings, may add further insights in future studies.

Affective responsiveness performance of relatives was closer to controls' than patients'. First-degree relatives seem to be more successful than patients in affectively responding to a written emotional situation and to correctly identify the emotional state. This might be related to better emotion regulation skills, which are believed to be a potential resilience factor of unaffected relatives of bipolar patients (Kruger et al., 2006).

Comparing these data in bipolar patients with our previous study in schizophrenia (Derntl et al., 2009b), we observed disease specific dysfunctions: Schizophrenia seems to more severely affect empathic competencies. In this regard, analyzing the impact of psychotic symptoms would be of high interest to differentiate the impact of schizophrenic and affective psychosis on empathy.

Despite several interesting findings the study has some limitations that have to be taken into account in interpreting the results. The small sample size and the great variety of pharmacological treatment did not allow for sub-analyses with respect to different medication effects on empathic abilities. We did not observe a general slowing of bipolar patients, which could be expected as one side effect of antidepressant or neuroleptic medication (Bora et al., 2009). The few studies on emotion recognition in bipolar disorders that explicitly tested the impact of medication found no significant impact (Addington and Addington, 1998; Derntl et al.,

2009a; Getz et al., 2003; Venn et al., 2004). For affective responsiveness one would also expect normalized rather than increased emotional responding in medicated patients (Roiser et al., 2009; M'Bailara et al., 2009). Previous studies on theory of mind did not examine medication effects (Bora et al., 2005; Montag et al., 2010; Olley et al., 2005; Wolf et al., 2010) making it hard to infer whether the unaffected perspective taking ability in our study is due to medication effects.

Our previous study comparing emotion recognition between bipolar I and II patients (Derntl et al., 2009b) showed deficits only in bipolar I patients. An exploratory analysis comparing the two subgroups of bipolar disorder did not reveal significant group differences on any of the three empathy task, though this might be due to the small sample size.

Notwithstanding these limitations, the current study highlighted empathic abilities in bipolar patients and their first-degree relatives thereby providing novel data on emotion recognition as a possible endophenotype of bipolar disorder.

### Role of funding source

UH, AF and BD were supported by the German Research Foundation (DFG, IRTG 1328, KFO 112, Ha3202). UH was further supported by the Interdisciplinary Centre for Clinical Research (IZKF) within the Faculty of Medicine at the RWTH Aachen University (TV N70, VV N68-j), the Federal Ministry of Education and Research (BMBF: FKZ 01GW0751) as well as the Helmholtz Alliance (016W0751). None of these funding institutions had a further role in study design; the collection, analysis and interpretation of data; in the writing of the report; and in the decision to submit the paper for publication.

### Contributors

Authors EMS, UH and BD designed the study. Author EMS managed literature searches and analyses and wrote the first draft of the manuscript. Authors AH and MD managed data acquisition. Author AF contributed to data analysis. All authors contributed to and have approved the final manuscript.

### Conflict of interest

Each author declares that they have no potential conflict of interest.

### Acknowledgments

The authors thank Ms. Maria Kreis who helped with data acquisition.

### References

- Addington J, Addington D. Facial affect recognition and information processing in schizophrenia and bipolar disorder. *Schizophrenia Research* 1998;32:171–81.
- Begley CE, Annegers JF, Swann AC, Lewis C, Coan S, Schnapp WB, et al. The lifetime cost of bipolar disorder in the US—an estimate for new cases in 1998. *Pharmacoeconomics* 2001;19:483–95.
- Bora E, Vahip S, Gonul AS, Akdeniz F, Alkan M, Ogut M, et al. Evidence for theory of mind deficits in euthymic patients with bipolar disorder. *Acta Psychiatrica Scandinavica* 2005;112:110–6.
- Bora E, Yucel M, Pantelis C. Cognitive endophenotypes of bipolar disorder: a meta-analysis of neuropsychological deficits in euthymic patients and their first-degree relatives. *Journal of Affective Disorders* 2009;113:1–20.
- Bozidakis VP, Tonia T, Fokas K, Karavatos A, Kosmidis MH. Impaired emotion processing in remitted patients with bipolar disorder. *Journal of Affective Disorders* 2006;91:53–6.
- Davis MH. The effects of dispositional empathy on emotional-reactions and helping—a multidimensional approach. *Journal of Personality* 1983;51:167–84.
- Decety J, Jackson PL. The functional architecture of human empathy. *Behavioral and Cognitive Neuroscience Reviews* 2004;3:71–100.
- Derntl B, Kryspin-Exner I, Fernbach E, Moser E, Habel U. Emotion recognition accuracy in healthy young females is associated with cycle phase. *Hormones and Behavior* 2008;53:90–5.
- Derntl B, Seidel EM, Kryspin-Exner I, Hasmann A, Dobmeier M. Facial emotion recognition in patients with bipolar I and bipolar II disorder. *British Journal of Clinical Psychology* 2009a;48:363–75.
- Derntl B, Finkelmeyer A, Toygar TK, Hulsmann A, Schneider F, Falkenberg DI, et al. Generalized deficit in all core components of empathy in schizophrenia. *Schizophrenia Research* 2009b;108:197–206.
- Derntl B, Finkelmeyer A, Eickhoff SB, Kellermann T, Falkenberg DI, Schneider F, et al. Multidimensional assessment of empathic abilities: neural correlates and gender differences. *Psychoneuroendocrinology* 2010;35:67–82.
- Derntl B, Seidel EM, Eickhoff SB, Kellermann T, Gur RC, Schneider F, et al. Neural correlates of social approach and withdrawal in patients with major depression. *Social Neuroscience* 2011;0:1–20.
- Doyle AE, Wozniak J, Wilens TE, Henin A, Seidman LJ, Petty C, et al. Neurocognitive impairment in unaffected siblings of youth with bipolar disorder. *Psychological Medicine* 2009;39:1253–63.
- Getz GE, Shear PK, Strakowski SM. Facial affect recognition deficits in bipolar disorder. *Journal of the International Neuropsychological Society* 2003;9:623–32.
- Glahn DC, Almasy L, Barguil M, Hare E, Peralta JM, Kent JW, et al. Neurocognitive endophenotypes for bipolar disorder identified in multiplex multigenerational families. *Archives of General Psychiatry* 2010;67:168–77.
- Goodwin FK, Jamison KR. Manic-depressive illness. New York: Oxford University Press; 1990.
- Gur RC, Sara R, Hagendoorn M, Marom O, Hughett P, Macy L, et al. A method for obtaining 3-dimensional facial expressions and its standardization for use in neurocognitive studies. *Journal of Neuroscience Methods* 2002;115:137–43.
- Habel U, Windischberger C, Derntl B, Robinson S, Kryspin-Exner I, Gur RC, et al. Amygdala activation and facial expressions: explicit emotion discrimination versus implicit emotion processing. *Neuropsychologia* 2007;45:2369–77.
- Habel U, Chechko N, Pauly K, Koch K, Backes V, Seifert N, et al. Neural correlates of emotion recognition in schizophrenia. *Schizophrenia Research* 2010;122:113–23.
- Henry C, Van den Bulke D, Bellivier F, Roy I, Swendsen J, M'Bailara K, et al. Affective lability and affect intensity as core dimensions of bipolar disorders during euthymic period. *Psychiatry Research* 2008;159:1–6.
- Houshmand K, Braunig P, Gauggel S, Kliesow K, Sarkar R, Kruger S. Emotional vulnerability and cognitive control in patients with bipolar disorder and their healthy siblings: a pilot study. *Acta Neuropsychiatrica* 2010;22:54–62.
- Kerr N, Dunbar RIM, Bentall RP. Theory of mind deficits in bipolar affective disorder. *Journal of Affective Disorders* 2003;73:253–9.
- Kessler RC, Akiskal HS, Ames M, Birnbaum H, Greenberg P, Hirschfeld RMA, et al. Prevalence and effects of mood disorders on work performance in a nationally representative sample of U.S. workers. *American Journal of Psychiatry* 2006;163:1561–8.
- Kruger S, Alda M, Young LT, Goldapple K, Parikh S, Mayberg HS. Risk and resilience markers in bipolar disorder: brain responses to emotional challenge in bipolar patients and their healthy siblings. *American Journal of Psychiatry* 2006;163:257–64.
- Lahera G, Montes JM, Benito A, Valdivia M, Medina E, Mirapeix I, et al. Theory of mind deficit in bipolar disorder: is it related to a previous history of psychotic symptoms? *Psychiatry Research* 2008;161:309–17.
- Lawrence NS, Williams AM, Surguladze S, Giampietro V, Brammer MJ, Andrew C, et al. Subcortical and ventral prefrontal cortical neural responses to facial expressions distinguish patients with bipolar disorder and major depression. *Biological Psychiatry* 2004;55:578–87.
- Lehrl S. Der MWT - ein Intelligenztest für die ärztliche Praxis. *Praxis für Neurologie und Psychiatrie*; 1996:488–91.
- M'Bailara K, Demotes-Mainard J, Swendsen J, Mathieu F, Leboyer M, Henry C. Emotional hyper-reactivity in normothymic bipolar patients. *Bipolar Disorders* 2009;11:63–9.
- Montag C, Ehrlich A, Neuhaus K, Dziobek I, Heekeren HR, Heinz A, et al. Theory of mind impairments in euthymic bipolar patients. *Journal of Affective Disorders* 2010;123:264–9.
- Montgomery SA, Asberg M. New depression scale designed to be sensitive to change. *British Journal of Psychiatry* 1979;134:382–9.
- Olley AL, Malhi GS, Bachelor J, Cahill CM, Mitchell PB, Berk M. Executive functioning and theory of mind in euthymic bipolar disorder. *Bipolar Disorders* 2005;7:43–52.
- Post RM, Leverich GS. The role of psychosocial stress in the onset and progression of bipolar disorder and its comorbidities: the need for earlier and alternative modes of therapeutic intervention. *Development and Psychopathology* 2006;18:1181–211.
- Roiser J, Farmer A, Lam D, Burke A, O'Neill N, Keating S, et al. The effect of positive mood induction on emotional processing in euthymic individuals with bipolar disorder and controls. *Psychological Medicine* 2009;39:785–91.
- Seidel E, Habel U, Finkelmeyer A, Schneider F, Gur RC, Derntl B. Implicit and explicit behavioral tendencies in male and female depression. *Psychiatry Research* 2010a;177:124–30.
- Seidel E, Habel U, Kirschner M, Gur RC, Derntl B. The impact of facial emotional expressions on behavioral tendencies in women and men. *Journal of Experimental Psychology. Human Perception and Performance* 2010b;36:500–7.

- Sheehan DV, Janavs J, Baker R, Harnett-Sheehan K, Knapp E, Sheehan M, et al. MINI - mini international neuropsychiatric interview—English version 5.0.0-DSM-IV. *Journal of Clinical Psychiatry* 1998;59:34–57.
- Summers M, Papadopoulou K, Bruno S, Cipolotti L, Ron MA. Bipolar I and bipolar II disorder: cognition and emotion processing. *Psychological Medicine* 2006;36:1799–809.
- Taylor GJ, Bagby RM. New trends in alexithymia research. *Psychotherapy and Psychosomatics* 2004;73:68–77.
- Vaskinn A, Sundet K, Friis S, Simonsen C, Birkenae AB, Engh JA, et al. The effect of gender on emotion perception in schizophrenia and bipolar disorder. *Acta Psychiatrica Scandinavica* 2007;116:263–70.
- Venn HR, Gray JM, Montagne B, Murray LK, Burt DM, Frigerio E, et al. Perception of facial expressions of emotion in bipolar disorder. *Bipolar Disorders* 2004;6:286–93.
- Wolf F, Brune M, Assion HJ. Theory of mind and neurocognitive functioning in patients with bipolar disorder. *Bipolar Disorders* 2010;12:657–66.
- Wolwer W, Frommann N, Halfmann S, Piaszek A, Streit M, Gaebel W. Remediation of impairments in facial affect recognition in schizophrenia: efficacy and specificity of a new training program. *Schizophrenia Research* 2005;80:295–303.
- Young RC, Biggs JT, Ziegler VE, Meyer DA. Rating-scale for mania—reliability, validity and sensitivity. *British Journal of Psychiatry* 1978;133:429–35.
- Yurgelun-Todd DA, Gruber SA, Kanayama G, Killgore WDS, Baird AA, Young AD. fMRI during affect discrimination in bipolar affective disorder. *Bipolar Disorders* 2000;2:237–48.
- Zarate CA, Tohen M, Land M, Cavanagh S. Functional impairment and cognition in bipolar disorder. *Psychiatric Quarterly* 2000;71:309–29.